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Fasting-mimicking Diets

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Abstract

Fasting-mimicking diets (FMDs) are designed to replicate the physiological effects of water-only fasting over a period of 5 consecutive days while minimizing the associated burden. By allowing individuals to consume light meals and limiting the fasting period to no more than once a month, FMDs provide a practical alternative to extended fasting. The human FMDs program is plant-based, low in protein and carbohydrates, and high in healthy fats, aimed at achieving fasting-like effects while supplying essential micronutrients (vitamins and minerals) to reduce the burden of fasting. Low protein intake reduces the activity of IGF-1 and mTOR, which are involved in growth and aging. Caloric and nutrient restriction induced by FMDs stimulates autophagy, a cellular cleanup process that removes damaged components and promotes cellular repair. FMDs activate beneficial metabolic and cellular processes that support weight loss, improve metabolic health, reduce inflammation, and enhance tissue regeneration. When implemented properly, FMDs can be a powerful tool for improving overall health and longevity. However, balanced nutrition during the restricted diet is crucial to provide essential nutrients, prevent deficiencies, and support overall health.

Introduction

In recent years, periodic cycles of fasting or fasting-mimicking diets (FMDs) have emerged as effective methods to potentiate the anti-cancer effects of chemotherapy, hormone therapy, and kinase inhibitors against cancer cells while reducing side effects. FMDs refer to a medically designed fasting-like state that allows periodic consumption patterns of plant-based ,very low-calorie, low-protein and high-healthy fat diet (Longo & Mattson, 2014). Sufficient fasting time causes organ and cellular atrophy, cycles of FMDs and refeeding allow cells and organs to activate breakdown processes that target dysfunctional cells, initiating regenerative or reprogramming phases during the refeeding period in which new or more functional cells are generated. An FMDs regimen of 5 consecutive days per month for 3 months was found to reduce body weight, trunk and total body fat, blood pressure, fasting glucose, IGF-1, triglycerides, total and low-density lipoprotein cholesterol, and C-reactive protein without causing serious adverse effects (Brandhorst et al., 2024).

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Concept of fasting-mimicking diets

1. Fasting-mimicking diets

1.1 Definition of fasting-mimicking diets

The fasting-mimicking diets (FMDs) are scientifically formulated dietary patterns designed to mimic the biochemical and physiological effects of traditional fasting while allowing for limited food intake. The diet aims to provide the health benefits associated with fasting, such as cellular regeneration, improved metabolic health, and potential longevity benefits, without requiring complete abstinence from food. The main components of an FMDs typically include consuming plant-based foods. This approach normally involves a significant reduction in calorie intake, with a specific focus on low-protein, low-carbohydrate, and high-fat composition, rich in nutrients. FMDs are generally followed for a short time, usually 5 days, and are often repeated cyclically, such as monthly (Lin & Gao, 2024; Boccardi et al., 2023).

1.2 Nutritional components of fasting-mimicking diets protocol

The nutritional components of FMDs involve a caloric restriction, typically to about 30-50% of normal daily consumption on day 1 and around 10–20% for the following days (days 2-5). On day 1, the dietary content of the FMDs is approximately 1,100 kcal, with energy distribution of 11% protein, 46% fat, and 43% carbohydrates. On day 2-5, the caloric intake is approximately 700 kcal, with an energy distribution of 9% protein, 44% fat, and 47% carbohydrates. The diet consists of plant-based ingredients, all generally recognized as safe according to the FDA. The cycle was repeated every four weeks, three times per year for healthy individuals (Longo et al., 2021), and up to a maximum of 8 consecutive cycles (Kikomeko et al., 2023; Longo, 2018).

