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Effect of Intermittent Fasting versus Continuous Caloric Restriction on Body Weight and Metabolic Parameters in Adults with Overweight or Obesity: A Narrative Review

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Abstract

Obesity and type 2 diabetes have reached epidemic proportions worldwide, including the Middle East and North Africa region. Intermittent fasting (IF) has been increasingly used to manage overweight/obesity and its metabolic complications. Physiologically, IF shifts the body's metabolism into ketosis (the metabolic switch) and induces cellular changes, which have a theoretical benefit over and above continuous caloric restriction (CCR). In this narrative overview of IF, the focus is on summarizing studies that compare IF to CCR in adults with overweight or obesity. The most commonly practiced types of IF (5:2, the alternate day fast, and the time-restricted eating) were included. Nine studies of 1-year duration or longer, with weight loss as the primary outcome, were summarized. The effect on body weight and improved metabolic parameters such as blood pressure, glycemic indicators, and lipid profile are described. Overall, IF was well tolerated and effective for weight loss in a manner comparable to CCR. The benefits were similar among adults with type 2 diabetes. There were no additional metabolic effects or benefits over and above CCR. However, more studies are needed to address specific details of IF, such as the type and timing of fasting and its application to different populations. In conclusion, IF is safe and beneficial for weight loss in adults with overweight/obesity with or without diabetes. It can be used as an alternative to CCR.

Keywords
- intermittent fasting
- time-restricted eating
- caloric restriction
- obesity
- weight loss

Introduction

Intermittent fasting (IF) is a dietary intervention that entails phases of little or no energy intake, followed by periods of ad libitum eating, in a recurring fashion.[1] From a cultural perspective, IF was a natural component of lifestyle habits, and it is only recently, with industrialization, three meals per day became the norm.[2] According to data from the National Health and Nutrition Examination Survey (NHANES), the median daily eating period among adults in America is

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around 14 hours, with only 10 to 15% of adults eating for 12 hours or less.[3,4] Similarly, three meals per day are generally consumed across the Middle East and North Africa (MENA) region, except during religious fasting.[5] Over the past decade, IF has emerged as the new dietary modification for weight loss and obesity.[6]

Obesity and Diabetes in the MENA Region

Obesity, as a world epidemic, includes the MENA region. In 2016, more than half of the adult population in several Middle Eastern countries, including Egypt, Kuwait, Qatar, Saudi Arabia, and the United Arab Emirates, was classified as overweight or obese.[7] The predilection for obesity in the MENA region which affects particularly women, is higher in upper-middle-income nations, and constitutes a significant public health concern.[8,9] The prevalence of obesity is projected to continue to rise.[10] Sedentary lifestyle, nutrition transition, urbanization, cultural, social, and economic changes all contribute to the obesity epidemic in the MENA region.[11] Thus, there is a pressing need for impactful measures to address the rising prevalence of obesity.

Moreover, over the past few decades, the prevalence of diabetes mellitus (DM) worldwide has been steadily rising.[12] As per the International Diabetes Federation (IDF), roughly 73 million adult men and women were living with DM in the MENA region in 2021. This number is projected to reach 95 million by 2030 and 136 million by 2045.[13] DM is associated with significant complications, and the MENA region has the highest rate of disability-adjusted life years and DM-related deaths among working-age people.[13] Therefore, DM should be addressed as a significant health issue, and interventions for prevention must be implemented to control risk factors such as obesity by addressing a healthy lifestyle and regular exercise.

Types of Intermittent Fasting

Sustained successful weight loss with caloric restriction has been limited by reduced adherence. IF, because it encompasses ad libitum food intake periods, has emerged as an attractive alternative to induce sustainable weight loss. Several types of nonreligious IF approaches exist. The most practiced are[6] are as follows:

1. Alternate day fasting (ADF): This practice involves alternating between a day of normal eating and fasting. As a result, no calories on fast days and unrestricted food intake on nonfast days.
2. Modified ADF: This approach differs from ADF in that it includes up to 25% of estimated total energy requirements on fast days, followed by unrestricted food intake on nonfast days.
3. The 5:2 diet involves fasting (between 0 and 25% of daily energy requirements) 2 days a week and eating ad libitum on the other 5 days.[6,14]
4. Time-restricted eating (TRE): This approach is the only IF subtype that does not place a strong emphasis on caloric restriction.[1] The fast's length and the eating window's timing are significant factors that could impact physiological outcomes.[15,16] Although there is heterogeneity between different TRE practices, with eating windows varying from as little as four hours[17,18] to as long as 12 hours[19,20] per day, the window duration most frequently reported in clinical studies is eight hours.[21,22] Early TRE protocols have the bulk of their calories distributed in the morning and early afternoon, while late TRE protocols have the eating window in the late afternoon.[1]

