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Review Article

Components of an Optimal Weight Loss Diet: What Darwin Would Say About Survival of the Fittest

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Abstract

Most North American adults will try to lose weight at some point, but likely regain what they lost. Many weight loss plans set dieters up for failure because they are predicated on gimmicks rather than science. If Charles Darwin were to comment on popular weight loss diets, he'd suggest the best ones include approaches that have been shown to work - "survival of the fittest". In this review, we identify five components of a commercial weight loss diet (referred to as the Diet), which have been shown to be effective at promoting weight loss. First, the weight loss diet includes nutrient-dense foods, providing most essential nutrients. Diets fail because they are not nutritionally complete. Second, the Diet is devoid of ultra-processed foods, which have been shown to decrease satiety, promote hunger, and foster overeating. Third, the Diet is anti-inflammatory, which fosters weight loss. Fourth, the Diet adopts an intermittent fasting approach - there is no snacking - so it produces an overnight fast of at least 12 hours. The Diet is also energy-restricted to 1,500 kcal, which is at least as good at promoting weight loss as an intermittent fasting diet. Fifth, the Diet offers microbiome support because it is rich in dietary fiber, which promotes satiety and a diverse microbiota. The weight loss Diet described herein is easy to follow, includes recipes and meal plans, and features meals that can be prepared in 20 minutes or less. Nearly 12,000 individuals have followed the Diet for three months. The average rate of weight loss was one to two pounds each week. After three months, the percentage of weight loss was considered to be medically significant, with a loss of at least 5%. Before starting any weight loss diet, it is important to determine if it is based on proven principles to support weight loss, and thus, if it has a "survival of the fittest" approach.

Keywords: Weight Loss; Anti-inflammation; Nutrient-Dense Foods; Nutritional Completeness; Optimal Weight Loss Diet

INTRODUCTION

Nearly three-quarters of Americans are overweight or obese and globally, 39% are overweight or obese [1,2]. Many of these individuals have tried dieting but recidivism is high, mainly because diets are not effective or sustainable long term [3]. People trying to lose weight may have a hard time adhering to a diet plan. Over a one-year period, individuals following four popular weight loss diets, experienced drop-out rates between 35% and 50%. This high drop-out rate implies that many popular diets don't work.

The ideal weight loss diet should be based on scientific principles shown to be effective, rather than on the latest fad. Even if healthy principles are assembled into a weight loss program, the program must offer tasty foods and be easy to adopt. We have identified a commercial weight loss diet (hereafter referred to as the Diet; https://epicure.com/) that is predicated on five scientific principles associated with weight loss.

If Charles Darwin were to review the Diet, then he'd agree that it is taking on a "survival of the fittest" approach to weight loss. In his 1869 book, *On the Origin of Species*, he suggested that organisms best adjusted to their environment are most successful in surviving and reproducing. As far as the Diet is concerned, it is analogous to the "organism" that is best adjusted to the environment because it

is easy to follow and based on sound science. Given this, the Diet has best chance of surviving - unlike fad diets that come and go because they lack scientific basis, are too hard to follow, or both.

The purpose of this review is to describe the merits of a commercial weight loss diet based on these five scientifically-sound principles: nutrient-dense/nutritional completeness, limited ultra-processed foods, anti-inflammatory, intermittent fasting, and microbiome support. For each of these five sections, the science behind each principle will be reviewed followed by an assessment of how the Diet conforms to each principle. Before these attributes are discussed, there is an overview of the Diet.

THE DIET

The commercial Diet reviewed herein is a 90-day program that was developed to produce weight loss of one to two pounds weekly. Other aspects of the Diet include:

- Designed by registered dietitians nutritionists, and reviewed by medical professionals, who are familiar with the principles of healthy eating, of emphasising plant-based protein options over animal proteins, and of promoting nutrient-rich foods like fruits, vegetables, whole grains, seeds/nuts, and low-fat dairy foods. Red meat and processed meats are limited.
- Focuses on frequency of food consumption
    - Embraces the principles of intermittent fasting, as the Diet provides three meals daily without snacking. This creates an overnight fast of at least 12 hours.
- Places emphasis on the qualtiy of food
    - Incorporates nutrient-dense, whole, unprocessed foods that are enhanced with herb and spice blends the Company sells.
    - Supports a healthy microbiome because it is rich in dietary fiber.
    - Eliminates ultra-processed foods, which are rich in salt, sugar, and saturated fats that are inflammatory.
    - Encourages both animal- and vegetable-based proteins, with 20-30 grams of dietary protein provided at each meal. The company sells a plant-based protein powder, supplemented with 1 billion probiotic cells, that can serve as the protein source of any meal.
- Teaches cooking skills and allows for a customized approach to food options
    - Designed for those who may not know how to cook or lack a wide variety of things they are comfortable cooking.
    - Feeds a family of four, so a single household could consume the same healthy meals.
    - Offerings are prepared in 20 minutes or less.
    - Meals are inexpensive with most costing $3.50 to $4.00 per serving. Those following the Diet state they spend less money on eating out, take-out meals, and junk foods and snacks, and have less waste because they stick to the Company-generated recipes and shopping lists.
    - Provides meal plans, recipes, and weekly shopping lists for both conventional grocery stores and the Company's herb and spice seasonings and protein powders (https://epicure.com/). The addition of these offering enhances the flavor of proteins, vegetables, fruits, and whole grains, thereby increasing compliance and diet quality.
    - Allows for substitutions (e.g., chicken for fish, broccoli for green beans) so compliance is enhanced.

