

Intermittent fasting and weight loss

Systematic review

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Abstract

Objective To examine the evidence for intermittent fasting (IF), an alternative to calorie-restricted diets, in treating obesity, an important health concern in Canada with few effective office-based treatment strategies.

Data sources A MEDLINE and EMBASE search from January 1, 2000, to July 1, 2019, yielded 1200 results using the key words *fasting, time restricted feeding, meal skipping, alternate day fasting, intermittent fasting, and reduced meal frequency*.

Study selection Forty-one articles describing 27 trials addressed weight loss in overweight and obese patients: 18 small randomized controlled trials (level I evidence) and 9 trials comparing weight after IF to baseline weight with no control group (level II evidence). Studies were often of short duration (2 to 26 weeks) with low enrolment (10 to 244 participants); 2 were of 1-year duration. Protocols varied, with only 5 studies including patients with type 2 diabetes.

Synthesis All 27 IF trials found weight loss of 0.8% to 13.0% of baseline weight with no serious adverse events. Twelve studies comparing IF to calorie restriction found equivalent results. The 5 studies that included patients with type 2 diabetes documented improved glycemic control.

Conclusion Intermittent fasting shows promise for the treatment of obesity. To date, the studies have been small and of short duration. Longer-term research is needed to understand the sustainable role IF can play in weight loss.

Editor's key points

- ▶ In all 27 trials examined, intermittent fasting (IF) resulted in weight loss, ranging from 0.8% to 13.0% of baseline body weight. Weight loss occurred regardless of changes in overall caloric intake. In the studies of 2 to 12 weeks' duration, body mass index decreased, on average, by 4.3% to a median of 33.2 kg/m². Symptoms such as hunger remained stable or decreased, and no adverse events were reported.
- ▶ While IF is a moderately successful strategy for weight loss, it shows promise for improving glycemic control, although it does pose a potential risk of hypoglycemia.
- ▶ The heterogeneity in the current evidence limits comparison of IF to other weight-loss strategies. Intermittent fasting shows promise as a primary care intervention for obesity, but little is known about long-term sustainability and health effects. Longer-duration studies are needed to understand how IF might contribute to effective weight-loss strategies.

Points de repère du rédacteur

► Dans l'ensemble des 27 études examinées, le jeûne intermittent (JI) s'est traduit par une perte pondérale allant de 0,8 à 13,0 % du poids corporel au départ. La perte pondérale s'est produite quels que soient les changements dans l'apport calorique global. Dans les études d'une durée de 2 à 12 semaines, l'indice de masse corporelle a connu une baisse, en moyenne, de 4,3 % à une réduction médiane de 33,2 kg/m². Les symptômes, comme la faim, sont demeurés stables ou ont diminué, et aucun événement indésirable n'a été rapporté.

► Si le JI est une stratégie qui connaît un succès modéré en ce qui concerne la perte pondérale, elle se révèle prometteuse pour améliorer le contrôle glycémique, quoiqu'elle comporte un risque potentiel d'hypoglycémie.

► L'hétérogénéité des données probantes actuelles limite les possibilités de comparer le JI à d'autres stratégies de perte de poids. Le jeûne intermittent est prometteur en tant qu'intervention en soins primaires pour l'obésité, mais sa durabilité et ses effets sur la santé à long terme sont peu connus. Des études plus prolongées sont nécessaires pour comprendre comment le JI pourrait contribuer à l'efficacité des stratégies de perte pondérale.

Jeûne intermittent et perte de poids

Revue systématique

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Résumé

Objectif Examiner les données probantes concernant le jeûne intermittent (JI) comme solution de rechange aux régimes faibles en calories dans le traitement de l'obésité, une importante préoccupation en matière de santé au Canada, compte tenu de la rareté des stratégies thérapeutiques efficaces applicables en clinique.

Sources des données Une recherche documentaire effectuée dans MEDLINE et EMBASE, du 1^{er} janvier 2000 au 1^{er} juillet 2019, a produit 1200 résultats à l'aide des expressions clés suivantes: *fasting, time restricted feeding, meal skipping, alternate day fasting, intermittent fasting* et *reduced meal frequency*.