1.2.1 Protein

Protein sources in FMDs protocol, the aim sources of protein for a fasting-mimicking diet protocol are derived from plants. Due to the low-protein nature of the diet, variety of protein sources must be consumed to ensure all essential amino acids are obtained and health requirements are met. Most animal protein have high biological value (HBV), containing all 10 essential amino acids (EAA) and scoring very near 1.00 on the protein digestibility corrected amino acid score (PDCAAS). The score reflects the quality of a protein based on both the amino acid requirements of humans and their ability to digest it. In contrast, plant proteins may have insufficient levels of one or more indispensable amino acids. Legumes, for instance, are frequently low in the sulfur-containing amino acids methionine and cysteine, while lysine is typically limiting in grains. Selecting plant protein sources with a PDCAAS of 1.00 is advisable; soy, canola, potato, pea, and quinoa have a PDCAAS of at least 0.75 (Hertzler et al., 2020; Langyan et al., 2022).

1.2.2 Carbohydrate

Low carbohydrate intake is a key focus of dietary patterns in FMDs. Simple sugars (monosaccharides such as glucose, fructose and galactose) can enter the bloodstream immediately, increasing blood glucose levels and triggering the rapid release of insulin by the pancreas, which can lead to a risk of insulin resistance and type 2 diabetes mellitus (T2DM). Complex carbohydrates (starch, glycogen, and fiber) must be broken down into simple sugars before they can be absorbed by the body. The glycemic index (GI) is a scale that ranks carbohydrate-containing foods from 0 to 100 based on their postprandial blood glucose response. Low-glycemic-index carbohydrates are generally considered to have a GI below 40, while those with a GI between 40 and 70 are considered to have a moderate glycemic index. Carbohydrates with a GI greater than 70 are classified as high GI. The glycemic load (GL) is calculated by multiplying the total amount of dietary carbohydrates in a food serving by the glycemic index of that food. Lower glycemic load strongly influences appetite through hormonal regulation: meals containing carbohydrates with low GL reduce hunger and promote satiety. Thus, low carbohydrate intake with low GI and low GL foods, such as all-bran, oats, bean, whole grains, and legumes, may result in weight loss, reduce blood sugar levels, and a lower risk of heart disease (Augustin et al., 2015; Longo, 2018).

1.2.3 Essential fats

The main fats commonly consumed are vegetable oils and fats, dairy fats, and animal-derived fats, such as lard, tallow, and fish oil. The 2015 dietary guidelines advisory committee, the dietary guidelines for Americans 2015–2020, and many other organizations consistently recommend limiting saturated fat intake to less than 10% of total energy intake, with a maximum of 35% of energy from total fat. In FMDs, essential fatty acids (EFA) play a crucial role. EFAs are polyunsaturated fatty acids (PUFA) that must be obtained from food because the body cannot synthesize them, yet

they are necessary for health. There are two families of EFAs: omega-3 (ω-3) and omega-6 (ω-6). The recommended amounts of essential fatty acids are linoleic acid (2.5–9% of energy), total n-3 PUFA (0.5–2% of energy), and EPA + DHA (250 to 2,000 mg/day) (Kaur et al., 2014; Longo, 2018; Rosqvist & Niinistö, 2024).

1.2.4 Multivitamin and mineral

Poor nutrient intake from diet alone, particularly in those who consume low-calorie diets or avoid certain foods (such as strict vegetarians and vegans), can lead to deficiencies. It can be postulated that a 44% reduction in energy intake might be accompanied by a proportional reduction in micronutrients. Individuals with medical conditions or diseases that impair digestion, absorption, or utilization of nutrients might benefit from taking a multivitamin/mineral (MVM) supplement. Therefore, it is recommended to follow a diet with high vitamin and mineral supplements and to complete it with a multivitamin buffer every three days (Longo, 2018; Zhang, 2024).

2. Effect of fasting-mimicking diet on physiological responses

The FMDs operate through a combination of reduced caloric intake, nutrient sensing pathway modulation, ketosis induction, enhanced stress resistance, improved metabolic health, cellular regeneration, and epigenetic changes. These mechanisms collectively contribute to the health benefits observed with FMDs, including weight loss, improved metabolic health, reduced inflammation, enhanced cognitive function, and potentially increased lifespan and health span.