The Diet is calorically restricted as it provides 1,500 kcal, which is 500 fewer calories than a normal diet (Table 1). The typical daily macronutrient composition is comprised of up to 90 g dietary protein, 170 g carbohydrate, and 56 g fat. Up to 30 grams of dietary fiber is provided at each meal. The Diet offers a full complement of essential nutrients approaching 100% of daily needs for most. Given that food plans and preferences vary daily, each essential nutrient need may not be met consistently so the Company is planning on offering a whole food-based multivitamin/mineral.

The Diet has a similar nutrient composition to other healhty diets like the Mediterranean diet and the Dietary Approaches to Stop Hypertension (DASH) diet. All these diet plans emphasize nutrient-dense, whole foods while limiting ultra-processed ones. However, in contrast to the Mediterranean and DASH diets, the Diet described herein provides the tools needed to prepare healthy meals, including meal plans, recipes, and shopping lists. In addition, the Company has an online established community and encourages their participants to journal their progress over the 90-day program. It also sells cookware to help prepare food quickly, along with color-coded, different sized scoops that correspond to a serving size for different food groups: green for fruits and vegetables, blue for lean proteins/dairy, yellow for whole grains/starchy vegetables, and purple for healthy fats.

Meal (Caloric contribution)	Meal plan (macronutrient amount, serving sizes*)	Examples of purchases from-Conventional grocery store ^The Company
Breakfast (400 kcal)	Protein or dairy (20 g dietary protein) Grain or starchy vegetable (1 scoop) Vegetable or fruit (two scoops) -Healthy fat (one scoop)	Egg, Greek yogurt ^Plant-based protein blend Whole-grain toast Two peaches Nut butter
Lunch (500 kcal)	Protein (20 g dietary protein) Grain/starchy vegetable (1 cup) Vegetables (2 cups) Healthy fat (one scoop)	Chicken breast, boneless, skinless ^Meal solution seasoning pack with recipe Zucchini and tomatoes -Olive oil
Dinner (500 calories)	Protein (20 g dietary protein) Grain/starchy vegetable (1 cup) Vegetables (2 cups) Healthy fat (one scoop)	Salmon ^Meal solution seasoning pack with recipe ^Dip for vegetables
Dessert (100-150 kcal)	Dairy (1/2 serving) Fruit (1)	Greek yogurt Fresh orange

Table 1: Overview of the Diet.

*Serving sizes are determined from different sized, and different colored scoops sold by the Company.

The Diet has been shown to be successful for many. Based on two different, 90-day weight loss sessions, data from nearly 12,000 individuals showed an average weight loss of at least one-pound per week weight loss. In addition, at the end of the 90 days, a medically significant weight loss of 6% was achieved [4] (Table 2). It would seem that Darwin would concur that the Diet has achieved the status of "survival of the fittest".

Table 2: Weight loss associated with the commercial Diet from two, 90-day programs.

Attribute	90 days of weight loss (September 13 to December 11, 2021)	90 days of weight loss (January 3 to April 2, 2022)
Number of participants	5,562	6,370
Average weight loss	13 pounds = 1 pound per week	12 pounds = 1 pound per week
Average percentage weight loss	6%	6%

NUTRIENT-DENSE/NUTRITIONAL COMPLETENESS

Nutrient density relates to the quality of the foods consumed, in terms of them providing many of the essential nutrients. Nutritional completeness refers to a day's worth of foods having the ability to provide the daily recommended amount of each essential nutrient. It is likely that all essential nutrients have been identified, and for the most part, these are universally agreed upon. Admittedly, the optimal daily amount to consume of each nutrient varies by country; however, these differences are minimal.

The best way to assure nutrient needs are met on a regular basis is to consume mostly nutrient-dense foods, while limiting those with poor nutrient quality. The food patterns that provide the highest nutrient density are the pescatarian diet pattern, followed by the vegetarian diet [5]. Most nutrient-poor foods are rich in salt, sugar, saturated fats, and refined grains. Simply removing up to three nutrient-poor foods daily improves diet quality and reduces energy intake.

Over the short-term, missing out on a few essential nutrients or not getting the optimal amount is likely not problematic [6]. However, long-term failure to meet essential nutrient needs can lead to chronic metabolic disruption, including mitochondrial decay that can lead to oxidative leakage and cellular aging. Deficiencies in many micronutrients may also cause DNA damage such as chromosome breaks.