Sélection des études Quelque 41 articles décrivant 27 études portaient sur la perte de poids chez les patients en surpoids et obèses: 18 petites études randomisées contrôlées (données probantes de niveau I) et 9 études comparant le poids après un JI avec le poids au point de départ et sans groupe témoin (données probantes de niveau II). Les études étaient souvent de courte durée (de 2 à 26 semaines), et la participation était peu nombreuse (de 10 à 244 sujets); 2 études ont duré 1 an. Les protocoles variaient, et seulement 5 études incluaient des patients atteints de diabète de type 2.

Synthèse Dans les 27 études sur le JI, une perte pondérale variant de 0,8 à 13 % s'est produite sans événements indésirables sérieux. Douze études comparant le JI et la restriction de calories ont fait valoir des résultats équivalents. Les 5 études qui comptaient des patients atteints de diabète de type 2 ont documenté un meilleur contrôle glycémique.

Conclusion Le jeûne intermittent semble prometteur pour le traitement de l'obésité. Jusqu'à présent, les études comptaient peu de sujets et étaient de courte durée. Des recherches à plus long terme sont nécessaires pour comprendre le rôle durable que peut jouer le JI dans la perte pondérale.

In 2018, 63.1% of Canadian adults were overweight or obese.¹ Obesity is a risk factor for cardiovascular disease and type 2 diabetes.^{2,3} As obesity rates climb, there is increasing focus on dietary interventions, the most common being calorie-restricted diets, which achieve initial but often unsustainable weight loss.⁴ There is recent interest in the use of fasting for the treatment of obesity⁵⁻⁷ and diabetes.^{8,9} *Intermittent fasting* (IF) refers to regular periods with no or very limited caloric intake. It commonly consists of a daily fast for 16 hours, a 24-hour fast on alternate days, or a fast 2 days per week on non-consecutive days.⁸ During fasting, caloric consumption often ranges from zero to 25% of caloric needs. Consumption on nonfasting days might be ad libitum, restricted to a certain diet composition, or aimed to reach a specific caloric intake of up to 125% of regular caloric needs.⁹ Various terms are used to describe regular intermittent calorie abstinence, including *intermittent fasting*, *alternate-day fasting*, *reduced meal frequency*, and *time-restricted feeding*. Intermittent fasting can be used with unrestricted consumption when not fasting or in conjunction with other dietary interventions. This review provides the most recent evidence on IF's effects on weight loss and the potential role it plays in primary care treatment of obesity.

— Data sources —

An EMBASE and MEDLINE search of articles from January 1, 2000, to July 1, 2019, returned 1200 unique results using the key words *alternate day fasting*, *intermittent fasting*, *fasting*, *time restricted feeding*, *meal skipping*, and *reduced meal frequency*. We included English-language studies that focused on weight loss for overweight and obese participants (body mass index [BMI] of ≥ 25 kg/m²) and excluded studies of very short duration (<2 weeks), studies of those requiring inpatient treatment, or studies focused on stroke, seizures, or other specific medical conditions. Following these exclusions 41 articles remained, describing 27 unique experiments: 18 small randomized controlled trials (level I evidence) and 9 trials comparing weight after IF to baseline weight with no control group (level II evidence) (Table 1).¹⁰⁻⁵⁰ Levels of evidence are classified according to the Canadian Task Force on Preventive Health Care.