Physiology of Fasting and Cellular Metabolic Benefits

Fasting elicits metabolic changes, primarily aimed at maintaining the glucose supply to the brain while providing energy to the remaining organs. During fasting, the body shifts from utilizing glucose as its primary energy source to using fatty acids and ketone bodies (synthesized de novo) as the primary fuel. This change is called the "metabolic switch" and is mainly driven by low insulin to glucagon hormonal milieu. In addition to maintaining a steady energy supply to the body, fasting promotes cellular responses that are considered beneficial physiologically and associated with an improved metabolic profile and healthier cells.[23–26] The caloric deficit and the accompanying ketosis partly induce these changes. de Cabo and Mattson describe three major cellular changes during fasting: autophagy, mitochondrial biogenesis, and increased insulin sensitivity.[26]

Autophagy is a cellular process that eliminates dysfunctional and damaged cell components. To preserve cellular homeostasis, a cell recycles and disassembles its proteins and organelles during autophagy.[1,26] Several important proteins are involved in the complicated molecular pathways that control autophagy, including the mTOR (mammalian target of rapamycin) pathway, which is shut down during fasting. When mTOR is blocked, the autophagy-related gene pathway and other proteins that promote autophagy are activated.[27] Numerous health advantages, such as improved insulin sensitivity, decreased inflammation, and defense against neurodegenerative diseases, have been associated with this increase in autophagy.[1,28,29]

Mitochondrial biogenesis denotes increased mitochondrial production, particularly in muscle and liver cells. This increase is attributed to be a protective response to fasting stress, as it ensures that cells have the energy they need to function. Several molecular mechanisms are involved in the increase in mitochondrial biogenesis, including the AMP-activated protein kinase pathway and the peroxisome proliferator-activated receptor gamma coactivator 1-α pathways. Fasting improves mitochondrial function and reduces oxidative stress in cells.[25,26]

IF is especially effective at improving insulin sensitivity by inducing the body to use stored glucose for energy, which can help to reduce insulin resistance. IF also aids in reducing inflammation and oxidative stress, as previously mentioned, which can contribute to insulin resistance.[26]

The above three cellular changes result in prolonged survival and improved cellular function and metabolism.

The “decluttered” cell ages less quickly and can function more efficiently.[26]

Intermittent Fasting versus Continuous Caloric Restriction

In contradistinction to IF, simple caloric restriction results in an energy deficit without reaching the metabolic switch and the resultant fasting physiology.[28] Nonetheless, there is ample evidence that a negative energy balance in overweight and obesity benefits health. As an example, the CALERIE (Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy) study was conducted between 2007 and 2010 on 218 healthy adults with a mean body mass index of 25.2 kg/m^2, who were randomly assigned to either 25% calorie restriction group or ad libitum eating group. Over 2 years, the calorie restriction group had a significant weight loss of −11% and a positive impact on several health indicators, such as blood pressure, cholesterol levels, and inflammation markers.[29] Although the CALERIE study did not specifically involve IF, there is some overlap in the mechanisms by which calorie restriction and IF may have similar effects. Both strategies have increased insulin sensitivity, decreased inflammation, and stimulated autophagy.[25–29]

Review Context, Rationale, and Methods

The question remains whether such benefits are seen beyond caloric deficit due to IF per se. Several studies have addressed this question concerning weight loss and metabolic benefits. More specifically, the present review aims at answering the following questions:

1. Is IF an effective and safe form of weight loss in overweight/obese adults with or without diabetes?
2. Does IF provide additional benefits in weight loss and metabolic improvement over and above caloric restriction?

