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Bioscience Research

Print ISSN: 1811-9506 Online ISSN: 2218-3973

Journal by Innovative Scientific Information & Services Network

REVIEW ARTICLE BIOSCIENCE RESEARCH, 2021 18(4): **OPEN ACCESS**

The Effect of Intermittent Fasting Regimens on Metabolic Syndrome: A Literature Review

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Metabolic syndrome (MetS) is a growing problem worldwide. Gulf countries, being part of the Middle East, have shown a high prevalence of metabolic syndrome. MetS typically reflect the clustering of individual cardiometabolic risk factors including central obesity, elevated fasting plasma glucose, dyslipidemia, and elevated blood pressure. Intermittent fasting (IF) has gained prominence as a promising approach for weight loss and mitigation of metabolic syndrome. This review investigates the effect of current evidence of intermittent fasting on metabolic syndrome. Three databases were used to identify studies between 2010 and 2021 using relevant selected keywords to explore the evidence of intermittent fasting's impact on metabolic syndrome. The article selection was made based on the inclusion and exclusion criteria concerning the participants' characteristics, study design, intervention protocols, and targeted dependent variables. We assessed 834 studies for eligibility and Twenty-one articles were identified and reviewed in our narrative synthesis. Overall, the available evidence suggests that IF is considered effective for losing weight, normalizing blood glucose, reducing lipids, and lowering blood pressure, particularly among obese subjects. Studies are urgently needed especially, randomized controlled trials with a long-term follow-up period of the abovementioned four variables.

Keywords: intermittent fasting; metabolic syndrome; hyperglycemia; abdominal obesity; dyslipidemia; blood pressure

Reference	Country	Study design/ duration/ sample	Objective/s of the study	Methods/Interventions	Main Outcomes
Arnason et al., (2017)	Canada	Design: Pilot study Duration: 6 weeks Sample: N=10 individuals with T2DM	To examine the short-term metabolic impact and therapeutic tolerability of intermittent fasting (IF) in adults with diabetes (T2DM).	Fasting for a period of 18-20 hr per day, with ad libitum zero-calorie coffee, tea, and water intake during fasting hours being permitted.	Short-term regular intermittent fasting (IF) can be a healthy and tolerable dietary strategy in T2DM patients, improving key outcomes such as body weight, fasting glucose, and postprandial variability.
Hutchison, Liu, et al., (2019)	Australia	Design: Randomized crossover trial Duration: one week Sample:N= 15 men at risk of T2DM	To evaluate the effectiveness of 9-hour restricted feeding or delayed TRF/d on glucose resistance in men at risk of T2DM.	-TRFe (eating window between 8 am and 5 pm) -TRFd (eating window between 12 pm and 9 pm) for 7 days, separated by a 2-week washout period.	Findings suggest that 1 week of TRF increases glucose responses to a meal in men at risk of type 2 diabetes, regardless of when TRF is launched.
Gabel et al., (2019)	United States	Design: Secondary analysis Duration:12months Sample: N=43 participants with insulin resistance.	To investigate the impact of ADF in subjects with insulin resistance, overweight or obesity on body weight and glucoregulatory factors.	-ADF consumed 25% of baseline energy needs as lunch on fast days and 125% of baseline energy needs on alternating feast days -CR consumed 75% of baseline energy needs over three meals every day	While comparable reductions in body weight have been observed, findings demonstrate that ADP in insulin-resistant participants can lead to greater reductions in fasting insulin and insulin resistance than CR.
Furmli et al., (2018)	Canada	Design: A case report Duration: Several months Sample: N=3 adults diagnosed with T2DM	To demonstrate the effect of therapeutic fasting in reversing insulin resistance and enabling patients to discontinue insulin therapy while maintaining blood sugar control.	-Patients followed alternating 24hr-fast 3d/wk	All three clients could postpone their insulin, with a general decrease in haemoglobin A1C (HbA1C) levels for all patients through fasting.
S. Carter et al., (2019)	Australia	Design: RCT Duration:12months Sample: N=137 adults with T2DM	To investigate the effect of intermittent or continuous energy restriction on glycemic management in subjects with type 2 diabetes mellitus.	-2DW 500-600 kcal/d for 2 non-consecutive days each week, and 5 days of habitual eating -CER diet of 1200-1500 kcal/d	In both the continuous and intermittent groups, the intention-to-treat analysis revealed an improvement in mean HbA1c levels at 24 months.
Corley et al., (2018)	New Zealand	Design: RCT Duration:12 weeks Sample: N=41 participants with T2DM	To verify the claim that non-consecutive days of caloric restriction along with prescription modification will decrease the overall risk of hypoglycemia in individuals with Type 2 diabetes on hypoglycemic medication and a 5:2 intermittent fasting diet	- Consecutive fast 2d/w - Non-consecutive fast 2d/wk	In people with Type 2 diabetes who adopted a 5:2 diet, intermittent fasting was attributed to a twofold rise in hypoglycemia on fasting days
Catenacci et al., (2016)	United States	Design: RCT Duration: 8 weeks Sample: N=26 Adults with obesity	To determine the safety and tolerability of alternate day fasting (ADF) and compare weight, body composition, lipids, and insulin sensitivity index (Si) improvements with those created by a normal weight loss diet, moderate daily caloric restriction (CR)	- ADF 100% energy restriction on a fasting day, ad libitum on fed days. Meals provided - CER almost 400 kcal/day deficit per day. Meals provided	ADF caused considerable enhancements in weight, body composition, lipids, and insulin sensitivity index (Si) after 8 weeks
Trepanowski et al., (2017)	United States	Design: RCT Duration: 12 weeks Sample: N=100 participants	To compare the effects of alternate-day fasting vs. daily calorie restriction on weight loss, weight maintenance, and risk factors for CVA disease.	- ADF 25% of baseline EI as lunch on fast days, 125% of baseline EI split between meals on fed days. Meals provided in the first 3 months - CER 75% of baseline EI split between three meals daily. Meals provided in the first 3 months - Control group; maintain baseline weight	Total weight loss was –6.0% (95% CI, –8.5% to –3.6%) for the alternate-day fasting group and –5.3% (95% CI, –7.6% to –3.0%) for the daily calorie restriction group, relative to controls, with no substantial variance between the intervention groups.
		Design: RCT	To investigate the effect of intermittent	-400/600 kcal (female/male) energy	After one year, weight loss was

