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Review article

The Use of Dietary and Caloric Restriction Models for Improved Cardio-Metabolic Health

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Abstract

Although weight loss is often the impetus for beginning a dietary program, multiple physiological benefits are typically observed when someone embarks on a dietary regimen involving reduced caloric intake. Many of these changes, such as a reduction in blood pressure, an improvement in blood lipids and insulin sensitivity, and a reduction in inflammation and oxidative stress, can be viewed as favorable in terms of cardio-metabolic health. The positive changes are not only realized if individuals follow a hypo-caloric diet. In fact, simply altering the timing of the overall caloric intake over the period of the day or week can result in profound benefits. Alternatively, manipulating the macronutrient composition of the diet can be met with favorable outcomes, in particular when the dietary plan includes high quantities of nutrient dense, fiber-rich foods. This brief review discusses four different dietary approaches that have been shown to be effective alternatives to the traditional dietary plans most commonly followed. The plans discussed include caloric restriction, alternate day fasting, intermittent fasting, and dietary restriction. Findings from both animal and human studies are discussed, as appropriate.

Abbreviations

ADF: Alternate Day Fasting;
CALERIE: Comprehensive Assessment of Long-term Effects of Reducing Caloric Intake;
CR: Caloric Restriction;
DR: Dietary Restriction;
IF: Intermittent Fasting;
HDL-C: High Density Lipoprotein;
LDL-C: Low Density Lipoprotein

Keywords: Caloric Restriction; Dietary Restriction; Alternate Day Fasting; Intermittent Fasting; Cardio-Metabolic Health

Introduction: The Problem

At any given moment, approximately 25% of men and 45% of women in the United States are "on a diet" [1]. The primary goal for most of these individuals is simply to lose weight. Indeed, overweight status (body mass index ≥25kg/m^2) and obesity (body mass index ≥30kg/m^2) is on the rise, not only within the U.S. but in most developed countries around the world [2]. Obesity impacts adults, adolescents, and children of all walks of life—specifically, 34.9% of adults are obese (78.6 million) and 17% (12.7 million) of children and adolescents are obese [3, 4]. The reality is that obesity is a lifestyle disease, with individuals' lack of physical activity and poor dietary choices being the main culprits for the rampant rise in this disease [5]. Moreover, obesity is strongly associated with other lifestyle diseases including type II diabetes [6,7] and cardiovascular disease (e.g., high blood pressure [7-10], stroke [11,12], and heart disease [13,14]). As a result, many individuals begin a diet each year, often prompted by their personal physician, for purposes of improving overall health [15].

Although many interesting and sometimes successful diets are written about and followed with success by many (e.g., low carb-high protein, Paleo, small and frequent feedings), many other fad diets are available and often marketed heavily [16]. In most cases, dietary plans involve some form of caloric restriction—either by design or by default [17]. Some involve manipulating the timing of meal consumption [18-20], while others involve consuming better quality, more nutrient dense foods [21]. Many of these ideas are rooted in well-investigated plans that have been studied in controlled laboratory settings—the results of which include not only weight loss, but many other cardio-metabolic health benefits often overlooked by the typical dieter [22-24]. This is likely the result of the fact that individuals can "see" weight loss but cannot see a reduction in blood pressure or blood lipids, or an improvement in insulin sensitivity or antioxidant status.

Regardless of the dietary plan, one reality exists: All diet plans will work. The problem is that the plan will only work for the time a person can actually adhere to it [25]. This is of particular concern for plans that call for a drastic reduction in calories, as most individuals lack the discipline needed to reduce caloric intake day in and day out [26]. Alternative approaches are necessary, some of which are discussed in this article.

Caloric Restriction

Since the early work of McCay and colleagues [27], there has been a great deal of scientific interest in calorie reduction plans designed to shed body weight, improve overall health, and possibly extend lifespan. In general, caloric restriction (CR) involves the purposeful reduction of caloric intake of 20-40% of *ad libitum* consumption, while maintaining adequate nutrient intake [28, 29]. The magnitude of the restriction appears related to the extent of longevity, up to the point that the plan does not induce starvation [30].