— Synthesis —

Study design

Study interventions incorporated IF in a variety of ways, from a 24-hour fast several days per week (eg, the “5 and 2” protocol)^{11,16,17,21,27,28,35,41,42,50} to a daily 16-hour fast.^{10,12,25,34} The most common study design was to alternate 24-hour periods of fasting with unrestricted consumption (alternating fast and feast days).^{13,15,19,20,22-24,29,33,38,43,47,49} Study protocols also varied in their recommendations on caloric intake, enrolment of patients with diabetes,

presence of a control group, and study duration. Some studies restricted calories while others allowed ad libitum consumption when not fasting. The rigour of fasting also varied, with several studies allowing 25% of regular caloric consumption during fasting periods. Comparator groups to IF diets followed a usual diet^{13,20,25,43,49} or calorie-restricted diet.^{11,15-17,19,22,27,28,33,41-43}

While patients with diabetes were commonly excluded (Table 2),^{10,11,13,15,19-25,27-29,32,33,35,37,38,40-43,47,49,50} 5 studies enrolled only those with type 2 diabetes (n=174 patients) (Table 3).^{12,16,17,21,34} In both diabetic and non-diabetic populations, cardiovascular risk factors were reduced. When diet composition was controlled, most protocols were consistent with Health Canada and American Heart Association guidelines at the time: 55% carbohydrates, 20% fat, and 25% protein.^{51,52} The most common alternative was unrestricted consumption. An enrichment of protein was considered in 5 studies at the expense of carbohydrate intake.^{12,15,16,28,50} Two followed a Mediterranean-type diet.^{27,42} Fat consumption was examined in 1 study, which compared dietary fat intake of 45% versus 25%, at the expense of carbohydrate intake.³⁷ Sixteen studies included dietary education, with participants choosing their own meals, while 11 supplied all or part of the diet.^{1,13,19,23,29,33,34,37,43,47,49} Others did not require a specific dietary composition outside of the fasting period.

Studies were of limited size and duration: 18 of 27 trials analyzed fewer than 60 participants and were 12 weeks or fewer in duration. The longest studies lasted 1 year and had 137 to 244 participants.^{17,28} Several studies had follow-up periods after the intervention ranging from 2 weeks to 1 year.^{12,15,18,19,41-43,50}

Weight loss

In all 27 trials (n=944 IF participants), IF resulted in weight loss, ranging from 0.8% to 13.0% of baseline body weight (Table 1).¹⁰⁻⁵⁰ Weight loss occurred regardless of changes in overall caloric intake.^{43,53} In the 16 studies of 2 to 12 weeks' duration that measured BMI, BMI decreased, on average, by 4.3% to a median of 33.2 kg/m².^{10,12,13,19-21,23-25,29,34,35,37,47,50} Waist circumference decreased by 3 cm to 8 cm in studies longer than 4 weeks that recorded it.^{13,21,23,24,27,33-35,37,41,42,47}

Twelve studies used calorie-restricted diets as a comparator to IF and found equivalent weight loss in both groups.^{11,15-17,19,22,27,28,33,41-43} Study duration was 8 weeks to 1 year, with a combined total of 1206 participants (527 undergoing IF, 572 using calorie restriction, and 107 control participants) and demonstrated weight loss of 4.6% to 13.0%.^{11,15-17,19,22,27,28,33,41-43} Adherence appears similar for both weight loss strategies.^{15,17,27,28} The largest study comparing IF with calorie restriction was by Headland et al in 2019 of 244 obese adults who achieved a mean 4.97-kg weight loss over 52 weeks versus a mean weight loss of 6.65 kg with calorie-restricted diets ($P=.24$).²⁸

Table 1. Summary of IF studies: Total IF participants = 944.