Over time, abnormal changes from nutrient deficiencies can foster the development of late onset chronic conditions, including cancer. Others have shown that chronic nutrient deficiencies are related to depression [7]. Based on the NHANES data, those who fail to meet the minimum daily recommended intakes for several nutrients (e.g., thiamin, dietary fiber, vitamin K, calcium, magnesium, iron, zinc, and copper) are at higher risk of developing depression than those who meet their nutrient needs. Long-term nutrient deficiencies also impair cognitive function. Interestingly, providing a daily multivitamin/multimineral supplement to an elderly cohort was shown to improve cognition [8].

Many popular diets focus on the macronutrient composition such as restricting fat or carbohydrates, or encouraging a high protein intake. Attention to micronutrient content is mostly neglected. One of the major reasons that diets don't work is that they fail to provide all of the essential nutrients - and if they are present, there are only sub-optimal amounts [9,10]. The micronutrient adequacy of four popular diets (Atkins, Zone, LEARN [Lifestyles, Exercise, Attitudes, Relationships, Nutrition], and Ornish) revealed that all posed a risk of inadequacy [9]. Both vitamins (e.g., vitamins C, E, and K, folate, thiamin) and minerals (e.g., zinc, iron, magnesium) were sub-optimal and deemed problematic.

The findings of nutrient adequacy from four different weight loss diets (South Beach, Atkins For Life, DASH diet, and Best Life) mirrored what others have found [9,10]. Based on these four diets, the most common under-consumed nutrients were: biotin, vitamin D, vitamin E, chromium, iodine and molybdenum [10]. The authors estimated that to meet all the nutrient needs from one of these weight loss diets, someone would need to consume more than 15,000 kcal, which is not only impossible to achieve, but also paradoxical, as this amount would promote weight gain. This study illustrates that focusing on macronutrient constraints (South Beach, Atkins for Life) or restricting foods that are rich in sodium and dairy fat, and that are fried, can make it difficult - if not impossible - to achieve all micronutrient goals.

Rather than imposing macronutrient restrictions to lose weight, others have proposed simply to reduce total energy intake (i.e., calorie restriction) by 25% of daily needs, which in most cases, would provide 1,500 calories [11,12]. This potentially would make it easier to meet all micronutrient needs, but only if just nutrient-dense foods were consumed. Admittedly, consuming an energy restricted diet would likely result in a corresponding reduction in micronutrient intake. But by playing careful attention to each micronutrient, widespread deficiencies may be overcome.

In order to assure all nutrient needs are met, some argue it is important to focus on the type of dietary protein consumed [13]. Based on mathematical modeling, achieving micronutrient needs is only assured if 45% to 60% of all dietary protein comes from animal sources. The rest of the dietary protein can then be met from plant-based proteins. Consuming lesser percentages of dietary protein from animal sources could make it difficult, if not impossible, to meet all micronutrient needs - it would be especially difficult to meet the needs of vitamin D, zinc, calcium, magnesium, iodine, and iron. Older individuals and young women should consume animal proteins at the higher end of this range to assure these nutrient needs are met.

Nutritional adequacy is not only important to preserve the health of the host, but also to promote weight loss. Nutrient-rich, fortified foods have been shown to promote satiety and a medically significant weight loss of at least 5% of the pre-diet weight after two months [4,14,15]. In addition, the use of the fortified foods resulted in a decrease in waist circumference and body weight, which is associated with a lower risk of hypertension, cardiovascular disease, and type 2 diabetes according to the National Heart, Lung, and Blood Institute of the National Institutes of Health (NIH) [16].

The diet

The commercial Diet reviewed herein incorporates nutrient-dense foods that lead to near-nutritional completeness, by approaching or meeting 100% of the Daily Value (DV) for each nutrient. Understandably, it is difficult to meet 100% of each nutrient need because the Diet only contains 1,500 kcal, which is 75% of the DV goal. Based on a typical 30-day period of the diet, the DVs for dietary protein and fiber are consistently met. Total dietary fat and saturated and trans fat intakes were below the DV; cholesterol is at the DV; and there is no DV for carbohydrates. The DVs for sodium and chloride are deliberately set below the DV, because heart-healthy recommendations for the two often are lower than the DV. Four other minerals (chromium, iodine, copper, and molybdenum) were not examined for DV because the mineral content in most foods is unavailable rendering these DV values meaningless.

The Diet provided at least 100% Daily Value (DV) for six vitamins (vitamins C, D, K. B6, and B12; niacin; and pantothenic acid) and three minerals (phosphorus, manganese, and selenium). The remaining vitamins and minerals fell below 100% DV, and most deviated within 20% of the DV. Mineral needs were harder to meet, mainly because the needs are often higher than for vitamins (e.g., calcium, potassium). Over the 90-day period, however, it is likely the nutrients that were sub-optimal over a sample period of 30 days would be made up because different offerings are provided over the Diet. In addition, it may be prudent to use a multivitamin/multimineral supplement to assure nutrient completeness; the Company will soon be offering one.

LIMITED PROCESSED FOODS

North Americans enjoy processed foods (now usually referred to as ultra-processed foods), because of the flavor and convenience. According to an article from the American Society for Nutrition, food processing likely began more than 700,000 years ago with the use of salting, smoking, and drying, mainly of meats [17]. It wasn't until the second half of the 20st century that the increased reliance on commercially processed foods was realized.