Literature Search

For this narrative review, relevant articles were searched on PubMed using the following MeSH keywords: “intermittent fasting,” “time-restricted eating,” “calorie-restricted diet,” and “low-calorie diet.” Chosen articles were those meeting the below inclusion criteria:

1. Written and/or available as full text in the English language.
2. At least 1 year-long randomized controlled trials (RCTs) comparing the effect of IF to continuous calorie restriction on weight loss and/or body mass index as a primary outcome among overweight/obese adults with/without type 2 diabetes (T2D), otherwise healthy.
3. The search spanned the literature for the past 20 years (from 2003 until February 28, 2023).

Results

There were 5,157 entries found, of which 16 studies fit the inclusion criteria. After scrutinizing the full text of the studies, only nine were deemed within the study’s objective. Therefore, nine studies were summarized in this review (►**Fig. 1**).

Weight Loss Outcomes

Continuous Calorie Restriction versus 5:2 Intermittent Fasting

In a 1-year RCT, Carter et al followed overweight adults with T2D, randomized to either a caloric restriction diet of 1200 to 1500 kcal/day or 5:2 IF with an intake of 500 to 600 kcal/day

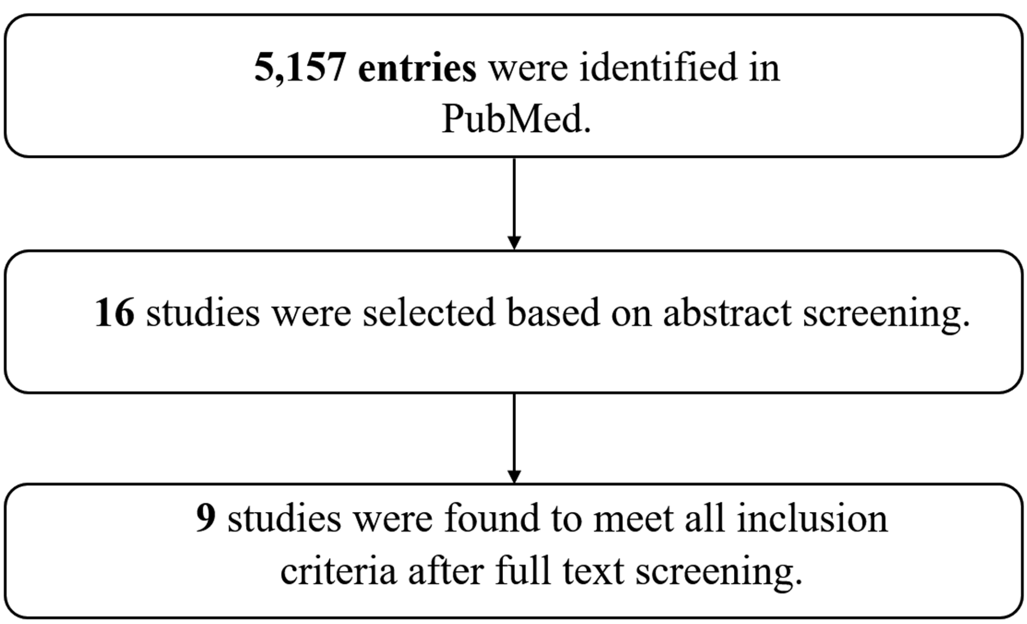

Fig. 1 Randomized controlled trials selection process.