Sundfør et al., (2018)	Norway	Duration: 12 weeks Sample: N=112 adults	energy restriction versus continuous energy restriction on losing weight, maintenance, and cardiometabolic risk factors in men and women with abdominal obesity and at least one other feature of metabolic syndrome	restriction on two non-consecutive fasting days; ad libitum energy intake on the remaining 5 days. -CER daily restriction of energy to match IER groups. Both groups reduced energy intake by 26%-28%.	comparable between the intermittent and continuous energy restriction groups (8.0 kg [SD 6.5] versus 9.0 kg [SD 7.1]; p =0.6)
Schübel et al., (2018)	Germany	Design: RCT Duration: 12 weeks Sample: N=150 overweight or obese	To examine if ICR, introduced as the "5:2 diet," has a greater influence on the expression of adiposis tissue, anthropometric and body composition indicators, and circulating metabolic biomarkers than CCR and a control regimen	-2 non-consecutive days with 75% energy restriction and 5 days with no restriction -Continuous energy restriction at 80% -No energy restriction (control)	The greatest loge relative changes in weight (mean±SEM) of −7.1% ± 0.7% was detected in the ICR group, followed by the CCR group (−5.2% ± 0.6%) and the Control group (−3.3% ± 0.6%) (*P* overall < 0.001, *P* ICR vs. CCR = 0.053).
Domaszewski et al., (2020)	Poland	Design: RCT Duration: 6 weeks Sample: N=45 non-smoking women	To evaluate the effectiveness of intermittent fasting (IF) in reducing body fat and lowering BMI.	-TRF abstinence from food intake for 16 h per day -Control subjects were permitted to eat ad libitum daily	Time-restricted feeding leads to a 2 kg reduction in body weight as well as other parameters linked to body fat mass after six weeks.
Bhutani, Klempel, Kroeger, Trepanowski, & Varady, (2013)	United States	Design: RCT Duration: 12 weeks Sample: N=64 Obese subjects	To evaluate whether the application of alternate day fasting (ADF) and exercise resulted in greater enhancements in body composition and plasma lipid levels than any intervention alone	-ADF consumed 25% of baseline on a fasting day, ad libitum on fed days+ Exercise 3d/week -ADF only - Exercise 3d/week - No Diet+ No Exercise	Over a 12-week duration, the application of ADF and resistance exercise resulted in greater body composition and lipid-altering effects than any intervention alone.
Krista A. Varady et al., (2013)	United States	Design: RCT Duration: 12 weeks Sample: N=32 subjects	To assess the impact of ADF on weight and heart disease among non-obese subjects.	-ADF consumed 25% of baseline on a fasting day, ad libitum on fed days. -Control subjects were permitted to eat ad libitum daily	By week 12, the ADF group had lost weight. The control group lost less weight. Fat mass reduction. There was no improvement in fat-free mass. Adiponectin levels increase as leptin levels decline.
Cai et al., (2019)	China	Design: RCT Duration: 12 weeks Sample: N=271 NAFLD patients	To investigate the effectiveness of ADF and TRF compared to placebo on weight and lipid profile in individuals with NAFLD.	-ADF consumed 25% of baseline on a fasting day, ad libitum on fed days. -TRF subjects with an 8-h open window and 16 hrs of fasting from energetic foods and beverages. -Control group consumed 80% of their energy needs every day.	Findings demonstrated a reduction in body weight in the ADF group by week 4. A more significant decrease by week12. Fat mass as well reduced in the ADF and TRF groups. Cholesterol was also reduced in both groups.
Ahmed et al., (2021)	Pakistan	Design: quasi-experimental trial Duration: 6 weeks Sample: N=40 participants with low HDL	To examine the efficacy of IF on lipid profile and HDL cholesterol in a group of South Asian adults.	-Fasting ~12 h 3d/week -Usual dietary pattern	The findings indicate that intermittent fasting boosts cardiovascular health by improving the lipid profile and increasing suboptimal HDL levels.
Maroofi & Nasrollahzadeh, (2020)	Iran	Design: Randomized, parallel-armed trial Duration: 8 weeks Sample: N=88 subjects with overweight or obesity and mild to moderate HTG	To evaluate the impact of CCR and ICR on weight loss and cardiometabolic markers in individuals with overweight and obesity and mild to moderate HTG.	-ICR group consumed 30% of the daily calories' requirement 3d/week and 100% of the daily calorie's requirement on the other days -CCR group consumed 70% of the estimated total energy expenditure	The findings specify that three days a week of ICR is comparable to a CCR diet for reducing triglycerides in subjects with HTG and that it tends to be more effective than continuous dieting in increasing insulin tolerance in the short term.
Conley et al., (2018)	Australia	Design: Parallel randomized-controlled trial Duration: 6 weeks Sample: N= 24 male war veterans	To ascertain whether the 5:2 diet would produce ≥5% weight loss and superior enhancements in weight and biochemical markers than a standard energy-restricted diet (SERD) in obese male war veterans.	-2DW restrict calorie intake to ~2500 kJ on two non-consecutive days per week: ad libitum intake on the remaining five days -SERD daily ~2100 kJ energy-restricted diet from the average requirement	When opposed to a SERD, the 5:2 diet seems to be a promising but not superior weight loss approach in male war veterans.

