Special Article

Effects of intermittent fasting on body composition and clinical health markers in humans

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Intermittent fasting is a broad term that encompasses a variety of programs that manipulate the timing of eating occasions by utilizing short-term fasts in order to improve body composition and overall health. This review examines studies conducted on intermittent fasting programs to determine if they are effective at improving body composition and clinical health markers associated with disease. Intermittent fasting protocols can be grouped into alternate-day fasting, whole-day fasting, and time-restricted feeding. Alternate-day fasting trials of 3 to 12 weeks in duration appear to be effective at reducing body weight (≈3%–7%), body fat (≈3–5.5 kg), total cholesterol (≈10%–21%), and triglycerides (≈14%–42%) in normal-weight, overweight, and obese humans. Whole-day fasting trials lasting 12 to 24 weeks also reduce body weight (≈3%–9%) and body fat, and favorably improve blood lipids (≈5%–20% reduction in total cholesterol and ≈17%–50% reduction in triglycerides). Research on time-restricted feeding is limited, and clear conclusions cannot be made at present. Future studies should examine long-term effects of intermittent fasting and the potential synergistic effects of combining intermittent fasting with exercise.

INTRODUCTION

The prevalence of obesity and overweight remains high throughout many parts of the world.[1,2] Weight loss and improvement of body composition (decreasing body fat and/or increasing muscle mass) through physical activity and dietary modifications can help decrease risk for obesity-related diseases.[3] While daily caloric restriction is perhaps the most prevalent form of dietary restriction, other methods are emerging. One alternative method of caloric restriction is intermittent fasting, a broad term that encompasses a number of specific fasting protocols. The common theme among intermittent fasting protocols is that individuals periodically abstain from eating for periods longer than the typical overnight fast. These programs typically lead to energy restriction, but the restriction is not necessarily maintained each day.

The majority of popular intermittent fasting protocols can be grouped into 1 of 3 categories: alternate day fasting, whole-day fasting, and time-restricted feeding. Each form of intermittent fasting utilizes different periods of feeding and fasting (Table 1). Alternate-day fasting involves alternating between *ad libitum* feeding days and fasting days, which typically consist of a single meal containing approximately 25% of daily calorie needs. Whole-day fasting is perhaps the simplest form of intermittent fasting and typically consists of 1 to 2 days of complete fasting per week plus *ad libitum* eating on the other days. Some programs, however, allow food intake of up to approximately 25% of total daily energy expenditure on fasting days.[4] Time-restricted feeding involves following the same eating routine each day, with a certain number of hours designated as the fasting window and the remaining hours as the feeding window.[5] It is important to note that fasting typically

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Table 1 **Examples of food intake schedules of different categories of intermittent fasting protocols**

Type of protocol	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Alternate day fasting	*Ad libitum*	25% kcal	*Ad libitum*	25% kcal	*Ad libitum*	25% kcal	*Ad libitum*
Time-restricted feeding	16–20 h of fasting, 4–8 h of feeding	16–20 h of fasting, 4–8 h of feeding	16–20 h of fasting, 4–8 h of feeding	16–20 h of fasting, 4–8 h of feeding	16–20 h of fasting, 4–8 h of feeding	16–20 h of fasting, 4–8 h of feeding	16–20 h of fasting, 4–8 h of feeding
Whole-day fasts	*Ad libitum*	*Ad libitum*	*Ad libitum*	*Ad libitum* or 24-h fast[a]	*Ad libitum*	*Ad libitum*	24-h fast

[a]Some programs utilize nonconsecutive fasting days, while others place multiple fasting days in succession.

refers to complete abstinence from caloric intake, but some intermittent fasting programs allow small amounts of food consumption (up to approximately 25% of daily caloric needs) during fasting periods, meaning they are actually utilizing modified fasting.

Several intermittent fasting protocols have gained popularity and boast impressive anecdotal health benefits, but it is unlikely that all intermittent fasting regimens lead to the same physiological changes, given their different patterns of fasting and feeding. Therefore, the purpose of this qualitative review is to provide a summary of the available human subject research pertaining to popular intermittent fasting protocols in order to determine the efficacy of these interventions, particularly how these protocols may alter body weight, body composition, and clinical health markers such as blood lipids and blood pressure. Unlike other recent publications, this review compares multiple categories of intermittent fasting (alternate-day fasting, whole-day fasting, and time-restricted feeding), which allows for a more direct assessment of their similarities, differences, and efficacy. Additionally, this review focuses on the effects of fasting or modified fasting programs that were specifically employed in order to improve health, not programs that are followed for other reasons (e.g., religious fasting). Finally, this review seeks to provide relevant information regarding the metabolic changes that occur during the short-term fasts practiced in intermittent fasting.

LITERATURE SEARCH

Searches were performed in PubMed and the university library's OneSearch resource using the following terms: "intermittent fasting," "alternate-day fasting," "meal frequency AND body composition," "reduced meal frequency," and "fasting calorie restriction." Inclusion criteria were as follows: 1) clinical trials conducted in human subjects; 2) male or female subjects of any age; 3) study duration of at least 3 weeks; 4) total sample size of $\geq$10 subjects; 5) utilization of complete or modified fasting; 6) reporting of changes in body weight and/or body composition; and 7) publication in the English language. Exclusion criteria were as follows: 1) animal studies; 2) study duration of less than 3 weeks; 3) total sample size of <10 subjects; 4) publications that were not in the English language; and 5) religious fasting. Twenty-one studies that matched the inclusion criteria were located.[6–18, 21–28]

EVALUATION OF EVIDENCE FOR POPULAR INTERMITTENT FASTING PROTOCOLS

Alternate-day fasting

With the exception of religious fasting, the most-studied form of intermittent fasting is alternate-day fasting. This protocol involves alternating *ad libitum* feeding days with fasting days, which typically consist of 1 meal consumed at lunchtime that contains approximately 25% of the baseline caloric needs for the individual. It is worth mentioning that alternate-day fasting utilizes modified fasting (since some caloric intake is allowed) and can involve different durations of modified fasting based upon an individual's schedule. The period of modified fasting, containing 1 small meal, could reasonably vary from 30 to 40 hours. For example, if an individual consumed his last meal on Monday (feeding day 1) at midnight and his first meal on Wednesday (feeding day 2) at 6 am, the duration would be 30 hours. However, if the last meal on Monday was eaten at 5 pm and the first meal on Wednesday was eaten at 9 am, the duration would be 40 hours. There could be differences in the alterations of metabolism and health markers between these two alternate-day fasting schedules, depending on the duration of modified fasting. Alternatively, alternate-day fasting can be viewed as two separate fasts, separated by a miniature feeding window consisting of the approximately 25% kcal lunch. In this case, the first fasting period would end when lunch was consumed midday and could reasonably vary from 12 to 19 hours, depending on when the last food intake on the previous day occurred. The second fasting period, beginning around 1 pm on a fasting day, could last from 17 to 20 hours, depending on when breakfast was consumed on the following feeding day.