STUDY, Y	N	POPULATION*	LEVEL OF EVIDENCE	DURATION	WEIGHT LOSS, % OF BASELINE WEIGHT	INTERVENTION*	KEY RESULT
Anton et al, ¹⁰ 2019	10	Obese, >65 y	II	4 wk	2.2	16-h daily fast; self-reported	IF is feasible in older adults and leads to weight loss
Antoni et al, ¹¹ 2018	41	Overweight and obese	I	Until 5% weight loss is reached	5.3	2-d fast (25% of caloric needs) and 5-d ad libitum calorie intake vs CR; self-reported	59 d to achieve 5% weight loss with IF; not statistically different in CR group (73 d)
Arnason et al, ¹² 2017	10	Obese, T2D	II	2 wk	1.4	18- to 20-h daily fast as a goal, but average fast was 16.8 h; 2-wk follow-up; self-reported	Short-term IF might be safe in patients with T2D and might improve glycemic control
Bhutani et al, ¹³ 2013 Bhutani et al, ¹⁴ 2013	64	Obese	I	12 wk	3.2	Alternated 25% of caloric needs with ad libitum calorie intake vs usual diet with or without exercise; self-reported	IF in combination with exercise is more effective than either method alone
Bowen et al, ¹⁵ 2018	136	Overweight and obese	I	16 wk	10.6	3-d fast, 3-d CR, and 1-d ad libitum intake vs CR; 8-wk maintenance; self-reported	CR combined with IF does not improve on weight loss of CR alone
Carter et al, ¹⁶ 2016	51	Obese, T2D	I	12 wk	5.9	2-d fast (1670 to 2500 kJ/d) and 5-d usual diet vs CR; self-reported	IF is a viable alternative to CR for weight loss and glycemic control in T2D
Carter et al, ¹⁷ 2018 Carter et al, ¹⁸ 2019	137	Obese, T2D	I	52 wk	6.8	2-d fast (25% of usual calorie intake) and 5-d usual diet vs CR; 1-y follow-up; self-reported	Similar decrease in HbA _{1c} level and weight with IF or CR; weight is stable and HbA _{1c} level climbs in follow-up
Catenacci et al, ¹⁹ 2016	26	Obese	I	8 wk	8.7	Alternated 0% usual calorie intake with ad libitum intake vs CR; 24-wk follow-up; monitored	IF is a safe weight-loss strategy; no increase in risk of weight regain
Cho et al, ²⁰ 2019	31	Overweight and obese	I	8 wk	5.0	Alternated 25% usual calorie intake with ad libitum intake vs usual diet with or without exercise; self-reported	Exercise does not improve weight loss for IF alone
Corley et al, ²¹ 2018	41	Obese, T2D	II	12 wk	0.8	2-d fast (2 small snacks, 1 light meal) and 5-d ad libitum intake; self-reported	IF safe in T2D; promotes weight loss and glycemic control
Coutinho et al, ²² 2018	35	Obese	I	12 wk	13.0	3-d fast (25% of caloric needs) and 4-d full caloric needs vs CR; self-reported	Similar weight losses result from IF and CR
Eshghinia and Gapparov, ²³ 2011	26	Obese women	II	4 wk	4.9	3-d fast (25% to 40% of usual caloric intake) and 4-d CR (10% decrease in usual caloric intake) per wk; self-reported	Short-term IF with CR is a viable weight-loss strategy in obesity