De Toledo et al., (2019)	Germany	Design: Observational study Duration: one-year Sample: N=1422 subjects	To test the effectiveness, therapeutic efficacy, and effects on the well-being of Buchinger periodic fasting in a large cohort for the first time in a prospective study.	Fasting periods of between 4 and 21 days. The participants fasted according to the Buchinger guidelines with a daily caloric intake of 200–250 kcal accompanied by a moderate-intensity lifestyle program.	Buchinger periodic fasting lasting 4 to 21 days was revealed to be healthy and well-tolerated for the first time in the study. It boosted emotional and physical well-being, as well as cardiovascular and general risk factors and subjective health complaints.
Sutton et al., (2018)	United States	Design: Randomized, crossover trial Duration: 5 weeks Sample: N=8 men with prediabetes	To assess whether eTRF will boost cardiometabolic fitness. To determine whether there are any benefits to IF that is not linked to weight loss or food intake.	- eTRF schedule ($6-hr eating period with 18 hr of daily fasting - Control schedule ($12-hr eating window with 12 hr of daily fasting)	The findings of 5 weeks of eTRF boosted insulin levels, insulin sensitivity, b cell tolerance, blood pressure, and oxidative stress levels in men with prediabetes—although food intake was matched to the control arm and no weight loss results.
Wilkinson et al., (2020)	United States	Design: Pilot study Duration: 12 weeks Sample: N=19 participants with metabolic syndrome	To evaluate whether TRE for 12 weeks increases health indicators in subjects with metabolic syndrome who are seeking routine medical treatment (including cholesterol and blood pressure medications).	- 14-h nightly fast and 10-h window	Findings verified that TRE intervention promotes cardiometabolic health in patients with metabolic syndrome who are seeking conventional medical treatment, including elevated rates of statins and antihypertensive use.
Erdem et al., (2018)	Turkey	Design: Prospective cohort study Duration: NA Sample: N=60 individuals	To evaluate the implication of intermittent fasting on BPV, central BP, and urinary sodium excretion in prehypertensive and/or newly diagnosed hypertensive patients	- Subjects had fasted for at least 1 week	The results reveal that intermittent fasting reduces office and ABPM BP values significantly but has little impact on central BP or home measurements.

Table 1: Literature, terms, and hits