Limited benefits come from ultra-processed foods, and relate to the contribution of some healthy and essential nutrients [18]. For example, a typical person who consumes ultra-processed foods may obtain about 55% of daily dietary fiber needs, 48% of calcium needs, and 43% of potassium needs. These benefits are outweighed by the contribution of constituents that should be limited and adversely affect health. For example, ultra-processed foods typically contribute 57% of daily energy requirements, 52% of the saturated fats requirements, 75% of added sugar allotment, and 57% of the sodium needs.

The ability to distinguish foods based on the extent of food processing has prompted investigations into the relationship between the degree of processing and health outcomes including obesity, cardiovascular disease, and type 2 diabetes [18,19]. Processed foods can be classified by a system referred to as Nova, which considers the physical, biological and chemical methods used during the food manufacturing process. Nova assigns foods into four groups: 1) unprocessed or minimally processed foods (e.g. fresh, dry or frozen fruits or vegetables grains; pasteurized milk; plain yogurt; and fresh or frozen meat); 2) processed culinary ingredients (e.g. table sugar, oils, butter, and salt); 3) processed foods (e.g. vegetables in salt, cheese, simple breads, fruits in syrup, and canned fish); and 4) ultra-processed foods (e.g. soft drinks, sweet or savory packaged snacks, candy, packaged breads, donuts, cakes, and cookies, and pre-prepared frozen or shelf-stable dishes).

The methods used to create the most highly processed foods - the ultra-processed ones - include the fractioning of whole foods into substances, applying chemical modifications of these substances, and then assembling the unmodified and modified food substances into the final food form [18]. The methods and ingredients used to manufacture ultra-processed foods are designed to create profitability for the manufacturer (e.g., low-cost ingredients, long shelf-life), to be convenient (ready to consume), and to be hyper-palatable so they displace unprocessed or minimally processed foods. Ultra-processed foods may be identified if the list of ingredients contains at least one item that is never or rarely used in kitchens (e.g., high-fructose corn syrup, hydrogenated oils, hydrolyzed proteins) or includes classes of additives designed to make the final product palatable (e.g., flavors, flavor enhancers, colors, emulsifiers).

A 2020 extensive review of the scientific literature identified the impact of consuming ultra-processed foods on health [20]. Twenty-three studies were included in the systematic review (ten cross-sectional and thirteen prospective cohort studies). According to the cross-sectional studies, consuming ultra-processed foods was associated with a 39% increased risk of becoming overweight/obese, a 102% risk of having low HDL cholesterol levels, and a 79% increased risk of having metabolic syndrome. For the prospective studies, which included 183,491 participants who were followed for 3.5 to 19 years, the highest consumption of ultra-processed foods was associated with a 25% increased risk of all-cause mortality ($P < 0.00001$) and a 29% increased risk of cardiovascular disease ($P < 0.0003$). In addition, cerebrovascular disease ($P = 0.01$) and depression ($P = 0.02$) risks were significantly increased by a high consumption of ultra-processed foods.

Others have shown that cancer risk is positively correlated with the increased intake of ultra-processed foods [21]. One study included more than 100,000 adults (with an average age of 43 years) and assessed cancer risk prospectively from repeated, 24-hour food intake records. A 10% increase in the proportion of ultra-processed foods in the diet was associated with a significant increase of greater than 10% of risk of overall cancer and breast

cancer. Thus, consumption of ultra-processed foods seems to not only adversely affect cancer risk, but also the risk of cardiovascular disease, obesity, depression, and all-cause mortality.

Much of the focus on ultra-processed foods is centered on their relationship to obesity [22]. Some have postulated that it is the sugar content in ultra-processed foods that promotes weight gain [23]. Based on a representative group of Americans (nearly 10,000 individuals), ultra-processed foods represent about 60% of all energy consumed. In most ultra-processed foods, added sugars represent one of every five calories, which is higher than processed foods and minimally processed foods. Thus, the sugar content of ultra-processed foods seems to be the main driver of weight gain.

Decreasing the consumption of ultra-processed foods could be an effective way of reducing the excessive intake of added sugars, potentially leading to weight loss. Much scientific attention is directed at determining why processed foods are so obesogenic, and exploring whether all calories are alike [24]. Ludwig., *et al*. aver that obesity is not caused by the concept of energy balance (i.e., energy intake is greater than energy expenditure), but rather on complex endocrine, metabolic, and nervous system signals that control food intake [25]. These authors postulate that rising obesity rates are caused by ultra-processed foods that are high in sugar and fat. The hormonal response to consuming these foods causes carbohydrates to favor fat deposition leaving fewer calories for the body's own metabolic needs. Thus, the body compensates by eating more.

Other investigators from the United Kingdom studied the direct effect of ultra-processed foods on adiposity in more than 6,000 adults [19]. Dietary intake was assessed using the Nova classification system. A dose response relationship was observed in men and women, showing that with a 10% increase in the consumption of ultra-processed foods, there was a corresponding increase of 18% in the prevalence of obesity in men and a 17% increase in women. These findings show that ultra-processed foods are related to obesity in a dose-dependent way.