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STUDY, Y	N	POPULATION*	LEVEL OF EVIDENCE	DURATION	WEIGHT LOSS, % OF BASELINE WEIGHT	INTERVENTION†	KEY RESULT
Eshghinia and Mohammadzadeh, ²⁴ 2013	15	Obese women	II	6 wk	7.1	3-d fast (25% to 30% of caloric needs), 3-d usual diet, and 1-d ad libitum intake; self-reported	Short-term IF is a viable weight loss strategy in obesity
Gabel et al, ²⁵ 2018 Gabel et al, ²⁶ 2019	46	Obese	I	12 wk	3.2	16-h fast daily vs usual-diet historical controls; self-reported	IF leads to weight loss compared with baseline and control group
Harvie et al, ²⁷ 2011	107	Obese women	I	24 wk	7.9	2-d fast (very low-calorie intake) and 5-d usual diet vs CR; self-reported	IF is as effective as CR for weight loss and insulin sensitivity
Headland et al, ²⁸ 2019	244	Obese	I	52 wk	5.6	2-d fast (25% of usual calorie intake) and 5-d usual diet vs CR; self-reported	IF and CR have similar weight loss results at 1 y
Hoddy et al, ²⁹ 2014 Hoddy et al, ³⁰ 2015 Hoddy et al, ³¹ 2016 Hoddy et al, ³² 2016	59	Obese	I	8 wk	4.2	Alternated daily 25% of baseline caloric needs with ad libitum caloric intake; self-reported	IF is a safe weight-loss strategy; no increased risk of disordered eating; might decrease insulin resistance
Hutchison et al, ³³ 2019	88	Overweight and obese women	I	8 wk	4.6	3-d fast (32%-37% of energy requirements) and 4 d at 100% or 145% of energy requirements vs CR and control group; self-reported	Combining CR and IF is more effective for weight loss than either alone
Kahleova et al, ³⁴ 2014	54	Obese, T2D	I	12 wk	3.9	16-h daily fast vs CR; self-reported	IF is more effective than CR for weight loss and glycemic control in T2D
Klempel et al, ³⁵ 2012 Kroeger et al, ³⁶ 2012	54	Obese women	II	8 wk	3.4	1-d fast (very low-calorie intake) and 6-d CR; self-reported	IF combined with CR promotes weight loss in obese women
Klempel et al, ³⁷ 2013 Klempel et al, ³⁸ 2013 Klempel et al, ³⁹ 2013 Varady et al, ⁴⁰ 2015	32	Obese women	II	8 wk	4.5	Alternated 25% of usual calorie intake with 125% of usual calorie intake; high-fat vs low-fat diet; self-reported	IF is effective for weight loss with a high-fat or low-fat diet composition
Schübel et al, ⁴¹ 2018	150	Obese	I	12 wk	6.4	2-d fast (25% of calorie requirements) and 5-d usual diet vs CR and control group; 12-wk maintenance; 26-wk follow-up; self-reported	Weight loss and maintenance is similar in IF and CR
Sundfjør et al, ⁴² 2018	112	Obese	I	26 wk	8.4	2-d fast (20% of calorie requirements) and 5-d usual diet vs CR; 26-wk maintenance; self-reported	Weight loss and maintenance are similar in IF and CR

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STUDY, Y	N	POPULATION*	LEVEL OF EVIDENCE	DURATION	WEIGHT LOSS, % OF BASELINE WEIGHT	INTERVENTION†	KEY RESULT
Trepanowski et al, ⁴³ 2017 Trepanowski et al, ⁴⁴ 2018 Kroeger et al, ⁴⁵ 2018 Kalam et al, ⁴⁶ 2019	79	Obese	I	24 wk	6.0	Alternated 25% of usual calorie intake with 125% of usual calorie intake vs CR and control group; 24-wk follow-up; self-reported	IF promotes weight loss and weight maintenance similar to CR
Varady et al, ⁴⁷ 2009 Bhutani et al, ⁴⁸ 2010	16	Obese	II	8 wk	5.8	Alternated 25% of energy needs with ad libitum caloric intake; self-reported	IF is a viable option for weight loss in obese individuals
Varady et al, ⁴⁹ 2013	30	Obese	I	12 wk	6.5	Alternated 25% of baseline energy needs with ad libitum caloric intake vs usual diet; monitored	IF is effective for weight loss in obese individuals
Zuo et al, ⁵⁰ 2016	40	Obese	II	12 wk	10.0	1-d fast (430 kcal) and 6-d high-protein diet; 52-wk follow-up; monitored	IF with a high-protein diet is effective for weight loss, with low risk of weight regain

CR—calorie restriction, HbA_{1c}—hemoglobin A_{1c}, IF—intermittent fasting, T2D—type 2 diabetes.

*Where sex is not specified, both men and women were enrolled.

†Self-reported indicates participants reported consumption in food diaries; monitored indicates investigators monitored participants' consumption.