As can be expected, reducing caloric intake by such a significant amount, results in weight loss [18, 31-35], which will aid in reducing the magnitude of obesity [31, 36]. Moreover, in many species, including drosophila [37-39], dogs [40], and primates [41-44], CR has been shown to increase longevity. To generate robust data, most studies involving animals initiate the CR during the weaning phase and then continue the plan throughout the animal's lifespan. Several investigations in animals have noted improved cardiovascular [45-49] and metabolic [42, 50, 51] health when following a CR regimen. This includes, but is not limited to a reduction in blood triglyceride [46, 52-55] and cholesterol [54-56], a reduction in resting heart rate and blood pressure [48, 49, 57, 58], a reduction in inflammation [55, 59, 60], a reduction in oxidative stress biomarkers [45, 51, 55-57, 61, 62], an improvement in glucoregulatory function and insulin sensitivity [54, 63, 64], and an improvement in immune function [65, 66]. All of the above may be reasons for the increased longevity and decreased incidence of disease associated with CR regimens [67].

While the majority of CR research has been done using animals, more human studies have been conducted recently, with promising results. Rather than measuring longevity directly, CR studies in humans typically measure biomarkers correlated with longevity, including those indicated above for animals. CR plans are typically implemented for a period of 6-12 months [68-80] but some studies have extended the timeframe beyond this point [26, 81-84]. The majority of published work has included healthy, middle aged, men and women with normal body mass. Much of the work is associated with the CALERIE (Comprehensive Assessment of Long Term Effects of Reducing Caloric Intake) program [26, 69, 71, 74-78, 81, 85], which investigates the responses of CR on free-living humans.

Alternate Day Fasting

While caloric restriction may be appropriate for some individuals, many simply do not have the discipline and will power to drastically reduce food intake each day, leading to a lack of compliance over time and ultimate failure. This fact is highlighted by recent statistics indicating that of those who begin a calorie restriction plan, only 38% maintain the plan after one year [86]. Clearly, alternative approaches are needed if we are concerned with long-term success.

One such alternative to CR is alternate-day fasting (ADF). This plan, as the name indicates, consists of two interchanging days of fasting and eating. On one day, individuals consume food *ad libitum*, sometimes significantly exceeding their usual daily intake. On the next day, food is reduced significantly (e.g., up to 500-600 calories) or withheld altogether [87]. The cycle repeats itself throughout the course of week, so that in a given two-week period, an individual would follow seven "fast" days and seven "feast" days [28]. Due to the fact that calorie restriction is not required every day, overall compliance to this plan may be better than with the usual caloric restriction regimen [28]. Of course, this is highly dependent on the individual.

Like CR, ADF has been noted to extend lifespan in several animal trials [88-90], which may be at least partly due to the fact that ADF has been shown to reduce or prevent the development of cardiovascular disease, diabetes, certain forms of cancer, and kidney disease, [90-92]. Many of the same cardio-metabolic outcomes shown to improve with CR are improved with ADF. For example, both resting heart rate and blood pressure are reduced following a period of ADF [92, 93]. ADF can also improve insulin sensitivity, resulting in lower fasting glucose and insulin concentrations and improved glucose tolerance [94], and lead to a lowering in inflammation [95-98] and oxidative stress [89, 96, 97, 99, 100].

Most human studies of ADF involve a maximum fasting period of up to 20 weeks, while some trials have lasted only a few days. Many subjects appear to tolerate this plan quite well, especially in the short-term [18]. Of course, subjects sometimes report hunger and irritability during fast days [18], which raises questions regarding the long-term compliance of this particular plan in a free-living environment.

Intermittent Fasting

Similar to ADF, intermittent fasting (IF) involves a period of fasting alternated with a period of eating [101]. However, this entire cycle is completed inside of a 24 hour period, rather than a two-day period as with ADF. With IF, individuals determine a 6-7 hour eating "window" during the day and consume all food and calorie containing beverages during that time [19]. For example, an individual might select to eat/drink all calories between 12:00 noon and 6:00 pm each day. This would often involve only two meals, one consumed at 12:00 noon and one consumed at 5:30 pm. If desired, a snack might be consumed at 3:00 pm. The total caloric load of these two meals (and snack if appropriate) might parallel what an individual would typically consume during a usual day of eating [102]. Then, they would go without food or calorie containing beverages from 6:00 pm that day until 12:00 noon the following day. For most individuals who go to bed at a reasonable hour (e.g., 10:00 pm), going without additional calories at night is not very difficult. If awakening at 6:00 am the next morning, waiting until 12:00 noon until consuming their first meal may be somewhat of a challenge. That said, individuals appear to adapt to this challenge rather quickly and find that success may be better on this particular plan as compared to CR and ADF [18]. Again, this is highly dependent on the individual following the plan.