2.1 Nutrient sensing pathways

The reduction in calories, proteins, and sugars leads to decreased activity of nutrient-sensing pathways such as IGF-1 (insulin-like growth factor 1), mTOR (mechanistic Target of Rapamycin), and AMPK (adenosine monophosphate-activated protein kinase) (Longo & Mattson, 2014). Reducing the activity of IGF-1 and mTOR pathways promotes cellular maintenance and repair mechanisms. Autophagy serves as an internal source of stored nutrients under conditions of nutrient limitation. Two main regulatory inputs for autophagy are AMPK and mTORC. Autophagy initiation can be promoted by AMPK-dependent phosphorylation during low ATP:AMP ratio. mTOR is activated by IGF-1at the outer lysosomal surface if cellular amino acids and glucose have recruited mTOR. Low nutrients promote autophagy by inhibiting of mTOR. Autophagy starts with the engulfment of cellular constituents,such as glycogen, lipids from lipid droplets, soluble proteins, ribosomes, and organelles, in a double membrane structure that then fuses with lysosomes, where the enzymatic breakdown occurs. The products of autophagy, which include basic nutrients (sugars, lipids, amino acid, and nucleosides), are then exported into the cytoplasm, where they may be used as a source of energy or re-used for anabolism (Efeyan et al., 2015).

2.2 Ketosis and metabolic shift

Fasting-mimicking diets (FMDs) induce ketosis through a combination of caloric restriction, reduced carbohydrate intake, and hormonal changes that promote the breakdown of fat stores and the production of ketone bodies. When carbohydrate and glucose levels are low, fatty acid production is stimulated by the release of adrenaline and glucagon. Acetyl CoA, produced from the β-oxidation of fatty acids, can enter the citric acid cycle. Excess acetyl-CoA from fatty acid oxidation is converted into ketone bodies (beta-hydroxybutyrate, acetoacetate, and acetone) to fuel the body. Within 24 hours of carbohydrate restriction, liver glycogen stores are depleted. Gluconeogenesis from amino acids maintains normal blood glucose levels, while fat stores are oxidised to provide energy for metabolic needs. Ketone bodies are produced in the liver and used as a fuel source throughout the body. Ketosis also leads to reduced hepatic glucose output and weight loss itself, which in turn affects insulin levels and sensitivity (Leonard, 2020).

Fasting-mimicking diet programs

Periodic fasting-mimicking diets (FMDs) programs typically last 4-5 consecutive days and involve a dietary pattern that includes plant-based diets with energy restriction. These diets are low in sugar and protein, primarily comprising complex carbohydrates and essential fats.

1. Fasting-mimicking dietary pattern

1.1 Plant-based diet

The fasting-mimicking dietary pattern follows a plant-based diet contains low amounts of animal products and high amounts of fibre-rich foods. The diet is low in protein, essential amino acids and sugars, and relatively high in fiber and unsaturated fats. It consists of fruits, vegetables, grains, legumes, nuts, seeds, herbs, and spices, excluding all animal products such as red meat, poultry, fish, eggs, and dairy products (Ostfeld, 2017).

1.2 Low protein diet

A prescribed low protein diet in FMDs programs is sufficient to meet daily requirements, with protein intake approximately 40-47 g per kg of body weight per day, or 30 g per day (11% of 1,100 kcal) on day 1, and 16 g per day (9% of 700 kcal) on days 2-5. Practically, this amounts to consuming 0.6-0.8 g of protein per kg of body weight per day (Brandhorst et al., 2015; Longo, 2018). The majority of protein intake is derived from plant sources such as legumes, lentils (e.g., green gram beans, red lentils, yellow pigeon pea, green and white peas, Bengal gram, black gram), soybeans, cereals or pseudocereals (e.g., rice, wheat and buckwheat), chia seeds, peanuts and other seeds (e.g., sunflower seeds, pumpkin seeds, almonds and cashews). Plant proteins differ regarding the amounts of limiting amino acids; therefore, using a variety of plant-based proteins should be considered as a replacement for animal proteins to meet nutritional requirements and increase the demand for protein from nutritional and other aspects.

