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Intermittent fasting as a nutritional tool

ORIGINAL RESEARCH Systematic review and network meta-analysis of RCTs

Intermittent fasting strategies and effects on body weight and other cardiometabolic risk factors

Semnani-Azad Z, Khan TA, Chiavaroli L, et al

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Study question What is the effect of intermittent fasting diets, compared with continuous energy restriction or unrestricted diets (ie, ad libitum), on intermediate cardiometabolic outcomes from randomised controlled trials (RCTs)?

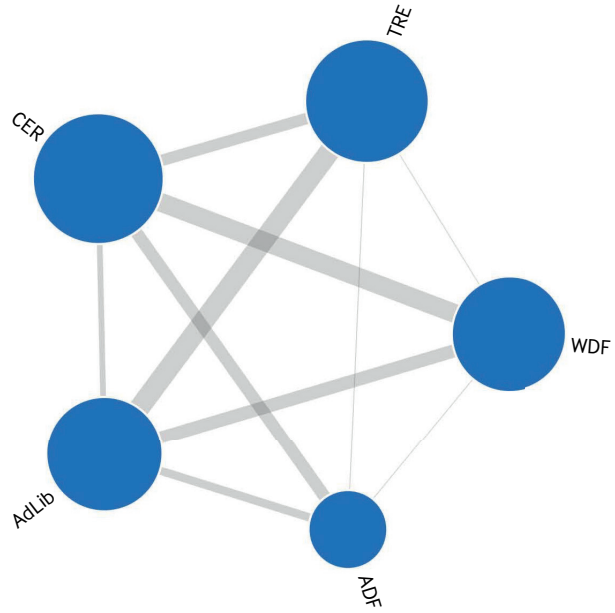
Methods In this systematic review and network meta-analysis, Medline, Embase, and Central databases were searched from inception to 14 November 2024. RCTs comparing intermittent fasting diets (alternate day fasting, time restricted eating, and whole day fasting) with continuous energy restriction and unrestricted diets were included. The primary outcome was body weight, with secondary outcomes including anthropometric measures, glucose metabolism markers, lipid profiles, blood pressure, C reactive protein, and liver disease markers. A network meta-analysis was performed, reporting mean differences with 95% confidence intervals (CIs), and evidence certainty was assessed using GRADE (Grading of Recommendations Assessment, Development and Evaluation).

Study answer and limitations 99 RCTs involving 6582 adults were identified and the results showed that while all intermittent fasting and continuous energy restriction diet strategies reduced body weight compared with ad libitum diet, alternate day fasting was the only intermittent fasting approach that showed significant weight reduction benefits compared with continuous energy restriction (mean difference −1.29 kg (95% CI −1.99 to −0.59), moderate certainty evidence). Short term studies (<24 weeks) had similar outcomes across interventions, but in moderate to long term trials (≥24 weeks), only comparisons between diet strategies and ad libitum approaches maintained significant weight reduction benefits. A limitation of the study is that the GRADE assessment downgraded the certainty of evidence owing to considerable heterogeneity and incoherence in body weight outcomes across diet strategy comparisons, with additional downgrades for imprecision and indirectness.

What this study adds Minor differences were noted between some intermittent fasting diets and continuous energy restriction, with some benefit for alternate day fasting strategy with weight loss in shorter duration trials. Intermittent fasting diets might have similar benefits to continuous energy restriction for weight loss and cardiometabolic risk factors.

Funding, competing interests, and data sharing See full paper on bmj.com for funding and competing interests. Additional data are available on request.

Study registration ClinicalTrials.gov NCT05309057.