One well-controlled study showed that consuming ultra-processed foods is addictive, and therefore, fosters weight gain [26]. Healthy, normal weight individuals (who were in a metabolic ward that controlled all food intake) were randomly assigned in a crossover design to consume as much as they wanted of only ultra-processed foods or a healthy diet. The diets were compared, and while consuming the ultra-processed foods, the participants consumed an average of 500 kcal more each day compared to those assigned to the healthy diet. These data suggest that eliminating ultra-processed foods from the diet decreases energy intake and results in weight loss; whereas a diet with a large proportion of ultra-processed foods increases energy intake and leads to weight gain.

Whether ultra-processed foods should become a part of dietary guidelines set by policy makers is of intense debate in the nutritional literature [27-29]. In 2022, the American Journal of Clinical Nutrition presented opposing arguments about the use of Nova, to classify foods based on the degree of processing. Some argued that the Nova classification system is important for policy makers to consider. Their view is that the Nova system is tied to health risk so recommending the avoidance of ultra-processed foods to optimize health should be incorporated into the government's dietary recommendations [28]. Others aver that it is not clear how much impact the Nova system has over more conventional ways of classifying foods such as fiber content, energy density, and glycemic index [29]. It may be easier for policy makers to just stick to the current assessment of diets instead of introducing a new - and more complicated - way, to determine the effect of diet on health.

The diet

The Diet includes no ultra-processed foods and, according to the Nova classification system, is primarily made up of unprocessed foods, which provide the bulk of the energy. As part of the Diet, the Company sells herb and spice blends that enhance the palatability of the unprocessed foods. Since most of these blends are devoid of energy, they would be considered to be a processed culinary ingredient according to the Nova classification system. All commercial herb and spice blends used in the Diet are low in sugar and devoid of high-fructose corn syrup, *trans* fats, and artificial colors and flavors. Thus, the Diet can successfully compete with the highly palatable ultra-processed foods, while including mostly unprocessed foods with some minimally processed offerings.

ANTI-INFLAMMATORY

Inflammation involves interactions among many cell types and the production of chemical mediators that serve as defense mechanisms, protecting the host from infection and other insults [30]. Specifically, the inflammatory response involves the synthesis and

secretion of anti-inflammatory cytokines and activation of regulatory cells, which are directly linked to the presence of inflammatory diseases. Historically, inflammation has been thought to be localized and related to physical pain in the joints or muscles [31]. Inflammation is easily identifiable in patients with arthritic pain - who, for the most part, are eager to take actions to down-regulate the inflammation.

However, over the past 30 years, there is growing appreciation of systemic inflammation and its association with chronic diseases [30,32-34]. This form of inflammation seems to be the root cause of many chronic conditions such as type 2 diabetes mellitus, cardiovascular disease, and cancer. Systemic inflammation is considered a low-grade and sub-clinical condition in that it is not associated with pain, so patients are slow to act on rectifying it [30]. This low-grade inflammation is often characterized by increased concentration of plasma and/or cellular biomarkers such as the acute phase protein, C-reactive protein (CRP) [30,32].

Obesity is likely the main driver of chronic inflammation and accompanies most inflammatory chronic conditions [31,35]. The link between obesity and elevated CRP levels has been well explained by several pathophysiological mechanisms [35]. The central role of chronic inflammation is attributed to the liver, where free fatty acids and triglycerides are drained from the circulation. This action prompts the release of cytokines (e.g., IL-6) by adipose tissue, which in turn, triggers the liver to release CRP.

The evidence for obesity being the root cause of inflammation is strong. Excess calorie intake leads to obesity, while a reduction in energy intake not only results in weight loss, but also the reduction of CRP and an improvement in metabolic markers like blood glucose, insulin, and lipids in adults and children [30,35]. Obesity also decreases adiponectin, an anti-inflammatory mediator. Thus, obesity caused by excess energy intake, increases inflammation, which drives chronic conditions. A reduction in calories promotes weight loss and improvement in many metabolic markers of chronic disease.

The relationship between diet and inflammation that leads to many chronic diseases is of intense scientific interest [30-34]. Most of the work in this area relates to the effect of a dietary pattern on inflammation. Less well studied is the effect of a single food or nutrient on inflammation [30]. A Western dietary pattern that has a high intake of red and processed meats, sugar-rich foods, refined grains, and ultra-processed foods is related to chronic inflammation. Even a diet consisting of mostly ultra-processed foods also fosters chronic inflammation [22]. In contrast, a prudent dietary pattern is rich in fruit, vegetables, legumes, whole grains, and plant-based proteins, and if animal proteins are consumed, they should come primarily from poultry and seafood. This prudent dietary pattern has a low inflammatory impact in the body.

The Mediterranean diet is a good example of a low inflammatory, prudent diet. It is characterized by a dietary pattern rich in plant-based foods, whole-grains, legumes, and fats from olive oil and nuts [30]. It allows for a moderate consumption of wine, but is low in meats and sugar-rich foods. Adherence to this dietary plan has been shown to lower makers of inflammation, including CRP.