Table 2[6–18] outlines the methods and results of alternate-day fasting experiments in humans. Body weight reduction[6,8–10,12–14,16,18] and decreases in fat mass[6,9,10,13,14,16,18] have been consistently observed during alternate-day fasting protocols. These results have been seen in obese,[8–10,12,14,16,18] overweight,[6,12,13,18] and normal-weight[6,13] subjects. No change in fat-free mass was observed in 3 alternate-day fasting studies in which body composition was measured,[10,13,14] while 3 studies have shown decreases[6,9,16] and 3 did not measure or did not report fat-free mass changes.[8,12,18] Heilbronn et al.[6] and Donahoo et al.[9] reported decreases in fat-free mass, but they used an alternate-day fasting protocol that utilized fasting days without any caloric intake, while many other studies placed 1 meal containing approximately 25% of daily caloric needs on the fasting days.[8,10–18] In fact, Heilbronn et al.[6] recommended that a small meal be added to the fasting days in future work. It is possible that adding this small meal helps promote lean-mass retention during fasting, since fat-free mass was not decreased in the majority of studies that placed a small meal on the fasting days.[10,13,14] A recent review by Varady[19] also noted that intermittent caloric restriction may provide superior fat-free mass retention when compared with daily caloric restriction. The effects of abstaining from the small fasting-day meal on clinical health markers is not clear because only limited blood lipid data are provided by the studies that excluded this meal.[6,9]

Alternate-day fasting has also been shown to be effective at improving several risk factors associated with cardiovascular disease. Reduction of total cholesterol,[8,10,13,14] triglycerides,[6,8,10,12–14] and low-density lipoprotein (LDL) cholesterol[10,12,14] have been observed, but not in every instance. Increases in high-density lipoprotein (HDL) were reported in 2 studies,[6,8] but 1 study reported an increase in women only and did not provide quantitative data.[6] The majority of studies found no difference in HDL concentrations. Small LDL particles have been associated with increased risk for cardiovascular disease,[20] and thus increasing LDL particle size might be regarded as a reduction in cardiovascular disease risk. Several alternate-day fasting studies have shown increased LDL particle size in subjects who followed the fasting protocol.[12,13,16] The vast majority of studies included in this review did not examine insulin sensitivity or action, but Donahoo et al.[9] found no change in insulin sensitivity in obese individuals after 8 weeks of alternate-day fasting.

There are a number of possible reasons why varying results were seen in different alternate-day fasting studies. Studies varied in experimental design, duration, and participant characteristics, including weight category (normal weight, overweight, obese), age, and gender. Some studies[6,7,9] allowed no caloric intake on fasting days, while others[8,10,11,13–18] allowed caloric intake of up to 25%–30% of weight maintenance needs. Macronutrient intake was not controlled in most studies, and adherence to the dietary protocol and the accuracy of reported adherence could have varied between studies.

Whole-day fasting

Some forms of intermittent fasting involve only 1 to 2 days per week of either complete food abstinence or severe calorie restriction instead of alternating between higher and lower food intakes each day. These protocols can be as simple as observing one 24-hour fast per week, although some include multiple fasts each week and/or fasts lasting longer than 24 hours.

Seven whole-day fasting studies are summarized in Table 3.[22–28] All studies combined intermittent fasting with caloric restriction (i.e., the total weekly diet was hypocaloric), and some utilized modified fasting by allowing small amounts of food intake on fasting days. Reductions in body weight and body fat were consistently seen in these studies. However, when total caloric restriction was equal between fasting groups (i.e., intermittent calorie restriction) and continuous calorie restriction, the losses in body weight and body fat were not different between groups.[23] When compared with control subjects who maintained their regular eating pattern, subjects who followed the whole-day fasting protocol showed significant reductions in body weight and body fat.[24,27,28]

Similar to alternate-day fasting studies, whole-day fasting studies have produced varying results, which might be attributable to a number of factors. Importantly, not all whole-day fasting studies used the same number of fasting days each week. Several utilized 1 day per week,[22,25,26] and the studies that required 2 fasting days differed in whether the days were consecutive[23] or nonconsecutive.[24,27,28] The information currently available is insufficient to make a definitive statement about which pattern is most beneficial, but it is possible that some differences in results could be attributed to these variations in the fasting protocol. Most whole-day fasting studies utilized middle-aged or older adults, but the gender and weight category of participants varied. Additionally, some studies[24,27] did not report blood lipid or blood pressure changes, which limits the ability to compare different experiments.