Network diagram for randomised controlled trials investigating the association of intermittent fasting strategies, continuous energy restriction, and ad libitum diets with body weight. ADF=alternate day fasting; AdLib=ad libitum; CER=continuous energy restriction; TRE=time restricted eating; WDF=whole day fasting. An interactive version of this graphic is available at https://public.flourish.studio/visualisation/23222926/

	Ad libitum	Continuous energy restriction	Alternate day fasting	Time restricted eating	Whole day fasting	Versus
Ad libitum		**-2.21† (-3.72 to -0.70) (n=3)**	**-3.63† (-5.91 to -1.35) (n=2)**	**-2.46† (-4.19 to -0.72) (n=2)**	**-1.88* (-3.37 to -0.39) (n=2)**	Ad libitum
Continuous energy restriction	**-2.09† (-2.77 to -1.41) (n=4)**		-1.42 (-3.44 to 0.61) (n=4)	-0.24 (-2.06 to 1.58) (n=3)	0.34 (-0.91 to 1.58) (n=7)	Continuous energy restriction
Alternate day fasting	**-3.37† (-4.16 to -2.59) (n=8)**	**-1.29* (-2.05 to -0.53) (n=11)**		1.17 (-1.42 to 3.77) (n=0)	1.75 (-0.53 to 4.04) (n=0)	Alternate day fasting
Time restricted eating	**-1.65* (-2.17 to -1.13) (n=23)**	0.44 (-0.25 to 1.12) (n=11)	**1.72* (0.87 to 2.58) (n=1)**		0.58 (-1.41 to 2.56) (n=0)	Time restricted eating
Whole day fasting	**-2.53† (-3.28 to -1.79) (n=14)**	-0.45 (-1.19 to 0.29) (n=16)	0.84 (-0.11 to 1.79) (n=1)	**-0.88* (-1.71 to -0.06) (n=1)**		Whole day fasting
Versus	Ad libitum	Continuous energy restriction	Alternate day fasting	Time restricted eating	Whole day fasting	

Network meta-analysis of body weight outcome from 93 randomised clinical trials by follow-up duration: ≥24 weeks (n=17, blue boxes) and <24 weeks (n=76, green boxes). Mean differences and 95% confidence intervals from 93 studies of body weight (kg). Total number of direct comparison studies are noted in the brackets below the confidence intervals. Statistically significant data are in bold. The minimally important difference for body weight is 2.0 kg. For body weight, the threshold classifications were classified as trivial* (<2.0 kg), small† (≥2.0 to <4.0 kg), moderate (≥4.0 to <10.0 kg), large (≥10.0 to <20.0 kg), and very large (≥20.0 kg)

COMMENTARY

Fasting is defined as the voluntary abstinence from food for a determined period. Although traditionally associated with religious purposes,[1] the practice has gained relevance today as a nutritional strategy, primarily for cumulative energy restriction. Fasting is used as an alternative to continuous caloric restriction, especially given the difficulties many individuals face in adhering to diets structured under strict parameters.[2] Adherence to a 30% caloric restriction is maintained during the first three months of the intervention; however, adherence progressively declines, reaching only a 9.5% restriction after 12 months, which compromises the sustainability of the clinical effects.[3]

In this context, intermittent fasting has emerged as a popular dietary intervention, in which popularity is spread mainly through social media, where its potential benefits for weight loss are emphasised. However, questions remain about its long term efficacy, feasibility in terms of adherence, and effects on cardiometabolic variables. A scarcity of rigorous comparative syntheses mean that uncertainty exists around whether any forms of intermittent fasting are superior, inferior, or equivalent to continuous caloric restriction in terms of clinical efficacy.

In their network meta-analysis, Semnani-Azad and colleagues synthesised findings from 99 randomised clinical trials that compared continuous energy restriction and ad libitum diets with any of the three main modalities of intermittent fasting: alternate day fasting, time restricted eating, and whole day fasting.[4] The results show that all

strategies produced significant weight reductions compared with ad libitum diets. Alternate day fasting was the only intervention with additional reductions in body weight (−1.29 kg), body mass index, and certain lipid parameters compared with continuous energy restriction, although with small effects and moderate certainty according to GRADE (Grading of Recommendations Assessment, Development and Evaluation).[4] Importantly, these differences did not reach the prespecified clinical relevance threshold of at least 2 kg defined for individuals with obesity. Nonetheless, randomised trials have shown that alternate day fasting can induce more substantial weight losses (around 4-6 kg in 8-12 weeks), accompanied by reductions in visceral fat and cardiometabolic improvements, particularly in adults with obesity or metabolic dysfunction associated steatotic liver disease (previously known as non-alcoholic fatty liver disease).[5-7]

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Why does this study matter?