Another prudent diet, the DASH diet (Dietary Approaches to Stop Hypertension), was also shown to be anti-inflammatory based on a meta-analysis [36]. The DASH diet recommends a high intake of fruit, vegetables, and other potassium-rich foods, which serve to replace sodium-rich processed foods. Based on six studies including 451 individuals, the DASH diet significantly decreased CRP levels compared to a Western diet that is typically consumed.

In addition to using dietary patterns to predict inflammation and thus chronic disease, dietary inflammatory indexes have been developed that assess multiple factors [34]. Two indexes exist to describe a diet's inflammatory potential: (1) an empirical dietary inflammatory pattern (EDIP) composed of food groups as reported on a food-frequency questionnaire (FFQ); and (2) a literature-derived dietary inflammatory index (DII) that focuses mainly on individual nutrients. Higher scores in both dietary indexes were associated with higher concentration of inflammatory markers (e.g., CRP) in both men and women.

Besides healthy meal patterns, the addition of herbs and spices to meals has an anti-inflammatory effect, thereby reducing the risk of chronic disease [37]. Based on a narrative review, selected herbs and spices were shown to be anti-inflammatory. Specific herbs that were shown to have anti-inflammatory properties included basil,

rosemary, oregano, coriander, thyme, and sage. Several spices had anti-inflammatory properties as well (e.g., cinnamon, cloves, ginger, turmeric, cumin, black pepper).

In a well-controlled study, investigators explored the anti-inflammatory impact of different amounts of spice blends in a group of overweight and obese subjects [38]. The spices consumed were: cardamom, cinnamon, coriander, cumin, garlic, ginger, paprika, red pepper, and turmeric. After four weeks of a medium intake of the spices (3.2 g), interleukin-6 (IL-6) in the plasma and IL-6 secretion from stimulated monocytes decreased. In addition, after four weeks, postprandial reductions were observed in plasma IL-1-beta, IL-8, and tumor necrosis factor-alpha concentrations after ingestion of daily meals containing a different spice dose (3.7 g).

Thus, it seems reasonable that the liberal use of herbs and spices coupled with a prudent, healthy eating pattern will not only reduce inflammation, but also the risk of developing chronic conditions.

The diet

The Diet is anti-inflammatory for several reasons. First, it promotes weight loss, which has been shown to be the root cause of inflammation. Second, it is a prudent diet in that it is replete with whole, unprocessed foods like whole grains, fruits, and vegetables, while at the same time, being low in meats and devoid of ultra-processed foods. Third, the Diet includes the regular use of herbs and spices, which have been shown to be anti-inflammatory. Each individual meal from the Diet is carefully balanced to contain a serving of protein from plants, animals, or both; a whole-grain starch; and fruits and vegetables. The Company products, rich in herb and spice blends, accompany most of these offerings.

INTERMITTENT FASTING

Caloric restriction has been shown to increase life expectancy, but it is rarely adopted because it creates uncontrollable hunger [39]. Instead, an intermittent fasting approach has been proposed as an alternative because it offers periods of time when the body is in a fasted state, thus mimicking the hormonal pattern that might occur with calorie restriction. One study in mice demonstrated that calorie restriction extended life by 30%, while intermittent fasting offered a 35% increase [39]. Thus, intermittent fasting has sparked the attention of many nutritional researchers, as it allows for the benefit of calorie restriction without hunger.

Intermittent fasting is the umbrella term for four approaches to this way of eating [40]:

- Zero-calorie alternate-day fasting, which involves alternating days of fasting (no calories) and ad libitum eating on the others.
- Modified alternative-day fasting, which alternates between days of ad libitum eating and days of fasting (up to 600 kcal per day for three to five days per week).
- The 5:2 diet, in which indivudals fasted for two days weekly (consuming up to 600 kcal daily) and have five days of ad libitum eating.
- Time-restricted eating, which involves fasting for 12 to 24 hours per day.

One early study from Serlie's lab showed a hypercaloric diet with high meal frequency increased intra-hepatic triglyceride content and abdominal fat independent of caloric content and body weight gain; whereas, increasing meal size did not [41]. This study suggested that snacking - a common feature in the Western diet - may independently contribute to hepatic steatosis and obesity. In addition, it showed meals consumed at one sitting, independent of energy content, allow for fasting in-between them, which is a healthier way to lose weight than consuming multiple meals and snacks throughout the day.

Numerous other studies and reviews have shown the benefits of intermittent fasting [40,42-44]. One umbrella review - based on 11 meta-analyses and 130 clinical studies, supported by moderate- to high-quality evidence - showed intermittent fasting improves anthropometric measurements (e.g., reduction in body weight, less body fat) and cardiometabolic outcomes (e.g., blood cholesterol, glucose, triglycerides), especially in overweight and obese adults [40].