Table 2 **Alternate-day fasting experiments in human subjects[a]**

Reference(s)	Purpose	Subjects (age in years)[b]	Methodology	Weight and body composition (kg or percent change)			Cholesterol (mg/dL or percent change)				Blood pressure (mmHg)	
				Body weight	Body fat	Fat-free mass	Total cholesterol	Triglycerides	LDL	HDL	Systolic	Diastolic
Heilbronn et al. (2005)[6] and Heilbronn et al. (2005)[7]	To determine the feasibility of ADF in nonobese subjects and to examine the effects of ADF on body weight, resting metabolic rate, fat oxidation, and biomarkers of longevity	16 normal-weight and overweight M (34 ± 3) and F (30 ± 1)	Subjects alternated between fasting days (no calorie intake) and *ad libitum* feasting days for 22 d. Body composition was measured by DXA	↓ −2.1 ± 0.3 kg (− 2.5 ± 0.5%)	↓ −4 ± 1%	↓ 53.4 to 52.8 kg[c]	NR	↓ in M only (data NR)	NR	↑ in F only (data NR)	NC	NC
Johnson et al. (2007)[8]	A pilot study to determine the feasibility and efficacy of intermittent CR in the treatment of patients with moderate asthma	10 obese inactive M and F with moderate asthma (age NR)	All subjects alternated between fasting days (320 kcal consumption for F and 380 kcal consumption for M via canned meal-replacement shake) and *ad libitum* feeding days for 8 wk. Body composition was not measured	↓ −8.5 ± 1.7 kg (−8.0 ± 1.4%)[d]	NR	NR	↓ 204.1 ± 7.9 to 183.6 ± 7.1 mg/dL	↓ 279.3 ± 105.4 to 161.0 ± 40.5 mg/dL	NC	↑ 44.0 ± 5.6 to 48.1 ± 5.9 mg/dL	NR	NR
Donahoo et al. (2009)[9]	To determine if IF results in greater weight loss and improvements in insulin sensitivity than CR	17 healthy obese subjects	Subjects randomized into CR and IF groups. Subjects in the IF group alternated between *ad libitum* feeding days and fasting days without food intake for 8 wk. Subjects in the CR group followed a 400 kcal/d deficit diet. Food was provided to subjects in both groups. Body composition was measured by DXA	IF[e]: ↓ −6.9 ± 1.3 kg (−7.4 ± 1.4%) CR[e]: ↓ −4.7 ± 1.3 kg (−4.2 ± 1.0%)	IF[e]: ↓ −3.9 ± 0.7 kg CR[e]: ↓ −2.8 ± 0.6 kg	IF[e]: ↓ −2.9 ± 0.8 kg CR[e]: NC	NR	NR	NR	NR	NR	NR
Varady et al. (2009)[10] and Bhutani et al. (2010)[11]	To examine the ability of ADF to facilitate weight loss and beneficially modulate key indicators of coronary artery disease risk in obese individuals	16 obese M and F (46 ± 2)	All subjects alternated between fasting days (≈25% of kcal needs as determined by Mifflin equation; consumed between 12 pm and 2 pm) and *ad libitum* feeding days for 8 wk. A 2-wk baseline control period preceded the 8-wk intervention. Body composition was measured by tetrapolar BIA	↓ −5.6 ± 1.0 kg (−5.8 ± 1.1%)	↓ −5.4 ± 0.8 kg 45 ± 2% to 42 ± 2%	NC	↓ −21 ± 4%	↓ −32 ± 6%	↓ −25 ± 10%	NC	↓ 124 ± 5 to 116 ± 3 mg/dL	NC

(continued)

Table 2 **Continued**

Reference(s)	Purpose	Subjects (age in years)[b]	Methodology	Weight and body composition (kg or percent change)			Cholesterol (mg/dL or percent change)				Blood pressure (mmHg)	
				Body weight	Body fat	Fat-free mass	Total cholesterol	Triglycerides	LDL	HDL	Systolic	Diastolic
Varady et al. (2011)[12]	To compare the effects of ADF, CR, and endurance exercise on changes in LDL and HDL particle size in overweight and obese subjects when a similar degree of weight loss is achieved	60 overweight and obese M and F (ages for 4 groups: ADF, 47 ± 2, CR, 47 ± 3, exercise, 46 ± 3; control, 46 ± 3)	Randomized, controlled, parallel-arm trial. Four groups were utilized (ADF, CR, EX, and control). Subjects in ADF and CR groups alternated between fasting days (≈25% of kcal needs as determined by Mifflin equation; consumed between 12 pm and 2 pm) and *ad libitum* feeding days for 12 wk. EX group participated in supervised exercise 3 times per week on stationary bikes and elliptical machines. Sessions progressed from 45 min at 60% HRmax to 60 min at 75% HRmax over the course of the study. Body composition was not measured	ADF: ↓ −5.2 ± 1.1% CR: ↓ −5.0 ± 1.4% EX: ↓ −5.1 ± 0.9% Control: NC	NR	NR	NC	↓ in ADF only −17 ± 5%	↓ in ADF: −10 ± 4% ↓ in CR: −8 ± 4%	↑ in EX only 16 ± 5%	NR	NR
Varady et al. (2013)[13]	To examine the effects of ADF on body weight, body composition, and CHD risk parameters in normal-weight and overweight adults	30 normal-weight and overweight M and F (ages for 2 groups: ADF, 47 ± 3; control, 48 ± 2)	Randomized, controlled, parallel-arm trial. Two groups were utilized (ADF and control). Subjects in ADF group alternated between fasting days (≈25% of kcal needs as determined by Mifflin equation; consumed between 12 pm and 2 pm) and *ad libitum* feeding days for 12 wk. Body composition was measured by DXA	↓ −5.2 ± 0.9 kg (−6.5 ± 1.0%)	↓ −3.6 ± 0.7 kg	NC	↓ in ADF[f] 201 ± 9 to 175 ± 12 mg/dL	↓ in ADF 109 ± 13 to 87 ± 9 mg/dL (−20 ± 8%)	NC	NC	↓ in ADF[f] 124 ± 4 to 117 ± 4	↓ in ADF 78 ± 3 to 72 ± 2
Klempel et al. (2013)[14] and Klempel et al. (2013)[15]	To compare the effects of HF and LF ADF diets on body weight, body composition, and CHD risk in obese adults	32 obese F (ages for 2 groups: ADF-HF, 42 ± 3; ADF-LF, 43 ± 2)	Subjects randomized into HF or LF groups. Subjects in both groups alternated between fasting days (≈25% of kcal needs as determined by Mifflin equation; consumed between 12 pm and 2 pm) and *ad libitum* feeding days for 8 wk. A 2-wk baseline control period preceded the 8-wk intervention. Body composition was measured by DXA	HF: ↓ −4.3 ± 1.0 kg (−4.8 ± 1.1%) LF: ↓ −3.7 ± 0.7 kg (−4.2 ± 0.8%)	HF: ↓ −5.4 ± 1.5 kg LF: ↓ −4.2 ± 0.6 kg	NC	↓ in HF 198 ± 11 to 172 ± 9 mg/dL (−13.0 ± 1.8%) ↓ in LF 193 ± 8 to 162 ± 7 mg/dL (−16.3 ± 1.7%)	↓ in both groups HF: −13.7 ± 4.8% LF: −14.3 ± 4.4%	↓ in HF: 109 ± 9 to 90 ± 7 mg/dL (−18.3 ± 4.6%) ↓ in LF: 113 ± 7 to 85 ± 7 mg/dL (−24.8 ± 2.6%)	NC	NC	NC