1.3 Essential fats

Food sources of essential fatty acids include; lax seeds, hemp seeds, canola, walnuts, pumpkin seeds, soybeans and its products such as tofu and tempeh. Dark green veggies such as kale, collards, chard, parsley, seaweed, and cereal grasses (wheat and barley grasses) are also good sources because all green (chlorophyll-rich) foods contain Omega-3 fats in their chloroplasts (Kaur et al., 2014; Longo, 2018; Rosqvist & Niinistö, 2024).

1.4 Low carbohydrate

The following low GI and GL foods based on data from the American Diabetes Association. Food sources of low GI and GL are grains, apples, bananas, carrots, barley, chickpeas, lentils, kidney beans, soya beans, and rice noodles (Atkinson et al., 2008).

1.5 Multivitamin and mineral supplements

The food and drug administration (FDA) sets the guidelines for the amounts of different vitamins and minerals an individual should consume daily, called daily value (DV) based on the recommended dietary allowance (RDA). RDA is the recommended daily intake of nutrients that meets the nutritional requirements of most healthy individuals.The following amounts of vitamins and mineral are shown in Table 1-2 as daily values (National Institutes of Health, 2024).

2. Five days of fasting-mimicking diets programs

Instructions for the FMDs cycle include fivecontinuous days eachmonth, followed by a returned to the usual diet for about 25 days. This cycle is repeated for no more than three months (Longo, 2018). The diet programs are shown in Table 3.

3. Fasting-mimicking diets of meal design for 5 days

An example of the fasting-mimicking diet meal plan designed for five days is shown in Table 4.

Table 1 Daily value (DV) for vitamins

Vitamin	Daily value (DV)
folate, or folic acid	400 µg of dietary folate equivalents
niacin	16 mg
pantothenic acid	5 mg
riboflavin	1.3 mg
thiamin	1.2 mg
vitamin A	900 µg of retinol activity equivalents
vitamin B6	1.7 mg
vitamin B12	2.4 µg
vitamin C	90 mg
vitamin D	20 µg
vitamin E	15 mg of alpha-tocopherol
vitamin K	120 µg

Remark: National Institutes of Health (2024)

Table 2 Daily value (DV) for minerals

Mineral	Daily value (DV)
calcium	1,300 mg
chloride	2,300 mg
chromium	35 µg
iodine	150 µg
iron	18 mg
magnesium	420 mg
manganese	2.3 mg
phosphorus	1,250 mg
potassium	4,700 mg
sodium	2,300 mg
zinc	11 mg
selenium	55 µg

Remark: National Institutes of Health (2024)

Effect of fasting-mimicking diets on health

1. Fasting-mimicking diets on health benefits

1.1 Cancer

Cancer cells have a distinct metabolism, with glucose uptake and preferential production of lactate, even in the presence of oxygen, which is also known as the Warburg effect. The FMDs are dietary interventions that protect healthy cells against stressors such as chemotherapy and other therapies. Healthy cells can switch toward a maintenance or repair state when nutrients are absent (fasting), as opposed to cancer cells, where oncogenes prevent the activation of such stress resistance. A molecular mechanism is insulin and IGF-1 signal immunosuppression. Fasting suppresses levels of circulating insulin and IGF-1, leading to a reduced

Table 3 Five days of fasting-mimicking diets programs

Day	Diet programs	Nutrition composition
Day 1	1. Energy 500 kcal derived from complex carbohydrates with low GI and Low GL such as whole wheat, whole grain, brown rice, mushroom, seeds, oats, broccoli, berries, green apple, banana and leaf vegetables. 2. Energy 500 kcal derived from essential fats such as nuts, olive oil, kale, collards, chard, parsley, seaweed, and cereal, etc. 3. Taking multivitamins, minerals, ω-3 and ω-6 supplements 4. Sugarless 5. Protein intake was 30 g/day from plant-based protein such as legumes, lentils, soy, and seeds. 6. Unlimited water	Total energy 1,100 kcal Carbohydrates approximately 43% of 1,100 kcal Protein 30 g/day (energy distribution of protein 11% of 1,100 kcal) Fat approximately 46% of 1,100 kcal
Day 2-5	1. Energy 330 kcal derived from complex carbohydrates with low GI and Low GL such as whole wheat, whole grain, brown rice, mushroom, seeds, oats, broccoli, berries, green apple, banana, and leaf vegetables. 2. Energy 300 kcal derived from essential fats such as nuts, olive oil, kale, collards, chard, parsley, seaweed, and cereal, etc. 3. Taking multivitamins, minerals, ω-3 and ω-6 supplements 4. Sugarless 5. Protein intake was 16 g/day from plant-based protein such as legumes, lentils, soy and seeds. 6. Unlimited water	Total energy 700 kcal Carbohydrates approximately 47% of 700 kcal Protein 16 g/day (energy distribution of protein 9% of 700 kcal) Fat approximately 44% of 700 kcal
Day 25 later Transition diet	Transition diet follows a normal diet based on complex carbohydrates with low GI and Low GL, essential fats, and minimizes the consumption of fish, lean meat, and skim milk.	Individual energy requirement Energy distribution as carbohydrates 50%: protein 20%: fat 30% of total energy