on fasting days. At the end of the intervention, the continuous caloric restriction (CCR) group sustained an average of 5.0 kg weight loss compared with 6.8 kg in the 5:2 group, which was not a significant difference.[30] Indeed, in a 12-month follow-up by Carter et al done a year later using the same study design, both groups maintained a −3.9 kg weight loss compared with baseline, with no statistically significant difference in weight loss using intention-to-treat analysis between the two groups.[31] Similarly, Sundfør et al found that among 112 obese adults with more than or equal to 1 metabolic syndrome component randomized to 5:2 fasting or continuous energy restriction (CER), weight loss and decrease in waist circumference were comparable among both groups. Nevertheless, participants from the 5:2 fasting group experienced a statistically significant mild weight regain of 0.3 kg ± 1.2 kg ($p < 0.05$).[32] Conversely, Headland et al randomized healthy obese or overweight adults to CER (1000–1200 kcal/day), 5:2 IF, or week-on-week-off (WOWO) fasting. Follow-up at 12 months revealed a significant weight loss achieved by participants of each interventional group but with no significant difference between the three groups.[33] A newer RCT with the same study design was conducted by Headland et al 2 years later. After a year-long intervention, follow-up at 12 months post-fasting revealed a weight loss of 4.5 kg±4.9 kg in the CER group, 2.8 kg±6.5 kg in the WOWO group, and 3.5 kg±5.l kg in the 5:2 fasting group, with no significant difference between CER and WOWO and CER and 5:2, showing that both types of IF regimens are not superior but equally effective to CER concerning weight loss.[34] Furthermore, similar results were reached by Schübel et al while comparing the 5:2 fasting regimen's effect on weight loss compared with CER. The authors randomized 150 overweight and/or obese nonsmoking adults to either 5:2 fasting (net weekly 20% caloric restriction), CCR (daily 20% caloric restriction), and control groups. Following the 12-week intervention phase, the most remarkable drop in body weight was noted in the 5:2 fasting group ($\log_e$ relative change -7.1% ± 0.7%) compared with the CCR group ($\log_e$ relative change −5.2% ± 0.6%) with a marginal difference ($p = 0.053$). Weight loss was maintained among all groups. However, the $\log_e$ relative weight change maintained compared with baseline weight at week 50 was the greatest in the fasting group (−5.2% ± 1.2%) compared with the CCR group (−4.9% ± 1.1%), but the difference was not significant.[35]

Continuous Calorie Restriction versus Alternate-Day Fasting

Alternate-day fasting, which involves rotating between fasting and "feasting" every other day, is another approach investigated concerning weight loss outcomes compared with daily caloric restriction (DCR). In their study, Trepanowski et al randomized 100 overweight/obese nonsmoker adults to ADF, DCR, and control (no intervention) groups. Follow-up at 6 months at the end of the weight loss phase revealed that overall weight loss and change in fat mass, lean mass, and visceral fat were comparable among all three groups. Moreover, weight regains at the end of the study did not differ significantly between the ADF and DCR groups (mean difference of the change between ADF and DCR −0.7%; 95% confidence interval [−3.1 to 1.6%]).[36] Nevertheless, there was a higher number of dropouts among participants belonging to the ADF group (13 of 34 [34%]) as compared with the DCR group (10 of 35 [29%]), indicating an increased challenge in adhering to the ADF diet.

Continuous Calorie Restriction versus Time-Restricted Feeding

Other types of IF, such as TRE, were compared with caloric restriction to assess whether the benefits of these diets can be attributed to the timing of food intake or the caloric intake itself. For this purpose, Pureza et al randomized 58 obese women with low income to either a hypoenergetic diet (HD) only or time-restricted feeding (TRF) with HD, whereby participants were restricted to a 12-hour eating window with the same caloric restriction as the HD group, followed by a 12-hour period of fasting. According to the authors, restricting the sample to only women allowed for a more homogeneous and representative investigation of the effect of time restriction on the health outcomes studied. At 12 months, women in the TRF + HD group ($n = 31$) lost 0.77% of their baseline weight as compared with a loss of 0.69% in the HD group ($n = 27$), which was not statistically significant ($p = 0.95$). Similarly, while an overall decrease in body mass index and waist circumference was observed, it did not differ between the groups. Nevertheless, the percentage of body fat was lower in the TRE group (-0.97) compared with the HD group (0.66), which is statistically but not clinically significant ($p = 0.02$).[20] The results of the latter study were comparable to those of a newer RCT conducted by Liu et al in 2022 in which healthy obese adults were randomized to either CCR or TRE between 8:00 AM and 4:00 PM over 12 months, with both groups having the same total daily caloric intake. Follow-up at the end of the intervention revealed that TRE and CCR achieved similar weight loss outcomes and reduction in body and visceral fat, therefore concluding that both interventions are equal in achieving desired weight loss goals.[37]

Eight of the above nine studies are summarized in ►**Table 1**. The study by Pureza et al was not shown in the table as it included only women.