The value of this study is not in establishing a universally superior strategy but in positioning alternate day fasting as an additional option within the therapeutic repertoire. Pursuit of an ideal diet applicable to the entire population is a reductionist approach that overlooks the necessity of personalised interventions. The choice of dietary scheme should consider medical history, food preferences, psychosocial context, and the feasibility of sustained adherence.[8 9]

The population included in Semnani-Azad and colleagues' analysis encompassed adults with overweight, obesity, type 1 and type 2 diabetes, metabolic syndrome, and metabolic dysfunction associated steatotic liver disease, resulting in a wide clinical scope of intermittent fasting. This strategy gains further relevance considering that, according to the World Health Organization in 2022, about 2.5 billion adults, 43% of the global adult population, were overweight, and about 890 million (16%) lived with obesity.[10]

Pursuit of an ideal diet applicable to the entire population is a reductionist approach

A relevant methodological limitation is that many comparisons, especially those including alternate day fasting, were conducted against ad libitum diets, which, although without explicit energy restriction, may include general nutritional recommendations. Within this framework, any structured intervention—including continuous energy restriction—could show benefits derived not only from the dietary pattern but also from professional support, planning, and nutritional education. Diet quality during free eating days could affect alternate day fasting outcomes; however, this association has not been systematically evaluated in clinical trials. Studies specifically designed to isolate this component and understand its impact on metabolic outcomes are required.[11 12]

Likewise, studies shorter than 24 weeks reported adherence above 80%, whereas trials with follow-ups longer than 52 weeks showed a marked decline in adherence, especially in the whole day fasting group, with levels below 22% after one year.[4] In this regard, the clinical goal should not focus solely on weight loss or punctual metabolic improvements but on fostering sustainable changes over time.[13] Intermittent fasting does not aim to replace other dietary strategies but to integrate and complement them within a comprehensive, patient centred nutritional care model.

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Impact of pay for performance in primary care

ORIGINAL RESEARCH Systematic review with quantitative synthesis

Effect of UK Quality and Outcomes Framework pay-for-performance programme on quality of primary care

Ho L, Mercer SW, Henderson D, Donaghy E, Guthrie B

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Study question What was the impact on recorded quality of care of the introduction and withdrawal of financial incentives in the UK Quality and Outcomes Framework (QOF)?

Methods This systematic review included studies of introduction and withdrawal of QOF incentives that had consistent measurement of quality of care for at least three time points before and three time points after the introduction or withdrawal of incentives. Impact was evaluated for incentive introduction (83 indicators) and incentive withdrawal (31 indicators) at one and three years, either as reported by the underlying studies or estimated de novo from raw data if not reported.

Study answer and limitations QOF incentives consistently improved recorded quality of care at one year beyond that predicted by pre-incentivisation trends (median change 6.1 (interquartile range 1.9-14.6) percentage points), but by three years the change in recorded quality was inconsistent and not consistently better than expected on the basis of previous trends (median change 0.7 (−2.1-8.9) percentage points). Gains from incentivisation seemed to reverse after withdrawal of incentives. The study could not distinguish changes in data recording from changes in the care

COMMENTARY Lessons from the UK Quality and Outcomes Framework

When introduced in 2004, the UK Quality and Outcomes Framework (QOF) was one of the largest pay-for-performance programmes globally. The programme offered financial incentives to general practices based on their achievement against specific clinical targets.[1] Two decades later, the systematic review by Ho and colleagues evaluated the programme's effectiveness. The findings raise important questions about the value of pay-for-performance programmes for patients, clinicians, and policy makers.[2]

Ho and colleagues did a systematic review with quantitative synthesis to evaluate studies that assessed the impact of the introduction of QOF incentives (83 indicators) and their withdrawal (31 indicators). The study found that the introduction of QOF incentives was associated with an initial improvement in recorded quality of care at one year (median increase 6.1%), although this effect decreased by three years (median increase 0.7%).[2] Conversely, incentive withdrawal led to a decline in recorded quality at both one and three years (median decreases of 10.7% and 12.8%, respectively). This suggests that the effects of pay-for-performance programmes are often not sustained without financial motivation.[3] Complex process indicators, such as foot screening in patients with diabetes, had larger declines than simple process indicators (for example, blood pressure measurement), intermediate outcomes (for example, blood pressure control), and treatment indicators (for example, antithrombotic therapy).