In addition, other seemingly unrelated benefits of intermittent fasting have been identified [43,44]. These include an improvement in the gut microbiome and in lifestyle behaviors such as sleep [43]. Intermittent fasting also increases life span and improves cognition [44]. Emerging evidence from animal and pre-clinical studies seems to support the use of intermittent fasting for reducing the risk of cancer, asthma, arthritis, and multiple sclerosis; and for pos-

sibly delaying the onset and progression of Alzheimer's disease and Parkinson's disease.

Despite the initial promise of intermittent fasting, some have questioned whether it is more beneficial than a modestly energy-restricted diet, which has no constraints regarding timing of meals [45,46]. The best study rebuking the superiority of intermittent fasting over this type of diet is a carefully controlled, one-year clinical trial [46]. The study included 139 obese individuals who were randomly assigned to eat between 8:00 a.m. and 4:00 p.m. without calorie restriction, or to eat an energy-restricted diet providing approximately 1,500 calories [46]. The results showed that a regimen of time-restricted eating was not more beneficial than daily caloric restriction in regard to a reduction in body weight, body fat, or metabolic risk factors.

In summary, it seems intermittent fasting takes on a variety of approaches, which not only result in weight loss, but also in an improvement in many metabolic parameters. However, the superiority of this approach compared to a modest, energy-restricted diet has not been shown to be true.

The diet

The Diet offers the best of two concepts: intermittent fasting and a modest energy restricted diet. First, the Diet provides three meals daily without snacking, thus abiding by the intermittent fasting concept of having at least 12 hours of fasting. In addition, it embraces the concept of energy-restriction, as it is designed to provide 1,500 kcal daily, which is a 500-kcal deficit to a weight that maintains body weight. The dual approach of the Diet has been shown to produce weight loss without hunger. It is not known if the use of the Diet leads to the health benefits associated with both approaches (e.g., loss of body fat, cardiometabolic improvement, better sleep, etc.), but anecdotal reports from those following the Diet would suggest so. The Company that offers the Diet plans to obtain such data to further strengthen this approach to losing weight.

MICROBIOME SUPPORT

For the past 100 years, much of the focus of nutritional research centered on macro- and micronutrients and their effect on health. The new trend is to focus on the microbiome and weave in how it is affected by diet and, ultimately, how it influences health [47]. Although exciting, this aspect of nutritional research is still in its infancy.

What is known is that the gut microbiota is a highly diverse and metabolically active part of the intestinal tract, consisting of ~3.9 x 10^{13} microbial cells [48]. The human gut microbiota consists of trillions of microbial cells and thousands of bacterial species [47]. These microbes participate in several beneficial functions, including the fermentation of undigested nutrients (mainly fiber), synthesis of vitamins, and interaction with the immune system.

Several diseases, including irritable bowel syndrome and type 2 diabetes mellitus, have been linked with disturbances in the gut microbiota [48]. Diet is the major influencer of the gut microbiota, which suggests the risk of developing these conditions may be reduced by dietary manipulation. Still unknown is what constitutes the ideal microbiome [47]. Inter-individual variation is great and one's own microbiome is resilient - and often resistant - to change. It makes the most sense, from what is known today about the microbiome, to focus on dietary fiber, dietary patterns, and probiotics from foods and supplements.

Dietary fiber

Dietary fiber seems like a logical place to start in regard to its influence on the microbiome, but according to a 2020 report from the Dietary Fibre Consensus from the International Carbohydrate Quality Consortium, of which David J. A. Jenkins was a member, there is still a lot to learn about dietary fiber [49]. For instance, the structure of the plant cell wall has not been fully elucidated. In addition, it is still unknown what the effects of chewing and passage through the gastrointestinal track have on dietary fiber, and thus, the microbiome itself.

What is known is dietary fiber seems to offer a wide variety of benefits to the microbiota [50]. Besides increasing the number of healthy bacteria like *Bifidobacteria* and *Lactobacilli*, dietary fiber also increases the production of beneficial metabolites, decreases protein fermentation and pathogenic bacteria, promotes calcium absorption, reduces allergy risk, and improves the overall immune defense system.

Based on a systematic review and meta-analysis comprised of 64 studies, dietary fiber interventions lead to higher fecal abundance of the so-called healthy bacteria, *Bifidobacteria* and *Lactobacillus* [48]. Two specific types of dietary fiber (fructans and

galacto-oligosaccharides) lead to the highest fecal abundance of these bacteria. Whole grains appear to be mostly bifidogenic, and resistant starch may promote the growth of *Ruminococcus bromii* and *Eubacterium rectale* [51]. What influence other fiber-rich foods (e.g., fruit, nuts, vegetables, seeds/nuts, and legumes) have on the microbiota is less clear. Thus, it would appear dietary fiber supports a healthy microbiome, and that obtaining fiber from different dietary sources may be important.

Dietary patterns

In a broad sense, the Western diet, which is rich in sugar, salt, and ultra-processed foods, has a worse impact on the human gut microbiota than a prudent diet [18,22,51,52]. For example, from a sample of 34 individuals - who underwent endoscopy where colonic mucosal cells were obtained - those who consumed a poor diet based on the Healthy Eating Index experienced a reduction in the relative abundance of potentially beneficial bacteria and an increase in the number of potentially harmful ones compared to those who ate a healthier diet [52].