While this particular plan is relatively new in terms of the scientific research, not many studies have been published in this area, at least relative to CR and ADF [101]. What we know at this point is the following: A majority of animal studies in mice [103-107], rats [108], and geese [109] demonstrate overall reductions in body weight following IF trials lasting between 4 and 16 weeks. Because IF has been shown to entrain circadian energy metabolism [110], the timing of the feeding window could have large implications on health outcomes. This is evidenced by the single study exhibiting a significant weight gain following an IF trial in which rats were restricted to feeding during their innate inactive period [111]. In addition to weight loss, improvements in blood lipid are also noted including reductions in total cholesterol [104, 105, 107, 112] and triglycerides [104, 107]. IF can also decrease insulin resistance [104, 113] and/or increase insulin sensitivity [105, 108] resulting in lower circulating glucose [104, 107, 112, 113] and less circulating insulin [104, 107, 113]. Taken together, these improvements in cardio-metabolic risk factors may contribute to the decreases in inflammatory markers [103-105].

Translational studies typically vary in length between 2 and 8 weeks and reveal similar outcomes as in animals, including weight loss [102, 114-120]. Improvements in blood lipids such as decreased total cholesterol [114, 115, 117-119], decreased LDL-C [102, 114, 115, 117-119], increased HDL-C [102, 114, 115, 118, 119], and decreased triglycerides [114, 115, 117-119] are also noted following an IF intervention. Although little change has been noted for fasting insulin levels, reductions in circulating glucose have been observed in many trials [102, 117, 118, 120, 121]. IF is somewhat similar to certain religious fasting practices such as Ramadan and has been well tolerated for centuries.

Dietary Restriction

For those individuals not interested in purposefully reducing calories or restricting the timing of their caloric intake, dietary restriction (DR) may be the best option. With this particular plan, individuals restrict one or more components of their intake with no planned reduction in total caloric intake. With regards to the extension of lifespan, protein and amino acid restriction has been reported to increase maximum lifespan [122, 123] and may account for approximately half of the life extending effects observed with CR [122]. Specifically, the amino acid methionine appears to be responsible for the observed benefits, by impacting mitochondrial reactive oxygen species generation and subsequent oxidative stress [123].

From a practical and human perspective, we have studied a dietary restriction model known as the "Daniel Fast" since 2009. The plan involves *ad libitum* intake of fruits, vegetables, whole grains, nuts, seeds, and oil [21]. This plan is a form of DR that resembles a vegan diet—which has been reported to yield health-enhancing properties [21, 124-127]. However, this plan is more stringent, in that in its purest sense, it does not allow for preservatives, additives, flavoring, sweeteners, alcohol, or caffeine. As with CR, ADF, and IF plans, we have noted multiple positive changes in health-specific outcomes when individuals follow this DR model for a period as short as three weeks. For example, we have noted reductions in body weight, blood pressure, blood lipids, blood insulin, blood oxidative stress biomarkers, and systemic inflammation [124-127]. Moreover, we have studied a modified version of the plan, inclusive of one serving per day of dairy and meat, and noted similar findings as with the pure vegan plan [126]. Of importance, long term compliance with this DR plan is excellent at approximately 80% at six months [128], which far exceeds most traditional dietary plans [129]. When considering that a dietary plan should not be merely adopted for a period of a few weeks but rather, as a lifestyle, DR models such as the Daniel Fast plan may be the best option for most individuals within a free-living environment. Although food choices are limited to some extent, freedom is provided in terms of how much an individual can consume and when they can consume their calories. No restrictions are placed on either of these variables, yet the health benefits are essentially similar to what might be expected with a traditional CR plan.

Conclusions

The concern over excess body weight and obesity status continues to grow in the United States and in other developed countries around the world. The regular consumption of processed, calorie-dense foods is fueling this problem. While many fad diets are available for consideration and use, the dietary plans discussed in this brief review have been well-tested and shown to provide benefit when used by men and women. While practitioners working with those requiring weight loss and health improvement might begin by adopting a standard CR plan in an attempt to jump start the weight loss process, individuals should then have the choice as to which plan they believe will be best for them to follow moving forward. Their individual lifestyle should be considered in the selection process, making certain that the plan they choose is flexible enough to work long-term. Of course, physical activity and regular, structured exercise should always be a part of every weight loss and general health program, as we know from the available evidence that success in eating well can be fueled by success in adhering to an exercise regimen [34, 130, 131].

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