Table 4 Example of the fasting-mimicking diets of meal design for 5 days

Day	Meals			
	Breakfast	**Lunch**	**Snack**	**Dinner**
Day 1	1. Coffee tea or cacao 2. Oats with almond milk or unsweetened plant-based milks, chocolate, nuts, and berries	Brown rice with Vegan stir-fry 1. Brown rice 2. Tofu 3. Leafly vegetable 4. Rice bran oil	1. Unsweetened plant-based milks 2. Nuts or seeds	Mix bean salad and green leaf vegetables, corn, potato or taro with olive oil vinaigrette.
Day 2-5	1. Coffee, tea or cacao 2. Unsweetened plant-based milks 3. Brown bread with butter nuts.	Vegan noodles 1. Rice noodles 2. Leafly vegetable 3. Tofu 4. Mushroom 5. spice	1. Boiled Sweet Potatoes 2. Nuts or seeds	Pasta or Noodles Vegan 1. Pasta 2. Tofu fried 3. Olives oil 4. Tomato

Remark: Longo (2018)

immunosuppression and increased immune activation, which has a positive antitumor effect. This effect involves a potent tumor promoter and tumor suppressor factors associated with cell growth, apoptosis, angiogenesis, invasion, and metastasis (Kikomeko et al., 2023). FMDs cycles appear to enhance the killing of cancer cells by causing system-wide changes that affect the ability of malignant cells to survive or adapt. These changes include reductions in IGF-1, insulin, glucose, leptin and cytokines, as well as likely changes in hundreds of enzymes or pathways. The action of cycles of FMDs cycles and refeeding activates immunosurveillance, promoting T-cell-dependent killing of cancer cells (Longo et al., 2021).

1.2 Diabetes

Fasting-mimicking diets (FMDs) promote the expression of Ngn3-driven β-cells in the islets of langerhans, generating insulin-producing cells. This effect is reversed by IGF-1 treatment and recapitulated by PKA and mTOR inhibition. FMDs cycles restore insulin secretion and glucose homeostasis (Cheng et al., 2017). Three FMDs cycles can restore glucose levels in pre-diabetics with fasting glucose >99 mg/dL to a normal range, which is maintained for at least 3 months following

the intervention. In the assessment of insulin resistance (HOMA-IR) before and after completion of the third FMDs cycle in pre-diabetics, HOMA-IR was reduced from 1.473 ± 0.85 to 1.209 ± 0.99 (Brandhorst et al., 2024). In a study involving one hundred type 2 diabetes patients in regular primary care, FMDs programs improved blood glucose and HbA1c levels despite the reduction in medication use, demonstrating safety in routine clinical practice over 12 months (van den Burg et al., 2024). After four cycles of FMDs, fasting plasma glucose (FPG), 2-hr plasma glucose (2hPG), and HbA1c were lower than in the control group (specific meal replacement foods) (Tang & Lin, 2020).

1.3 Obesity

The efficacy of FMDs in reducing body weight was studied in 38 healthy subjects who were randomized to either the FMDs for 5 days every month for 3 months (3 cycles) or to continue their usual diet. In the FMDs group, body weight was reduced by 3.1%, and relative lean body mass was increased after three FMDs cycles, indicating maintenance of muscle mass (Fanti et al., 2021).