The study findings highlight both the potential and the limitations of incentive based quality improvement.[4] Although the initial gains in quality indicators suggest that structured incentives can drive better data recording and adherence to guidelines, the lack of sustained improvement at three years raises concerns about long term clinical benefits. The reversal of quality gains following incentive withdrawal underscores the risk that financial incentives may encourage superficial compliance rather than deeply embedded improvements in care delivery.[5]

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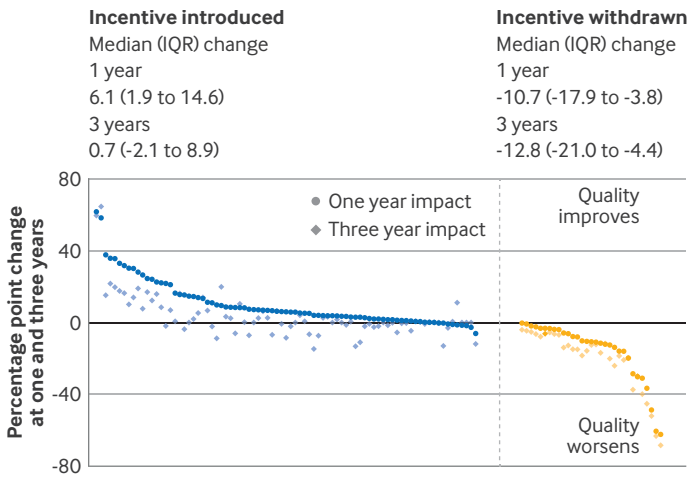

Change in recorded quality at one and three years after introduction and removal of incentives. Indicators ordered in descending order of one year impact/change, paired with three year impact/change on same vertical. IQR=interquartile range

actually provided to patients, and some indicators were already near maximum before incentivisation, limiting likely benefit.

What this study adds The financial incentives deployed under the UK QOF did not seem to provide sustained improvements in recorded quality of care, although on introduction they did stimulate activity in practices. Whether or how best to deploy financial incentives in primary care therefore remains uncertain, although financial incentives may have a role for engaging practices in broader quality improvement initiatives.

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Study registration Prospero CRD42023467627.

Pay-for-performance schemes such as the QOF provide structured targets that can standardise data recording and improve care. But the study also suggests that such incentives do not foster enduring improvements, thereby raising concerns about whether the financial rewards justify the associated administrative burden on primary care teams.[6] Moreover, "crowding out" effects may also be seen, whereby the focus on incentivised conditions may have come at the expense of important but non-incentivised aspects of healthcare.

What the findings mean

Ho and colleagues' work highlights the importance of robust evaluation to distinguish true changes in quality of care from underlying trends.[7] The study also identifies some key gaps in knowledge that warrant further research. For example, what are the underlying mechanisms that lead to the decline in quality following incentive withdrawal? Is it a reflection of reduced documentation, or do structural and behavioural changes revert in the absence of financial motivation? Secondly, how do pay-for-performance schemes interact with broader system factors, such as workforce shortages, workload pressures, and funding shortfalls? The study also raises important methodological considerations for future evaluations. The reliance on recorded quality metrics as opposed to patient reported outcomes means that some of the observed improvements could be artefacts of better data entry rather than true clinical benefits.