Not all studies suggest that diet quality is best for the microbiome. Some studies showed that differences in microbial populations are not apparent between those who follow a vegetarian/vegan diet and those who consume animal proteins [47]. A more beneficial dietary pattern may be the Mediterranean diet, which focuses on including a wide variety of plant-based foods while de-emphasizing, but not eliminating, animal products. Such a diet also encourages a variety of foods (fruits, vegetables, legumes, unsaturated fats, and limited red meat). Epidemical studies show that diets like the Mediterranean diet are associated with a risk reduction of multiple chronic diseases. Although few studies have examined the impact of a Mediterranean diet on the microbiome, those that are available seem to show this diet produces favorable microbiota profiles and metabolites. For example, closer adherence to the Mediterranean diet was associated with a lower ratio of *Firmicutes* and *Bacteroidetes*, and a higher detection of fecal short-chain fatty acids.

Dietary plans that incorporate herbs and spices in substantial quantities appear to favorably affect the gut microbiota compared to those that don't include them or only include them in small amounts [53]. In a prospective, cross-over design, participants at risk for cardiovascular disease were randomly assigned to one of three herb-spice regimens - low (0.5 g/day); moderate (3.3 g/day); and high (6.6 g/day) - for four weeks each, with a two-week wash-out period in-between each treatment. The addition of herbs and spices to a typical diet resulted in numerous changes to the gut bacterial composition (alpha diversity, beta diversity, and changes in the number of specific organisms). However, the clinical relevance of these changes cannot be determined so more work is needed.

Probiotics from foods and dietary supplements

Modification of the intestinal microbiota to restore and maintain a favorable balance can be achieved through the provision of probiotics from selected foods like some yogurts and dietary supplements containing probiotics [54,55]. Dietary supplements of probiotics such as *Lactobacillus* and *Bifidobacterium* are subjected to food regulations to assure safety.

Many of the studies on probiotic administration focused on treating conditions of the gastrointestinal tract such as Crohn's disease, ulcerative colitis, lactose intolerance, irritable bowel syndrome, infectious diarrhea, and peptic ulcers [54,55]. Other conditions have also been investigated, such as obesity, insulin resistance syndrome, non-alcoholic fatty liver disease, allergies, and atopic dermatitis. These findings have been inconclusive so today, it is not possible to assign certain probiotic strains and corresponding amounts to treat any of these conditions.

A new approach for probiotic administration combines probiotics and prebiotic fibers. This is referred to as synbiotics [54]. A combination of *Bifidobacterium* or *Lactobacillus* genus bacteria with fructooligosaccharides seems to be the most popular. It may be that the development of formulas containing both appropriate microbial strains and synergistic prebiotics may lead to the best outcomes in gastrointestinal health.

Ultra-processed foods that contain excessive amounts of fat and insufficient amounts of fiber-rich foods, wreak havoc with the human microbiota. Therefore, individuals who consume most of their energy from ultra-processed foods may benefit from including sources of probiotics from foods or dietary supplements coupled with dietary fiber from food or dietary supplements. These additions to a poor diet may improve symptoms associated with enteral conditions and overall health. However, despite how attractive a symbiotic approach may seem, more work is needed to understand the complex system of the microbiome and its effect on health, and

how different dietary patterns affect the health of the gastrointestinal system [56].

The diet

The Diet would appear to support a healthy microbiota because it is close to the Mediterranean diet and incorporates a variety of dietary fibers. Like the Mediterranean diet, the Diet focuses on including a wide variety of plant-based foods while de-emphasizing, but not eliminating, animal products. In addition, fiber comes from a variety of sources including fruits, vegetables, legumes, nuts, seeds, and whole grains. Unlike the Mediterranean diet, the Diet incorporates generous amounts of herbs and spices shown to have a favorable effect on the microbiome. The Diet does not include dietary components that may interfere with a healthy microbiota like saturated fats, which are minimized, and ultra-processed foods, which are eliminated. Many meals that are part of the Diet provide a synbiotic approach where both probiotics (e.g., yogurt, plant-protein product containing 1 billion probiotic *Bacillus coagulans* cells) and prebiotics (e.g., dietary fiber from a variety of foods) are consumed at the same time.

CONCLUSION

Weight loss is a goal of many and there are multiple ways to achieve it. However, most diets are simply fads and not based on sound science. Moreover, those that can be scientifically supported often only adopt one approach to weight loss, such as energy restriction. Darwin would not ascribe "survival of the fittest" to any of these weight loss approaches.

A multi-pronged approach is needed to successfully lose weight [57]. The Diet reviewed herein is unique in that it is based on multiple principles of sound science. This approach to weight loss is predicated on: nutritional completeness, limited processed foods, being anti-inflammatory, intermittent fasting, and microbiome support. It makes sense to use this Diet to lose weight and avoid others that are based on fads or just one scientific tenant. Darwin would certainly claim the Diet is truly a "the survival of the fittest" approach and likely to stand the test of time.

Acknowledgements/Conflict of Interest

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