(continued)

Table 2 **Continued**

Reference(s)	Purpose	Subjects (age in years)[b]	Methodology	Weight and body composition (kg or percent change)			Cholesterol (mg/dL or percent change)				Blood pressure (mmHg)	
				Body weight	Body fat	Fat-free mass	Total cholesterol	Triglycerides	LDL	HDL	Systolic	Diastolic
Bhutani et al. (2013)[16] and Bhutani et al. (2013)[17]	To investigate the effects of combining ADF and endurance exercise on body weight, body composition, and CHD risk factors	64 obese M and F (ages for 4 groups: combo, 45 ± 5; ADF, 42 ± 2; EX, 42 ± 2; control, 49 ± 2)	Randomized, controlled, parallel-arm feeding trial. 4 groups were utilized (ADF + EX [combo], ADF, EX), and control). The combo and ADF groups alternated between fasting days (≈25% of kcal needs as determined by Mifflin equation; consumed between 12 pm and 2 pm) and *ad libitum* feeding days for 12 wk. Body composition was measured by tetrapolar BIA	↓ in combo, ADF, and EX (−6 ± 4 kg, −3 ± 1 kg, −1 ± 0 kg)	↓ in combo and ADF (−5 ± 1, −3 ± 1) kg	↓ in ADF[g] −1 ± 1 kg	NC	NC	↓ in combo[g] −12 ± 5%	↑ in combo[g] 18 ± 9%	↓ in ADF[g] −3 ± 1%	↓ in ADF[g] −2 ± 2%
Eshghinia & Mohammadzadeh (2013)[18]	To examine the effects of modified ADF on body weight, total body fat mass, and CVD risk factors	15 overweight and obese F (33 ± 6)[h]	For 6 wk, all subjects consumed very low-calorie diets (25%–30% of energy needs) on the 3 weekly fasting days (Saturday, Monday, and Thursday) and consumed a diet of 1700–1800 kcal/d on feeding days. A 2-wk baseline control period preceded the 6-wk intervention. Body composition was measured by tetrapolar BIA	↓ 84.3 ± 11.4 kg to 78.3 ± 10.2 kg	↓ 45.8 ± 4.2% to 43.0 ± 4.0%	NR	NC	NC	NC	NC	↓ 114.8 ± 9.2 to 105.1 ± 10.2	↓ 82.9 ± 10.6 to 74.5 ± 10.8

Abbreviations and symbols: ADF, alternate-day fasting; BIA, bioelectrical impedance analysis; CHD, coronary heart disease; CR, caloric restriction; CVD, cardiovascular disease; DXA, dual-energy X-ray absorptiometry; EX, exercise; F, females; FFM, fat-free mass; HDL, high-density lipoprotein; HF, high-fat; HRmax, maximal heart rate; IF, intermittent fasting; LDL, low-density lipoprotein; LF, low-fat; M, males; NC, no change; NR, not reported; ↓, decreased; ↑, increased.

[a]Data reported as mean and standard error of the mean unless otherwise noted.

[b]Weight categories based on World Health Organization classifications, which are based on BMI (normal weight: 18.5–24.99 kg/m^2, overweight: 25–29.99 kg/m^2, obese: $\geq$30 kg/m^2).

[c]Numerical value for standard error of the mean not provided.

[d]Type of error reported was not specified.

[e]No significant between-group changes.

[f]Was not significantly different than control group at week 12.

[g]No changes in other groups.

[h]Mean ± standard deviation.