Table 2. Outcomes of risk factors for cardiovascular disease and type 2 diabetes in 26 individual studies of 22 intermittent fasting trials enrolling obese adults without type 2 diabetes

RISK FACTOR	OUTCOME	N	STUDIES
Blood pressure	↔	324	Examined in 16 studies, with no change in 9 studies ^{10,13,27,29,35,37,42,43,47}
	↓	226	Examined in 16 studies, with a decrease in 7 studies ^{11,15,21,24,25,49,50}
Body weight	↓	764	Decrease seen in 22 studies ^{10,11,13,15,19,20,22-25,27-29,33,35,37,41-43,49,47,50}
BMI	↓	566	Decrease seen in the 16 studies measuring BMI ^{10,13,15,19,20,23-25,28,29,35,37,42,43,47,50}
Diabetes			
• Glucose level	↔	409	Examined in 17 studies, with no change in 11 studies ^{10,19,24,25,27,32,35,38,40,42,43}
	↓	192	Examined in 17 studies, with a decrease in 5 studies ^{13,15,20,23,41}
	↑	24	Examined in 17 studies, with an increase in 1 study ¹¹
• HbA _{1c} level	↓	54	Decrease seen in the 1 study measuring HbA _{1c} level ⁴²
• Insulin level	↓	407	Decrease in 8 studies, decreasing trend in 3 of 11 studies measuring insulin level ^{11,13,15,19,20,25,27,32,35,41,43}

BMI—body mass index, HbA_{1c}—hemoglobin A_{1c}.

Table 3. Outcomes of risk factors for cardiovascular disease and type 2 diabetes in 5 intermittent fasting studies enrolling obese adults with type 2 diabetes

RISK FACTOR	OUTCOME	N	STUDIES
Blood pressure	NA	NA	Not studied in obese patients with type 2 diabetes
Body weight	↓	174	Decrease seen in all 5 studies ^{12,16,17,21,34}
BMI	↓	174	Decrease seen in all 5 studies ^{12,16,17,21,34}
Diabetes			
• Glucose level	↓	78	Decrease seen in the 3 studies measuring glucose level ^{12,21,34}
• HbA _{1c} level	↓	164	Decrease seen in the 4 studies measuring HbA _{1c} level ^{16,17,21,34}
• Insulin level	↓	27	Decrease seen in the 1 study measuring insulin level ³⁴

BMI—body mass index, HbA_{1c}—hemoglobin A_{1c}, NA—not available.

All of the 11 other comparisons of IF and calorie-restriction diets also found similar results between both groups.^{11,15-17,19,22,27,33,41-43} In several of these studies, those in the IF group consumed the same amount of calories^{22,41-43} or less^{19,27,33} than those in the calorie-restriction group. Four studies combined fasting and calorie restriction on the non-fasting days and found comparable weight loss to other studies (3.4% to 10.6%).^{15,23,33,35} In a direct comparison of 88 participants over 8 weeks, IF combined with restricting calories to 30% less than their calculated energy requirements led to greater weight loss versus IF alone ($P \leq .05$).³³

Most of the weight loss with IF is fat loss.^{13,17,19,20,22,28,29,33,35,43,47,53} A 2011 study by Harvie et al calculated that 79% of weight loss was owing to loss of fat specifically (level I evidence).²⁷ Participants regained some weight during follow-up after intervention, although average body weight remained statistically significantly lower than baseline levels.^{15,18,19,41-43,50} Weight regain did occur after 6 months. Five studies followed participants for 6 months or longer after completing IF interventions of 8 weeks to 1 year and most studies saw body weight increase by 1% to 2% of their weight nadir.^{18,19,41,43,50} Catenacci et al found a mean 2.6-kg regain over 6 months,¹⁹ and Schübel et al⁴¹ and Trepanowski et al⁴³ each found a regain of 2% of baseline body weight. The year-long study by Carter et al of 137 participants was the exception, demonstrating a maintained weight loss.¹⁸ Zuo et al saw a BMI increase of less than 1% during a year-long follow-up period after 12 weeks of IF.⁵⁰ In 6 comparisons of IF and calorie restriction, the amount of weight regained after IF and calorie restriction was similar.^{15,18,19,41-43} The 2016 study by Catenacci et al showed differing patterns of weight regain. In the 11 IF patients who completed follow-up, this was limited to lean body mass, while the 10 calorie-restricted patients who completed follow-up regained both fat and lean body mass.¹⁹