1.4 Neurodegeneration

FMDs were shown to protect neurons and ameliorate cognitive impairment. The important roles of the ketone body β-hydroxybutyrate and the mitochondrial sirtuin SIRT3 in the neuroprotective mechanism of FMDs. Ketone bodies may be protective against GABAergic interneuron degeneration through a mechanism dependent on SIRT3, which was shown to reduce anxiety-like behavior and improve hippocampus-dependent memory in Alzheimer's disease (AD). FMDs cycles decrease hippocampal microglia number and neuroinflammation (Boccardi et al., 2023). Hunger is an adaptive response to food deprivation that involves sensory, cognitive and neuroendocrine changes that motivate and enable food-seeking behaviors. It has been proposed that hunger-related neuronal networks, neuropeptides and hormones play pivotal roles in the beneficial effects of energy restriction on aging and disease susceptibility (Longo & Mattson, 2014).

1.5 Cardiometabolic diseases

The effects of 5-day FMDs on trimethylamine N-oxide (TMAO) levels, a cardiometabolic biomarker produced by the gut microbiota after the consumption of animal-derived products, were studied alongside other metabolic parameters. The FMDs resulted in a decrease in plasma TMAO levels and a weight loss of 2.8 ± 0.2 kg. Additionally, the FMDs led to a significant elevation in plasma ketone bodies and a decrease in IGF-1 levels by 37 ± 8 ng/mL. Fasting glucose and C-peptide levels also decreased, indicating improved insulin sensitivity and a decreased HOMA-IR index. The reduction in TMAO levels could be an additional benefit of FMDs, potentially leading to a reduced risk of cardiometabolic diseases (Videja et al., 2022).

1.6 Skin health

Caloric restriction (CR) and fasting-mimicking diets (FMDs) have demonstrated improvements in multiple skin properties. The metabolic alterations mediated by CR might include changes in cellular signaling, epidermal barrier function, and skin structure during aging, which are underpinned by various molecular activities. The metabolome-induced catabolism of biomolecules and increased oxidative stress alter activities in upper glycolysis and glycerolipid biosynthesis, leading to decreased protein and polyamine biosynthesis in aged skin. CR stimulates respiratory rates by enhancing mitochondrial biogenesis and stimulating uncoupling between oxygen consumption and oxidative phosphorylation. As a result, both the epidermis and dermis become thinner, and there is increased expression of the senescence markers p16 and p21, as well as lipid peroxidation, due to long-term carbohydrate restriction (Choi, 2020). Additionally, FMDs may reduce intestinal inflammation and stimulate protective members of the gut microbiome, such as *Lactobacillaceae* and *Bifidobacteriaceae*. *Bifidobacteriaceae,* in particular, has been found to protect against UV-induced changes in transepidermal water loss and skin hydration. Three consecutive monthly cycles of FMDs resulted in a significant increase in skin hydration and maintained skin texture (Maloh et al., 2023).

2. Limitation of fasting-mimicking diet

The FMDs program provides plant-based foods, that increase the risk of iron and vitamin B12 insufficiency. Limiting meals with fish to a maximum of two or three times per week should be a prevented. Fish, crustaceans, and mollusks with a high ω-3, ω-6, and vitamin B12 content such as salmon, anchovies, sardines, cod, sea bream, trout, clams, and shrimp were added (Longo, 2018). It is important to avoid high-fat from saturated fat and to select essential fat instead. Balanced nutrition, when the diet is restricted, provides essential nutrients to prevent deficiencies and support overall health.

3. Awareness of using fasting-mimicking diets programs

Commonly, the FMDs programmes caused mild adverse effects such as fatigue, headache, dizziness, weakness, nausea, and dehydration, transient signs of

energy deficit and hypoglycemia (van den Burg et al., 2024). The FMDs programmes did not find these adverse effects, but they may still cause harm when practiced frequently for many days consecutively. Importantly, more fasting could lead to malnutrition, eating disorders, susceptibility to infectious diseases, or moderate damage to organs (Horne et al., 2015). The programme is typically followed for 5 consecutive days no more than once a month, for three months. During 5 days of FMDs programmes, intake of essential nutrients is important, such as vitamins and mineral supplements, in relation to the nutrient requirement for adequate health, which is expressed as the recommended dietary allowance.