Metabolic Outcomes

Continuous Calorie Restriction versus 5:2 Intermittent Fasting

Most of the studies mentioned above further expanded their investigations to include a comparison of different types of IF regimens to CCR concerning metabolic outcomes such as glycemic control and cardiovascular risk modifiers (total cholesterol, high-density lipoprotein [HDL]-cholesterol, low-density lipoprotein [LDL]-cholesterol, triglycerides, and blood pressure). While IF is a promising diet for achieving a healthier metabolic profile, current data fails to provide strong enough evidence to declare its superiority over other

Table 1 Data of the randomized controlled trials on IF versus CCR for weight loss

Author	N of participants	Mean age in years (SD)		*n*, gender		Population characteristics and baseline BMI (kg/m^2)	Type of fast		Duration of intervention	Change in weight in kg or % (SEM)	
		CCR	IF	CCR	IF		CCR	IF		CCR	IF
Trepanowski et al (2017)[36]	100	43 (12)	44 (10)	F = 29 M = 6	F = 30 M = 4	Overweight or obese nonsmoker adults otherwise healthy **CCR** 35 (4) **IF** 34 (4)	75% of baseline intake daily	25% of baseline intake on "fast" days and 125% of baseline intake on "feast" days	1 month baseline phase, 6 months weight-loss phase, 6 months weight-maintenance phase	−5.3%[a] [95% CI −7,6; −3.0]	−6.0%[a] [95% CI −8.5; −3.6]
Schübel et al (2018)[35]	150	50.5 (8.0)	49.4 (9.0)	F = 24 M = 25	F = 24 M = 25	Overweight or obese nonsmoker adults otherwise healthy **CCR** 31.2 (4.0) **IF** 32.0 (3.8)	20% energy restriction daily	5:2 (75% energy restriction for 2 consecutive days, with net weekly restriction of 20%)	12 weeks intervention, 12 weeks maintenance, 26 weeks follow-up	−4.9% (1.1)	−5.2% (1.2)
Sundfør et al (2018)[32]	112	47.5 (11.6)	49.9 (10.1)	F = 30 M = 28	F = 26 M = 28	Obese adults with ≥1 metabolic syndrome component **CCR** 35.3 (3.5) **IF** 35.1 (3.9)	Daily calorie restriction equivalent to weekly 5:2 average	5:2 (400–600 kcal/day)	6 months weight loss, 6 months maintenance	−9.4 kg[b] (5.3)	−9.1 kg[b] (5.0)
Carter et al (2018)[30]	137	61.0 (9.2)	61.0 (9.0)	F = 38 M = 29	F = 39 M = 31	Overweight adults with diagnosed T2DM managed with diet, OHA +/− insulin, otherwise healthy **CCR** 37 (5.7) **IF** 35 (5.8)	1200–1500 kcal/day	5:2 (500–600 kcal/day)	12 months intervention	−5.0 kg (0.8)	−6.8 kg (0.8)
Carter et al (2019)[31]	137	61 (9.2)	61 (9.0)	F = 38 M = 29	F = 39 M = 31	Overweight adults with diagnosed T2DM managed with diet, OHA +/− insulin, otherwise healthy **CCR** 37 (5.7) **IF** 35 (5.8)	1200–1500 kcal/day	5:2 (500–600 kcal/day)	24 months (including 12 months-follow up)	−3.9 kg (1.1)	−3.9 kg (1.1)
Headland et al (2019)[33]	332	51.7 (13.0)	**WOWO** 49.0 (13.2) **5:2** 47.5 (14.5)	F = 85 M = 19	**WOWO** F = 94 M = 16 **5:2** F = 97 M = 21	Overweight or obese adults otherwise healthy **CCR** 32.6 (4.1) **WOWO** 33.9 (4.9) **5:2** 32.6 (4.7)	1000–1200 kcal/day	**WOWO** (1000–1200 kcal/day) **5:2** (500–600 kcal/day)	12 months	−6.6 kg (6.1)	**WOWO** −5.1 kg (5.4) **5:2** −5.0 kg (4.9)

Table 1 (*Continued*)