We need to retain the most effective elements of programmes such as the QOF

For policy makers, the study offers an assessment of the long term impact of the QOF. Although the scheme showed initial quality gains, its failure to sustain improvements over time suggests that financial incentives alone are insufficient to drive lasting changes in quality of care. This has important implications for the design of future pay-for-performance programmes. Policy makers must consider how to transition from short term financial incentives to mechanisms that embed quality improvement into everyday practice—for example, by promoting greater continuity of care.[9] The findings also suggest that incentive structures should be designed with a focus on their sustainability.

Going beyond QOF

The mixed results of the QOF programme in the UK illustrate that although financial incentives can drive short term improvements, they do not necessarily build a resilient, self-sustaining system of high quality care. Policy makers must therefore be wary of over-reliance on pay-for-performance programmes and consider integrating financial incentives within a wider strategy for quality improvement.[10] As health systems globally continue to grapple with the challenge of improving quality of care in an era of financial restrictions, the lessons from the QOF programme in the UK can help in developing more effective and sustainable approaches to incentivising high quality primary care.

The UK has already begun to diverge in its approach to the implementation of the QOF in primary care, with Scotland abolishing its own programme in 2016.[11] In England, and in other countries that have similar schemes, we need to retain the most effective elements of programmes such as the QOF, particularly areas focused on the early detection and management of long term conditions (such as hypertension and heart failure), while discarding the less useful parts (for example, non-clinical indicators such as those focused on workforce). The aim should be to incentivise long term quality improvements while minimising administrative burdens and unintended consequences.[12 13] An effective QOF programme that focuses on key clinical areas and that makes best use of developments in information technology remains essential for the NHS if we are to reduce health inequalities, increase healthcare efficiency, and improve health outcomes.

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Comparative effectiveness of interventions to facilitate deprescription of benzodiazepines and other sedative hypnotics

Zeraatkar D, Nagraj SK, Ling M, et al

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Study question What are the most effective strategies for deprescribing benzodiazepines and related sedative hypnotics (BSH) in patients with insomnia?

Methods Studies eligible for this systematic review randomised adults using BSH for insomnia to interventions aimed at deprescribing BSH, strategies to implement these interventions in healthcare settings, or usual care or placebo. Reviewers worked independently and in duplicate to screen search results, extract data, and assess risk of bias. Similar interventions were grouped together, frequentist random effects meta-analysis performed, and the certainty of evidence assessed using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach.

Study answer and limitations The evidence to guide patients and clinicians on the effectiveness of strategies to discontinue BSH is uncertain. Low certainty evidence suggests that educating patients (144 (95% confidence interval 61 to 246) more per 1000 patients), medication review (104 (34 to 191) more), and enabling pharmacists to educate patients and doctors (491 (234 to 928) more) may increase the proportion of patients who discontinue BSH. No compelling evidence was found that tapering, education of doctors, the combination of education of patients and doctors, cognitive behavioural therapy, mindfulness, other pharmacist led interventions, and drug supported tapering and withdrawal strategies are effective. Low certainty evidence suggests that multicomponent interventions may be more effective at facilitating discontinuation of BSH than single component interventions. Despite rigorous searching of the literature, eligible trials might have been missed. Insufficient data were available for subgroup analyses to determine whether the effects of interventions differ according to various characteristics.

ANDRIY POPOV/ALAMY

Summary of results of interventions that may increase proportion of patients who discontinue BSH

Intervention (versus usual care)	Discontinuations	Odds ratio (95% CI)
Education of patients	144 more (95% CI 61 more to 246 more) per 1000 (8 trials; 4055 patients)	2.53 (1.58 to 4.04)
Medication review	104 more (95% CI 34 more to 191 more) per 1000 (2 trials; 736 patients)	2.04 (1.31 to 3.17)
Pharmacist led educational intervention	491 more (95% CI 234 more to 928 more) per 1000 (1 trial; 301 patients)	4.78 (2.80 to 8.14)*

BSH= benzodiazepines and related sedative hypnotics; CI=confidence interval.
*Risk ratio.

What this study adds This study suggests that certain strategies, such as patient education, medication review, and pharmacist led educational interventions, may increase the chances of discontinuation of BSH in patients with insomnia.

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