Table 3 **Whole-day fasting experiments in human subjects[a]**

Reference(s)	Purpose	Subjects (age in years)	Methodology	Weight and body composition (kg or percent change)			Cholesterol (mmol/L or percent change)				Blood pressure (mmHg)	
				Body weight	Body fat	Fat-free mass	Total cholesterol	Triglycerides	LDL	HDL	Systolic	Diastolic
Williams et al. (1998)[22]	To determine whether moderate CR with intermittent VLCD therapy improves weight loss or glycemic control compared with moderate CR alone, and to determine the optimal frequency of VLCD therapy	47 obese M and F with type II diabetes (ages for 3 groups were 54 ± 7, 51 ± 8, and 50 ± 9)	Subjects randomized to SBT, VLCD-1, or VLCD-5. Subjects in SBT consumed 1500–1800 kcal/d throughout the study. Subjects in VLCD-1 consumed a VLCD (400–600 kcal/d) 1 d per week for 15 wk. Subjects in VLCD-5 consumed a VLCD for 5 consecutive days during weeks 2, 7, 12, and 17 of the study. On non-VLCD days, subjects consumed 1500–1800 kcal/d. During the first week and the last 3 wk of the 20-wk study, all subjects consumed a diet of 1500–1800 kcal/d. Body composition was not measured	SBT: ↓, −5.4 ± 5.9 kg VLCD-1: ↓, −9.6 ± 5.7 kg VLCD-5: ↓, −10.4 ± 5.4 kg	NR	NR	↓ in all groups[b] SBT: 5.5 ± 1.2 to 5.2 ± 1.1 mmol/L VLCD-1: 5.6 ± 1.0 to 5.3 ± 1.3 mmol/L VLCD-5: 5.3 ± 0.9 to 5.0 ± 0.8 mmol/L	↓ in all groups[b] SBT: 2.6 ± 1.8 to 1.9 ± 1.0 mmol/L VLCD-1: 2.2 ± 0.9 to 1.1 ± 1.0 mmol/L VLCD-5: 1.8 ± 0.8 to 1.5 ± 0.8 mmol/L	NC	NC	NR	NR
Harvie et al. (2011)[23]	To investigate the difference between energy restriction (25%) delivered as IER or CER on anthropomorphic and metabolic variables in overweight and obese premenopausal women	107 overweight and obese premenopausal F (40 ± 4 for both groups)	Subjects randomly assigned to IER (25% energy restriction via 2 consecutive VLCD days per week) or CER (daily 25% energy restriction) for 6 mo. CER group consumed a Mediterranean-type diet (30% fat, 45% low-glycemic-load carbohydrate, 25% protein). IER group consumed ≈650 kcal on VLCD days. Body composition was measured by BIA	↓ in both groups[b] IER[c]: −6.4 (7.9–4.8) kg CER[c]: −5.6 (6.9–4.4) kg	↓ in both groups[b] IER[c]: 40.5% (39.0–42.0) to 37.3% (35.2–39.3) CER[c]: 40.5% (38.7–42.3) to 38.0% (35.8–40.3)	↓ in both groups[b] IER[c]: 47.6 (46.3–49.0) to 46.4 (44.9–47.9) kg CER[c]: 49.1 (47.7–50.5) to 48.3 (46.7–49.9) kg	↓ in both groups[b] IER[c]: 5.1 (4.9–5.4) to 4.8 (4.5–5.0) mmol/L CER[c]: 5.2 (5.0–5.4) to 4.7 (4.5–5.0) mmol/L	↓ in both groups[b] IER[c]: 1.2 (1.0–1.4) to 1.0 (0.9–1.2) mmol/L CER[c]: 1.3 (1.1–1.4) to 1.0 (0.8–1.2) mmol/L	↓ in both groups[b] IER[c]: 3.1 (2.9–3.3) 2.8 to 2.8 (2.6–3.1) mmol/L CER[c]: 3.1 (2.8–3.3) to 2.8 (2.6–3.0) mmol/L	↓in CER only[b,c] 1.6 (1.4–1.7) to 1.5 (1.4–1.6) mmol/L	↓ in both groups[b] IER[c]: 115.2 (111.2–119.2) to 111.5 (107.7–115.2) CER[c]: 116.8 (113.1–120.4) to 109.3 (105.3–113.2)	↓ in both groups[b] IER[c]: 76.7 (73.9–79.4) to 72.4 (68.9–76.0) CER[c]: 75.4 (72.3–78.4) to 69.7 (66.4–72.9)

(continued)

Table 3 **Continued**

Reference(s)	Purpose	Subjects (age in years)	Methodology	Weight and body composition (kg or percent change)			Cholesterol (mmol/L or percent change)				Blood pressure (mmHg)	
				Body weight	Body fat	Fat-free mass	Total cholesterol	Triglycerides	LDL	HDL	Systolic	Diastolic
Teng et al. (2011)[24]	Pilot study to investigate the feasibility of FCR and its effect on quality of life, food intake, and body composition in elderly Malaysian men	25 normal-weight/overweight M (control group, 58 ± 6; intervention group, 59 ± 3)	Subjects randomized into intervention (FCR) and control groups. Daily caloric intake in FCR group was reduced by 300–500 kcal/d and subjects fasted for 2 nonconsecutive days per week. Control group maintained their regular eating pattern. Study lasted 12 wk, and body composition was measured by BIA	↓ in FCR[d] FCR: −3.14% (71.6 ± 6.0 to 69.3 ± 6.0 kg) CON: +1.1% (72.9 ± 8.5 to 73.7 ± 8.4 kg)	↓ in FCR[d] FCR: −6.35% (26.4 ± 3.9 to 25.3 ± 3.8 kg) CON: +2.7% (25.0 ± 2.9 to 25.5 ± 2.9 kg)	FCR[d]: −0.9% CON: + 0.4%	NR	NR	NR	NR	NR	NR
Klempel et al. (2012)[25] and Kroeger et al. (2012)[26]	To examine the effects of an intermittent fasting protocol combined with CR on body weight, body composition, and CHD risk factors. The use of liquid meals was also examined	54 obese F (IFCR-L group, 47 ± 2; IFCR-F group, 48 ± 2)[f]	Subjects randomized into primarily liquid (IFCR-L) or primarily food-based (IFCR-F) groups. Groups were isocaloric and utilized a 30% energy restriction. Both groups consumed calorie restricted diet for 6 days each week and fasted for 24 h (~120 kcal intake from juice powder). Study lasted 10 wk, and body composition was measured by DXA	↓ in both groups[g] IFCR-L[f]: −3.9 ± 1.4 (−4.1 ± 1.5%) kg IFCR-F[f]: −2.5 ± 0.6 (−2.6 ± 0.4%) kg	↓ in both groups[g] IFCR-L[e]: −2.8 ± 1.2 kg IFCR-F[e]: −1.9 ± 0.7 kg	NC	↓ in both groups[f] IFCR-L: −19 ± 10% IFCR-F: − 8 ± 3%	↓ in IFCR-L (−17%)	↓ in both groups[f] IFCR-L: −20 ± 9% IFCR-F: −7 ± 4%	NC	NC	NC
Hussin et al. (2013)[27]	To examine the effects of FCR on depression and mood in aging Malaysian men	32 normal-weight and overweight M (FCR group, 60 ± 7; control group, 60 ± 6)	Subjects randomized into intervention (FCR) and control groups. Daily caloric intake in the FCR group was reduced by 300–500 kcal/d and subjects fasted for 2 nonconsecutive days per week. Control group maintained their regular eating pattern. Study lasted 12 wks, and body composition was measured by BIA	↓ in FCR[d] FCR: −3.8% (74.2 ± 7.8 kg to 71.4 ± 7.2 kg) CON: −0.9%	↓ in FCR[d] FCR: −5.7% (26.4 ± 2.4% to 24.9 ± 2.5%) CON: +1.1%	NR	NR	NR	NR	NR	NR	NR

(continued)