The practical length of a fast to effect changes in weight appears to be 16 hours. In IF studies with a daily fasting intervention, a total of 120 participants were able to maintain a minimum daily fast of about 16 hours (15.8 to 16.8 hours), with an 8-hour eating window each day.^{10,12,25,34} Arnason et al found that participants were able to fast for an average of 16.8 hours per day, rather than the 18- to 20-hour goal they had set.¹² Combining exercise with IF improved weight loss in a 2013 study by Bhutani et al of 64 obese patients. They found weight loss doubled (6 kg) when exercise was added to IF (level I evidence).¹³ In 2019, Cho et al found no improvement in weight loss when exercise was added to IF ($n=31$) (level I evidence).²⁰ There were high dropout rates ($\geq 25\%$) in several IF studies,^{11,13,20,25,28,43,50} which compare poorly to the 12% to 14% dropout rates of other long-term diets: Atkins, Zone, LEARN (Lifestyle, Exercise, Attitudes, Relationships, and Nutrition), and Ornish.⁵⁴ In direct comparisons of IF to calorie restriction, the 2 have similar dropout rates.^{11,15-17,19,22,27,28,33,41-43} Across the IF

studies, adherence to fasting ranged from 77% to 98% ($n=265$).^{10,11,13,17,21,29,38} In a 2009 study, Varady et al found weight loss was directly related to percentage of adherent days per week (level II evidence).⁴⁷

Intermittent fasting studies generally find that hunger levels remain stable^{22,31} or decrease during IF.^{38,45} A study of 30 participants over 12 weeks by Varady et al found reports of hunger during IF were no higher than with unrestricted consumption (level I evidence).⁴⁹ Kroeger et al found that among those with the highest weight losses over 12 weeks of IF, hunger decreased and fullness increased.⁴⁵ In the study by Harvie et al, 15% of participants reported hunger.²⁷ Sundfør et al saw higher reported hunger in the IF group compared with those in the calorie restriction group.⁴²

Ramadan is a culturally determined example of IF for many Muslims. Those who fast often do so for approximately 14 hours per day for 30 days, presenting a real-world opportunity for examining effects of fasting.⁵⁵⁻⁶² Eight Ramadan studies examined weight loss in obese adults ($n=856$).⁵⁵⁻⁶² Weight losses ranged from 0.1 kg⁵⁸ to 1.8 kg⁶¹ (level II evidence). Studies enrolling participants with diabetes saw a modest improvement in glycemic control.^{58,60,62} Diabetes Canada issued detailed recommendations on management of patients with diabetes during Ramadan in February 2019.⁶³ Their expert panel recommends individualized risk stratification, glucose monitoring, and treatment with medications with low hypoglycemia risk profiles.⁶³

Diabetes

While IF is a moderately successful strategy for weight loss, it shows promise for improving glycemic control. Five studies exclusively enrolled individuals with type 2 diabetes (**Table 3**).^{12,16,17,21,34} Kahleova et al compared a daily fast of at least 16 hours to caloric restriction ($n=54$).³⁴ Both groups experienced decreases in insulin levels but IF participants had significantly lower fasting glucose levels (-0.78 mmol/L vs -0.47 mmol/L, $P < .05$). Increased oral glucose insulin sensitivity, decreased C-peptide levels, and decreased glucagon levels were also statistically significantly greater in the IF group. The decrease in hemoglobin A_{1c} level was similar between the IF and calorie-restricted groups—a 0.25% decrease over 12 weeks (level I evidence).³⁴

In a 2016 pilot study, Carter et al implemented a fast 2 days per week with an otherwise usual diet versus caloric restriction every day in participants with diabetes ($n=51$).¹⁶ Medication use was reduced and hemoglobin A_{1c} levels decreased significantly (by 0.7%) during the 12-week study ($P < .001$), but the effect of IF on weight did not differ from that of caloric restriction (level I evidence).¹⁶ The 2018 trial that followed ($n=137$) saw the same result over 12 months of IF or calorie restriction (level I evidence).¹⁷ The improvements in hemoglobin A_{1c} level were lost during the 12 months after IF, although