Conclusion

The human fasting-mimicking diets (FMDs) program is a plant-based, low-protein, low-carbohydrate, and high- healthy-fat program designed to attain fasting-like effects while providing micronutrient nourishment (vitamins and minerals) and minimizing the burden of fasting. The idea is to trick the body into a fasting state while promoting the same benefits as complete fasting, Benefits include improved metabolic health, reduced inflammation, and cellular regeneration, without the need to completely abstain from food. Periodic fasting-mimicking diet (FMDs) programs lasting 4–5 consecutive days are designed to mimic the physiological effects of water-only fasting while minimizing its burden by allowing individuals to consume light meals during the fasting period and confining it to a limited number of days of no more than once a month.

Typically, three cycles of FMDs are recommended to achieve health benefits without adverse effects. Given the low-protein nature of FMDs, it is advisable to include plant protein sources with high biological value and Protein Digestibility-Corrected Amino Acid Scores (PDCAAS) similar to those of animal proteins, while limiting marine foods. The quality of fatty acids is crucial; therefore, nuts and seeds, which are rich in essential fatty acids, should be included in a high-fat program. Balanced nutrition is important during restricted diets to ensure adequate intake of essential nutrients. To prevent deficiencies, it is suggested to take a multivitamin supplement every three days. Overall, the FMDs presents a promising approach to enhancing health and longevity by combining the benefits of fasting with controlled nutrient intake.

References

Atkinson, F.S., Foster-Powell, K., & Brand-Miller, J.C. (2008). International tables of glycemic index and glycemic load values: 2008. *Diabetes Care, 31*(12), 2281–2283.

Augustin, L.S.A., Kendall, C.W.C., Jenkins, D.J.A., Willett, W.C., Astrup, A., Barclay, A.W., … Poli, A. (2015). Glycemic index, glycemic load and glycemic response: An international scientific consensus summit from the international carbohydrate quality consortium (ICQC). *Nutrition, Metabolism, and Cardiovascular Diseases: NMCD, 25*(9), 795–815.

Boccardi, V., Pigliautile, M., Guazzarini, A.G., & Mecocci, P. (2023). The potential of fasting-mimicking diet as a preventive and curative strategy for alzheimer's disease. *Biomolecules, 13*(7), 1133.

Brandhorst, S., Choi, I.Y., Wei, M., Cheng, C.W., Sedrakyan, S., Navarrete, G., … Longo, V.D. (2015). A periodic diet that mimics fasting promotes multi-system regeneration, enhanced cognitive performance, and healthspan. *Cell Metabolism, 22*(1), 86–99.

Brandhorst, S., Levine, M.E., Wei, M., Shelehchi, M., Morgan, T.E., Nayak, K.S., … Longo, V.D. (2024). Fasting-mimicking diet causes hepatic and blood markers changes indicating reduced biological age and disease risk. *Nature Communications, 15*(1), 1309.

Cheng, C.W., Villani, V., Buono, R., Wei, M., Kumar, S., Yilmaz, O.H., … Longo, V.D. (2017). Fasting-mimicking diet promotes ngn3-driven β-cell regeneration to reverse. *Diabetes. Cell, 168*(5), 775–788.e12.

Choi, Y.J. (2020). Shedding light on the effects of calorie restriction and its mimetics on skin biology. *Nutrients, 12*(5), 1529.

Efeyan, A., Comb, W.C., & Sabatini, D.M. (2015). Nutrient-sensing mechanisms and pathways. *Nature, 517*(7534), 302-310.

Fanti, M., Mishra, A., Longo, V.D., & Brandhorst, S. (2021). Time-restricted eating, intermittent fasting, and fasting-mimicking diets in weight loss. *Current Obesity Reports, 10*(2), 70–80.