Table 3 **Continued**

Reference(s)	Purpose	Subjects (age in years)	Methodology	Weight and body composition (kg or percent change)			Cholesterol (mmol/L or percent change)				Blood pressure (mmHg)	
				Body weight	Body fat	Fat-free mass	Total cholesterol	Triglycerides	LDL	HDL	Systolic	Diastolic
Teng et al. (2013)[28]	To expand on the previous pilot study[24] and determine if FCR improves metabolic parameters and DNA damage in aging men	56 normal-weight and overweight M (control group, 59 ± 6; intervention group, 60 ± 5)	Subjects randomized into intervention (FCR) and control groups. Daily caloric intake in the FCR group was reduced by 300–500 kcal/d and subjects fasted for 2 nonconsecutive days per week. Control group maintained their regular eating pattern. Study lasted 12 wk, and body composition was measured by 8-polar BIA	↓ in FCR[d] 73.1 ± 7.1 to 70.6 ± 6.7 kg	↓ in FCR[d] 26.4 ± 3.1% to 25.1 ± 3.1%	NC	↓ in FCR[d] 5.95 ± 0.9 to 5.48 ± 0.9 mmol/L	NC	↓ in FCR[d] 4.0 ± 0.9 to 3.71 ± 0.8 mmol/L	NC	↓ in FCR[d] 142 ± 18 to 136 ± 15	↓ in FCR[d] 84 ± 10 to 82 ± 8

Abbreviations and symbols: BIA, bioelectrical impedance analysis; CER, continuous energy restriction; CHD, coronary heart disease; CON: control; CR, caloric restriction; DXA, dual-energy X-ray absorptiometry; F, females; FCR, fasting calorie restriction; HDL, high-density lipoprotein; IER, intermittent energy restriction; IFCR-F; intermittent fasting caloric restriction, food-based; IFCR-L, intermittent fasting caloric restriction, liquid-based; LDL, low-density lipoprotein; M, males; NC, no change; NR, not reported; SBT, standard behavioral therapy; VLCD, very-low calorie diet; ↓: decreased.

[a]Data reported as mean ± standard deviation unless otherwise noted.

[b]No between-group differences.

[c]Data reported as mean (95% confidence intervals).

[d]Group × time effect.

[e]Mean ± standard error of the mean.

[f]Larger change observed in IFCR-L group.

Time-restricted feeding

Time-restricted feeding protocols involve adhering to a daily routine that requires fasting for a certain number of hours and feeding for the remaining hours in a 24-hour period.[5] Only 1 time-restricted feeding study[21] that met the criteria for this review was located.

One popular time-restricted feeding program involves a 20-hour "undereating" phase followed by a 4-hour "overeating" phase during each 24-hour period.[29] Stote et al.[21] utilized a very similar eating pattern in normal-weight males. The study involved a randomized crossover design with two 8-week periods of eating either 1 meal per day or 3 meals per day, separated by an 11-week washout period. All food was provided to the subjects during the study. The subjects were allowed 4 hours in the evening to eat their single meal during the 1-meal-per-day phase of the study. After subjects consumed 1 meal per day, decreases were seen in their body weight (65.9 ± 3.2 kg vs 67.3 ± 3.2 kg after 3 meals/d) and fat mass (14.2 ± 1.0 kg vs 16.3 ± 1.0 kg after 3 meals/d). Interestingly, fat-free mass was higher after subjects consumed 1 meal per day (50.9 ± 0.4 kg) than after they consumed 3 meals per day (49.4 ± 0.4 kg), but the difference was not statistically significant ($P = 0.06$). If following this intermittent fasting protocol could lead to a concomitant decrease in fat mass and increase in fat-free mass, it would be a beneficial and appealing dietary strategy to many individuals. The results on cardiovascular markers in the 1-meal-per-day group were mixed. Higher concentrations of total cholesterol (217 ± 5 mg/dL in 1 meal/d vs 191 ± 5 mg/dL in 3 meals/d) and LDL (136 ± 4 mg/dL in 1 meal/d vs 113 ± 4 mg/dL in 3 meals/d) were observed, as were higher concentrations of HDL (62 ± 2 mg/dL in 1 meal/d vs 57 ± 2 mg/dL in 3 meals/d) and lower concentrations of triglycerides (93 ± 8 mg/dL in 1 meal/d vs 102 ± 8 mg/dL in 3 meals/d).[21]

Stote et al.[21] designed the study to examine the effects of the change in meal frequency without caloric restriction, but the subjects ate approximately 65 fewer kilocalories during the 1-meal-per-day phase of the study because of the extreme fullness they felt during the feeding window. It is possible that individuals would have eaten even less during the 1-meal-per-day phase of the study if they had been free to choose their level of caloric intake. There was also a 28.6% withdrawal rate from the study (with the typical withdrawal rates for studies at the facility being ≈ 4%–7%),[21] indicating that some individuals may not be able to adhere to this pattern of eating. However, only 1 of the 6 participants who withdrew reported that withdrawal was due to the imposed eating pattern (i.e., consuming all calories in 1 meal); the rest cited scheduling conflicts and health problems unrelated to the study. It is likely that individuals have differing abilities to consume large amounts of calories at one time, and this could affect the feasibility of following an intermittent fasting protocol that requires all calories to be consumed in a brief window of time.

While no studies have specifically examined the popular 16-hour fasting to 8-hour feeding pattern, it can be viewed as a more conservative time-restricted feeding protocol, since the feeding period is fairly long. The eating pattern is much more similar to a normal eating pattern than other intermittent fasting protocols. Many individuals even adhere to this eating pattern unintentionally, as it approximates to skipping breakfast and not eating after dinner each day.

The extremely limited number of time-restricted feeding studies that were included in this review makes it difficult to draw clear conclusions about the efficacy of time-restricted feeding or to compare time-restricted feeding with alternate-day fasting or whole-day fasting. However, one potentially important difference between time-restricted feeding and other fasting regimens is that time-restricted feeding does not allow for entire *ad libitum* days, but rather just a number of *ad libitum* hours each day. If the time-restricted feeding window is short enough, it is conceivable that an individual would not be able to eat enough calories to make up for the deficit achieved during the fasting hours. A recent review by Rothschild et al.[5] discusses animal and human studies of time-restricted feeding and includes studies that were excluded from the present review (i.e., trials that lasted a minimum of 2 weeks, and studies of religious fasting).