Author	N of participants	Mean age in years (SD)		*n*, gender		Population characteristics and baseline BMI (kg/m^2)	Type of fast		Duration of intervention	Change in weight in kg or % (SEM)	
		CCR	IF	CCR	IF		CCR	IF		CCR	IF
Headland et al (2020)[34]	109	56.4 (8.8)	**WOWO** 55.0 (12.3)	F = 31 M = 7	**WOWO** F = 28 M = 6	Healthy overweight or obese adults	1000–1200 kcal/day	**WOWO** (1000–1200 kcal/day)	24 months	−4.5 kg (4.9)	**WOWO** −2.8 kg (6.5)
			5:2 2.4 (11.4)		**5:2** F = 23 M = 2	**CCR** 33.4 (4.8); **WOWO** 34.4 (5.7); **5:2** 32.9 (5.0)		**5:2** (500–600 kcal/day)			**5:2** −3.5 kg (5.1)
Liu et al (2022)[37]	139	32.2 (8.8)	31.6 (9.3)	M = 35 F = 35	M = 36 F = 33	Healthy overweight or obese adults; **CCR** 31.3 (2.6); **IF** 31.8 (2.9)	1500–1800 kcal/day for men, 1200–1500 kcal/day for women	Time restricted eating between 8:00 AM and 4:00 PM with same caloric intake as CCR	12 months	−6.3 kg (−7.8 to −4.7)	−8.0 kg (−9.6 to −6.4)

Abbreviations: CI, confidence interval; CCR, continuous calorie restriction; F, female; IF, intermittent fasting; M, male; SD, standard deviation; SEM, standard error of the mean; WOWO, week-on-week-off.
[a]Reflects the mean difference in weight change versus the control group.
[b]Reports on results at the end of the 6-month intervention.

lifestyle interventions. Indeed, the study by Carter et al showed no difference in hemoglobin A1c (HbA_1c) levels between both groups at 24 months (+0.4% in the CCR group as compared with 0.1% in the 5:2 group; $p = 0.32$). Moreover, fasting blood glucose, total cholesterol, triglycerides, and LDL-cholesterol remained relatively stable compared with baseline.[31] In line with these findings, Sundfør et al reported no significant difference in improving metabolic outcomes (blood pressure, serum lipid levels, and HbA_1c) among obese adults with more than or equal to 1 metabolic syndrome component randomized to 5:2 fasting or CER.[32] Moreover, Headland et al found that while serum lipid levels decreased in both RCTs conducted (cholesterol and triglycerides in the 2018 RCT and total cholesterol only in the 2020 RCT), the drop was comparable among all three groups (CER, WOWO, and 5:2) and HbA_1c levels remained unchanged from baseline.[33,34] A more detailed investigation of the 5:2 fasting regimen's effect on metabolic biomarkers compared with CER was conducted by Schübel et al, who concluded that the only significant difference between the 5:2 fasting and CCR groups was observed in fasting glucose levels, whereby the CCR group achieved lower fasting glucose at week 12 of the intervention compared with baseline (Log_e relative change of $-2.9\% \pm 1.2\%$ vs. $-7.6\% \pm 1.2\%$; $p = 0.01$). As for its effect on serum levels of triglycerides, HDL, cholesterol, adipokines, liver function tests, insulin, brain natriuretic peptide, insulin-like growth factor-1, resistin, homeostatic model assessment for insulin resistance (HOMA-IR), as well as inflammatory markers (C-reactive protein, interleukin-6, interleukin-8, interferon-Y, and tumor necrosis factor- -α), no significant difference was demonstrated between the two groups with an overall decrease observed in all three interventions.[35]

Continuous Calorie Restriction versus Alternate-Day Fasting

Similarly, investigations on ADF failed to show any superiority to CCR in reducing blood pressure, heart rate (HR), plasma lipids, glucoregulatory and inflammatory markers.[36]

Continuous Calorie Restriction versus Time-Restricted Feeding

In their study, Liu et al noted a reduction in systolic and diastolic blood pressures (DBP and SBP), HR, triglycerides, total cholesterol, LDL-cholesterol, glucose levels, HOMA-IR index values, and insulin disposition index at the 12-month follow-up in both CCR and TRE interventions, with no significant difference noted between the two groups.[37] Although cardiovascular health markers were not measured, Peruza et al investigated the impact of TRE and CCR on vital signs, including SBP, DBP, and HR, noting a decrease in SBP (−4.59 mm Hg in HD; −7.47 mm Hg in HD + TRF) and DBP (−4.22 mm Hg in HD; −2.22 in HD + TRF) but with no difference between the two groups. Moreover, there was no difference in HR between the two groups.[20]

The metabolic changes for serum fasting glucose, HDL-cholesterol, and triglycerides, which are reported in similar units, are displayed in ►**Fig. 2.**