weight losses and medication reductions remained.¹⁸ In the 2017 Saskatchewan study by Arnason et al, 10 participants with type 2 diabetes fasted an average of 16.8 hours per day for 2 weeks.¹² They found improved glycaemic control with lower morning, postprandial, and average mean daily glucose levels (level II evidence).¹² These improvements regressed once participants returned to their usual diets. Corley et al enrolled 41 individuals with diabetes in a 2018 study of twice-weekly 1-day fasts for 12 weeks; fasting glucose levels decreased by 1.1 mmol/L and hemoglobin A_{1c} levels by 0.7% (level II evidence),²¹ a decline similar to that in the earlier study by Carter et al.¹⁶ Kahleova et al found a more modest decrease in blood glucose levels (-0.78 mmol/L) with a daily 16-hour fast; no adverse events were reported.³⁴


Use of IF in patients with diabetes poses a risk of hypoglycemia. Olansky suggests adjusting medication in patients with type 2 diabetes taking insulin or insulin secretagogues (eg, sulfonylureas).⁶⁴ Other hypoglycemic agents such as metformin, glucagonlike peptide 1 agonists, dipeptidyl peptidase 4 inhibitors, and α -glucosidase inhibitors are considered less likely to cause hypoglycemia (level III evidence).⁶⁴ Olansky indicates that adjustments might not be required to long-acting basal insulin, but that short-acting analogues should be reduced on fasting days to reflect the timing of meals and anticipated carbohydrate intake (level III evidence).⁶⁴ Premixed insulins (ie, intermediate-acting and short-acting insulin) are not recommended during IF, as they are not adaptable to changes in meal timing and calories.⁶⁴ Corley et al reduced any insulin use by up to 70% on fasting days.²¹ Hypoglycemic events (blood glucose level \leq 4.0 mmol/L) in that study (n=41) were experienced on average every 43 days, with no severe hypoglycemic events (ie, requiring assistance of another person).²¹ Carter et al proposed lessening the risk of hypoglycemic events through pretrial discontinuation of all insulin and sulfonylureas when participants' baseline hemoglobin A_{1c} levels were less than 7%; discontinuation of insulin only on fast days if hemoglobin A_{1c} levels were between 7% and 10%; and no change in medication if hemoglobin A_{1c} levels were greater than 10%.^{16,65} This protocol was later modified to decrease long-acting insulin by 10 units while fasting.¹⁷ Arnason et al found no hypoglycemia among 10 participants with type 2 diabetes during a 2-week period with daily fasts averaging 16.8 hours; however, their study excluded those taking insulin.¹²

Adverse events

No serious adverse events were reported in the 27 IF trials. Fasting-related safety concerns include mood-related side effects and binge eating, among other symptoms. Obese participants observing a fast every second day did not develop binge-eating patterns^{19,26} or purgative behaviour,^{26,30} and reported improved body image and less depression.^{26,30} During the 6-month

study by Harvie et al, 32% of participants reported less depression and increased positive mood and self-confidence.²⁷ Study participants also occasionally reported dizziness,^{10,26,30,42} general weakness,^{26,27,30,41} bad breath,³⁰ headache,^{10,27,41,42} feeling cold,^{27,41} lack of concentration,^{27,41} sleep disturbance,^{42,30} nausea,⁴² and constipation.^{27,30} When compared with baseline, these symptoms were unchanged with fasting.^{26,30}

Conclusion

Obesity treatment will always be a challenge in primary care. We have limited effective options to recommend to overweight and obese patients, many of whom have doubtless already participated in calorie-restricted diets. The heterogeneity in the current evidence limits comparison of IF to other weight-loss strategies. Intermittent fasting shows promise as a primary care intervention for obesity, but little is known about long-term sustainability and health effects. Longer-duration studies are needed to understand how IF might contribute to effective weight-loss strategies. 

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Contributors

All authors contributed to the concept and design of the study; data gathering, analysis, and interpretation; and preparing the manuscript for submission.

Competing interests

None declared

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This article has been peer reviewed.

Cet article a fait l'objet d'une révision par des pairs.

Can Fam Physician 2020;66:117-25