METABOLIC CHANGES DURING SHORT-TERM FASTING

Studies examining short-term fasting reveal important information about metabolic changes that may occur during the brief fasts used in intermittent fasting protocols. These metabolic changes may be the basis for the benefits seen in individuals who follow an intermittent fasting program. Studies on starvation have been conducted for over 100 years, and there is a substantial amount of research examining varying durations of food deprivation.[30–37] However, a major concern arises when fasting and starvation literature is applied to intermittent fasting protocols. The majority of short-term starvation studies examine periods of approximately 2 to 4 days of food abstinence. Although this is considered "short-term,"[38] intermittent fasting typically utilizes periods of fasting that are considerably shorter. The fasts in intermittent fasting range from slightly longer than an overnight fast (i.e., ≈16 h) to a maximum of 1.5 days, although most fasting periods do not exceed 24 hours of complete food abstinence. The durations of fasts used in intermittent fasting fall into the category of the postabsorptive state (or "early fasting state" – up to ≈12–18 h without food), although some fasts extend into the earlier stages of the fasting state, which is considered to be approximately 18 hours to 2 days without food.[39] The majority of experimental studies of food deprivation extend through the fasting state but often do not contain information about the time course of changes in health markers and metabolic processes during the first 24 hours of fasting.[33,34,40–46] An additional complication is that there are potentially different outcomes of a one-time short fast as opposed to habitual short-term fasts. Together, these factors may call into question the applicability of a large portion of the acute short-term fasting studies. Despite these challenges, the literature can still be cautiously examined to give a picture of metabolic changes that may occur during brief fasting. Two studies that tracked metabolic changes at multiple time points in the very early stages of fasting were also identified.[43,47]

Soeters et al.[38] recently published a thorough review of the interrelationships between lipid and glucose metabolism during short-term starvation, detailing how the occurrence of a large switch in substrate utilization decreases reliance on carbohydrate and increases reliance on fatty acids as a fuel source.[38] Short-term starvation studies have shown that blood glucose concentrations decline and whole-body lipolysis and fat oxidation significantly increase within the first 24 hours of food deprivation.[38,47,48] The increase in lipolysis is thought to occur because of reduced plasma insulin concentration, increased sympathetic nervous system activity, and a higher concentration of growth hormone in the blood.[38,49] Plasma fatty acid concentrations rise early in fasting and have been seen to increase within 14 hours after the last meal.[31,38]

Klein et al.[47] performed an informative study of the events of early fasting in normal-weight young adult men. They examined whole-body lipid and glucose metabolism in healthy men at 12, 18, 24, 30, 42, 54, and 72 hours of fasting. The time points of 12, 18, 24, and 30 hours are particularly applicable to the events that may occur during intermittent fasting protocols. Klein et al.[47] found that the rate of plasma glycerol appearance, reflecting whole-body lipolysis, and the increase in plasma glycerol concentration were greatest between 12 and 24 hours of fasting and accounted for 50% to 60% of the total glycerol increase during the 72-hour fast. The rate of glycerol appearance was significantly greater between 18 and 24 hours than it was between 12 and 18 hours or between 24 and 72 hours. The time interval between 18 and 24 hours also exhibited an approximately 50% increase in fat oxidation and an approximately 50% decrease in glucose oxidation,[47] which supports the shift in substrate utilization described by Soeters et al.[38] As mentioned, declines in plasma insulin may contribute to the increase in lipolysis seen in brief fasting due to the decrease in insulin's inhibition of lipolysis.[38,49] Klein et al.[47] found that plasma insulin decreased between 12 and 72 hours of fasting (64.6 ± 12.9 pmol/L to 30.1 ± 7.9 pmol/L), with 70% of this decline occurring during the first 24 hours. As insulin concentration falls during short-term fasting, plasma glucagon rises substantially.[33,34,50,51] Glucagon concentrations increased from 51.6 ± 7.8 pmol/L in the postabsorptive state to 93.4 pmol/L after 3 days of fasting, while epinephrine and cortisol concentrations did not change significantly.[33,43] Although epinephrine concentrations do not increase, the lipolytic response to epinephrine infusion is increased by 2 to 3 days of fasting.[35,44]

These results provide valuable information for evaluating intermittent fasting protocols. First, it appears that the relatively short fasts of 18 to 24 hours are beneficial in promoting the breakdown of stored triglycerides and fat oxidation. Increasing lipolysis may increase fatty acid mobilization and utilization within adipocytes and uptake and oxidation in other tissues, thus increasing energy expenditure and providing a potential target for the prevention and treatment of obesity.[52,53] Secondly, these results reveal potential benefits of fasts that extend to a full 24 hours, owing to the impressive increase in triglyceride breakdown and fat oxidation between 18 and 24 hours of fasting.[47]

Zauner et al.[43] also conducted a study of brief fasting in healthy lean male and female subjects. They found that resting energy expenditure increased significantly from 14 to 36 hours of starvation (3.97 ± 0.9 kJ/min to 4.37 ± 0.9 kJ/min), apparently owing to increased norepinephrine concentrations. Between those same time points, increases in plasma fatty acids and β-hydroxybutyrate as well as a decrease in respiratory quotient and plasma triglycerides were observed.[43] Together, these changes provide additional support for the transition to reliance on fat for energy during brief fasting.