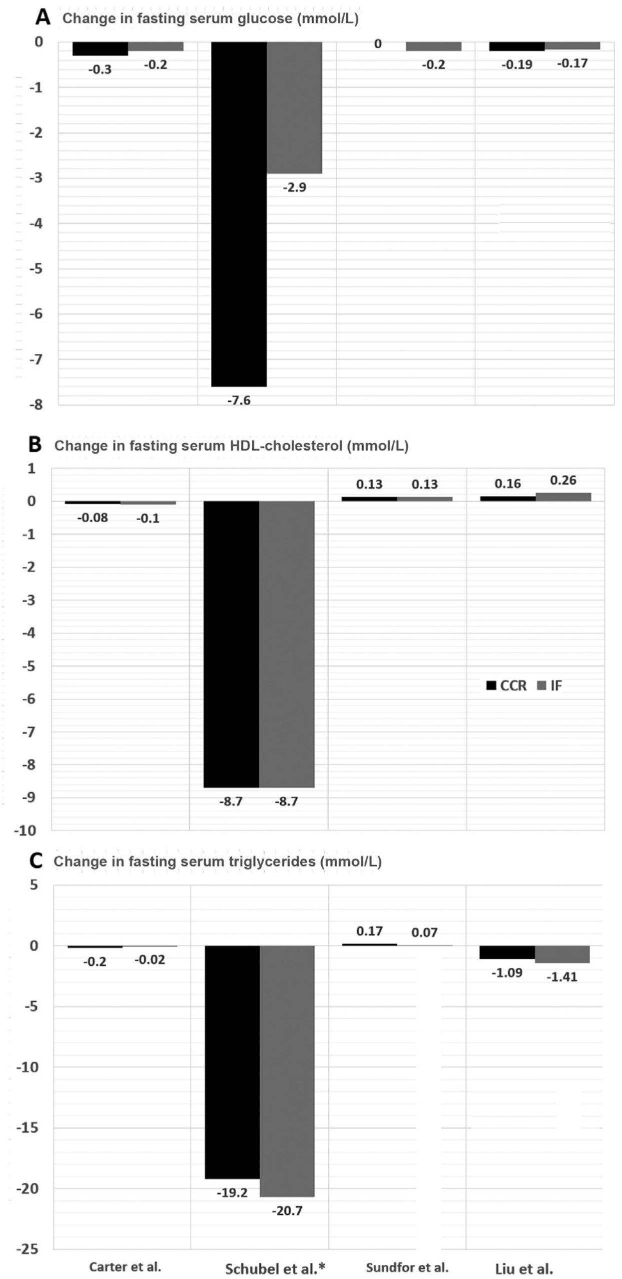

Fig. 2 Changes in select metabolic outcomes among four studies assessing intermittent fasting (IF) versus continuous caloric restriction (CCR): (**A**) Fasting serum glucose; (**B**) fasting serum high-density lipoprotein (HDL)-cholesterol, and (**C**) fasting serum triglycerides. *signifies that the numbers from this study are presented as "log e" whereas the remainder share a similar unit.

Conclusion

The above studies shed light on the efficacy of IF for long-term weight loss and maintenance in healthy overweight/obese individuals with or without T2D. Overall, there was a mild weight loss of around 5% baseline body weight at 1 year for both conventional calorie restriction and IF. Moreover, there was a similar degree of metabolic benefit. The three types of fast, 5:2, ADF, and TRE, were well-tolerated over at least 1 year.

Looking more specifically at the MENA region, given its high burden in obesity and T2D,[38] there are no reported long-term, controlled studies assessing the effect of IF on weight and metabolic outcomes. Most published studies report on the safety of fasting during Ramadan among participants with DM. Given that eating habits are highly influenced by climate, culture, and lifestyle, assessing the feasibility and efficacy of IF among the different populations in the MENA region would be essential.

In summary, IF is a feasible, attractive alternative to a conventional diet for weight and metabolic control. Studies are needed to further assess its applicability to the people of the MENA.

Compliance with Ethical Principles

No ethical approval is required for review article types of studies.

Authors' Contribution

J.A. and J.J. each wrote significant components of the manuscript. J.J. reviewed the literature and extracted the data into tables and figures. M.N. was responsible for the manuscript's concept, reviewing, and editing.

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None.

Conflict of Interest

None declared.

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