Hertzler, S.R., Lieblein-Boff, J.C., Weiler, M., & Allgeier, C. (2020). Plant proteins: assessing their nutritional quality and effects on health and physical function. *Nutrients, 12*(12), 3704.

Horne, B.D., Muhlestein, J.B., & Anderson, J.L. (2015). Health effects of intermittent fasting: Hormesis or harm? A systematic review. *The American Journal of Clinical Nutrition, 102*(2), 464–470.

Kaur, N., Chugh, V., & Gupta, A.K. (2014). Essential fatty acids as functional components of foods-a review. *Journal of Food Science and Technology, 51*(10), 2289–2303.

Kikomeko, J., Schutte, T., van Velzen, M.J.M., Seefat, R., & van Laarhoven, H.W.M. (2023). Short-term fasting and fasting mimicking diets combined with chemotherapy: A narrative review. *Therapeutic Advances in Medical Oncology, 15,* 17588359231161418.

Langyan, S., Yadava, P., Khan, F.N., Dar, Z.A., Singh, R., & Kumar, A. (2022). Sustaining protein nutrition through plant-based foods. *Frontiers in Nutrition, 8,* 772573.

Leonard, T. (2020). The physiology of ketosis and the ketogenic diet. *Southern African Journal of Anaesthesia and Analgesia, 26*(6), S94–S97.

Lin, X., & Gao, Y. (2024). A bibliometric analysis of the fasting-mimicking diet. *Frontiers in Nutrition, 11,* 1328450.

Longo, V.D., & Mattson, M.P. (2014). Fasting: molecular mechanisms and clinical applications. *Cell Metabolism, 19*(2), 181–192.

Longo, V. (2018). The longevity diet: Discover the new science behind stem cell activation and regeneration to slow aging, fight disease, and optimize weight. New York: Penguin.

Longo, V.D., Di Tano, M., Mattson, M.P., & Guidi, N. (2021). Intermittent and periodic fasting, longevity and disease. *Nature Aging, 1*(1), 47-59.

Maloh, J., Wei, M., Hsu, W.C., Caputo, S., Afzal, N., & Sivamani, R.K. (2023). The effects of a fasting mimicking diet on skin hydration, skin texture, and skin assessment: A randomized controlled trial. *Journal of Clinical Medicine, 12*(5), 1710.

National Institutes of Health. (2024). *Nutrient recommendations and databases.* Retrieved July 11, 2024, from https://ods.od.nih.gov/HealthInformation/nutrientrecommendations.aspx

Ostfeld, R.J. (2017). Definition of a plant-based diet and overview of this special issue. *Journal of Geriatric Cardiology: JGC, 14*(5), 315.

Rosqvist, F., & Niinistö, S. (2024). Fats and oils-a scoping review for nordic nutrition recommendations 2023. *Food & Nutrition Research, 68,* 10.29219/fnr.v68.10487.

Tang, F., & Lin, X. (2020). Effects of fasting-mimicking diet and specific meal replacement foods on blood glucose control in patients with type 2 diabetes: A randomized controlled trial. *Oxidative Medicine and Cellular Longevity, 2020,* 6615295.

van den Burg, E.L., Schoonakker, M.P., van Peet, P.G., van den Akker-van Marle, E.M., Lamb, H.J., Longo, V.D., … Pijl, H. (2024). Integration of a fasting-mimicking diet programme in primary care for type 2 diabetes reduces the need for medication and improves glycaemic control: A 12-month randomised controlled trial. *Diabetologia, 67*(7), 1245–1259.

Videja, M., Sevostjanovs, E., Upmale-Engela, S., Liepinsh, E., Konrade, I., & Dambrova, M. (2022). Fasting-mimicking diet reduces trimethylamine n-oxide levels and improves serum biochemical parameters in healthy volunteers. *Nutrients, 14*(5), 1093.

Zhang, W., Chen, P., Huo, S., Huang, X., & Zhao, Y. (2024). Requirements for essential micronutrients during caloric restriction and fasting. *Frontiers in Nutrition, 11,* 1363181.