One concern that arises during short-term fasting is that body protein may be lost. While it is known that humans adapt to prolonged starvation by conserving body protein,[31,54] increased proteolysis has been seen during short-term fasting.[33,34,40,55] Increased amino acid release from muscle was consistently seen in these studies, but the majority of these studies made comparisons between an overnight fast and a period ≥60 hours later.[33,34,40] Since the duration of fasts during popular intermittent fasting protocols are much shorter than 60 hours, it is possible that this would not be seen in studies examining shorter fasts. As discussed previously, there have been mixed results regarding the retention of fat-free mass during intermittent fasting. One fasting study showed that the appearance of urea nitrogen, reflecting muscle proteolysis, was not increased at 36 hours of fasting, but was increased at 60 hours.[43] In a recent study specifically examining intermittent fasting, Soeters et al.[56] found that short-term alternate-day fasting (alternating between 20 hours fasting and 28 hours feeding) did not alter whole-body protein metabolism in lean healthy men. Early fasting literature showed that protein catabolism did not begin to increase until the third day of fasting, and that the energy used by the body during the first 2 to 3 days of fasting was largely derived from glycogen breakdown and fat metabolism.[30]

While it appears that there is no change in 24-hour energy expenditure during reductions in meal frequency (down to 2 meals per day),[57–63] resting metabolic rate has been shown to increase during short-term starvation. However, the increases in resting metabolic rate were significant at 36 and 48 hours of fasting,[43,44] which is longer than most fasts used in intermittent fasting protocols.

DISCUSSION

From the available research, it appears that intermittent fasting programs are able to reduce body weight and body fat. Alternate-day fasting has been shown to reduce body weight (3%–7%), body fat (3–5.5 kg), total cholesterol (10%–21%), and triglycerides (14%–42%) in normal-weight, overweight, and obese humans. Reductions in LDL and blood pressure and increases in LDL particle size have also been seen in some, but not all, alternate-day fasting studies. Whole-day fasting has also been shown to reduce body weight (3%–9%), body fat, total cholesterol (5%–20%), and triglycerides (17%–50%). However, some studies indicate that neither alternate-day fasting nor whole-day fasting provides greater body composition improvements than isocaloric caloric restriction.[23,19,64] The extremely limited number of time-restricted feeding studies precludes definitive conclusions about this form of intermittent fasting.

As discussed, the variability of results in studies of alternate-day fasting and whole-day fasting could be attributable to a number of reasons, including differences in experimental design, subject characteristics, and participant adherence. As discussed elsewhere,[5] the failure to report energy intake and energy expenditure could also reasonably affect the outcomes of intermittent fasting studies.

On the basis of the findings discussed in this review, intermittent fasting appears to be a reasonable alternative to daily caloric restriction, which has been shown to have poor long-term results.[65,66] However, individuals following an intermittent fasting program will likely experience different degrees of energy restriction, depending on their individual implementation of the program. There are health risks of diets that restrict energy too severely, such as semistarvation and very low-calorie diets. Periods of semistarvation can lead to hyperphagic responses and increases in fat mass beyond initial levels.[67,68] Safety concerns associated with very low-calorie diets (<800 kcal/d) include increased risk of nutrient deficiencies and electrolyte abnormalities,[69] and diets implemented without medical supervision can lead to even more severe risks.[70] Very-low calorie diets do not produce greater long-term weight loss than diets with less-severe restriction.[69] Additionally, a reduction in energy intake can trigger a variety of biological adaptations that can promote weight regain after weight loss,[71] and most individuals do not maintain weight loss after dieting.[69,72] There are well-known risks associated with deficient intakes of protein[73,74] and other nutrients.[75] Very-low calorie diets could potentially lead to suboptimal protein intake and subsequent protein deficiency, depending on the macronutrient composition of the diet. Therefore, it is recommended that individuals implementing intermittent fasting utilize appropriate supervision and do not employ severe energy restriction each day.

Very little information about the optimal duration of intermittent fasting programs is available. Some authors have reported that intermittent fasting can extend lifespan and promote resistance to age-related diseases.[76,77] These potential health benefits, along with others described in this review, may be support for using intermittent fasting as a lifestyle, rather than a short-term diet plan. However, it may not be advisable to continue practicing forms of intermittent fasting that impose energy restriction sufficient to elicit weight loss after sufficient weight loss has been achieved. Intermittent fasting programs can be modified to be part of a long-term weight-maintenance program (e.g., the feeding window or *ad libitum* days could be increased until sufficient calories are consumed to allow for weight maintenance rather than weight loss).

Future research should seek to differentiate between caloric deficits induced by intermittent fasting programs and specific health benefits of fasting. The optimal programs for effectiveness and user compliance should also be identified. Both the short-term and long-term metabolic changes that occur during different intermittent fasting protocols should be detailed, with special attention given to substrate utilization and markers of disease risk. The nutritional profile of foods consumed during *ad libitum* feeding periods and modified fasting periods should be investigated because different nutrients have different effects on satiety and other health-related factors (e.g., the ability of dietary protein to promote fat-free mass retention during weight loss[78]). Additionally, interactions between intermittent fasting and physical activity should be examined, as it is thought that disease risk and body composition are best modified by a combined dietary and physical activity regimen.[79–82] Only one study that examined the combination of an intermittent fasting protocol and exercise program was identified through the literature search,[16] and endurance exercise on stationary bikes and elliptical machines was the only form used. Resistance training may be of particular importance because it may be able to better combat the losses in fat-free mass that were seen in some experiments.[6,9,16,23,24]

There are several limitations of this review and the current body of evidence on intermittent fasting. The relatively small amount of available research, particularly in the case of time-restricted feeding, the lack of control of macronutrient intake, and the few comparisons of differing nutrient intakes (both during *ad libitum* eating and during fasting periods) are limitations of the available studies. Additionally, unless multiple experiments were conducted by a single laboratory, there is considerable variation in the experimental protocols used, even within a particular category of fasting. Some limitations of this review are the exclusion of religious fasting studies, animal studies, and publications that were not in English. The broad inclusion criteria for research studies represent another potential limitation. A wide variety of subjects and experimental designs were used in the included studies, which hinders the direct comparison of different intermittent fasting programs presented in this review.

CONCLUSION

On the basis of the information presented in this review, it is recommended that intermittent fasting be considered as an alternative to daily caloric restriction for individuals who are interested in improving body composition and overall health. It is important, however, to consider the current limitations of intermittent fasting research and the unequal amount of information available on each style of intermittent fasting. Additionally, medical supervision is always recommended for individuals who participate in a weight-loss program. There are numerous opportunities for continued research in the area of intermittent fasting, and future studies should help fill many of the gaps in the current knowledge, particularly regarding optimal intermittent fasting regimens.

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