National Institute for Health and Care Excellence

Final

Overweight and obesity management: preventing, assessing and managing overweight and obesity

[F] Evidence reviews for the effectiveness of different diets in achieving and maintaining weight loss

NICE guideline NG246

Evidence reviews underpinning recommendations 1.16.1 to 1.16.12 and research recommendations in the NICE guideline

January 2025

Final

These evidence reviews were developed by NICE

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Contents

Effectiveness of different diets in achieving and maintaining weight loss

1.1 Review question

What is the effectiveness and cost effectiveness of total or partial meal replacements, intermittent fasting, plant-based and low carbohydrate diets, in achieving and maintaining weight loss in adults living with overweight or obesity?

1.1.1 Introduction

Dietary interventions are a treatment option for people living with overweight or obesity. The 2014 NICE guidance on obesity identification, assessment and management (CG189) included a number of recommendations on general dietary approaches, low-calorie diets and very low-calorie diets. The guideline stipulated that the main requirement of a dietary approach to weight loss is that total energy intake should be less than energy expenditure. The guideline also recommended that low calorie diets should be considered but these are less likely to be nutritionally complete and that very-low-calorie diets should only be considered as part of a multicomponent strategy, for people who are living with obesity and who have clinically assessed need to rapidly lose weight.

During the surveillance process, evidence was identified on the use of low and very low-energy diets. Based on this finding, an update was conducted that explored the effectiveness and cost effectiveness of different diets including energy restricted diets (low-energy and very-low-energy diets), macronutrient diets (low carbohydrate and very-low carbohydrate diets), plant-based diets and intermittent energy restriction.

1.1.2 Summary of the protocol

Table 1: PICO table for effectiveness of different diets in achieving and maintaining weight loss

Population	**Inclusion:** • Adults over the age of 18 living with overweight or obesity Where possible people with type 2 diabetes or prediabetes will be stratified and analysed separately **Exclusion:** • Pregnant women • People of healthy weight
Intervention	**Energy restricted diets:** • Low energy (total or partial replacement) diets including low energy liquid diets (defined as diet containing 800-1200 calories per day) • Very low (total or partial replacement) energy diets (defined as diets containing less than 800 calories per day) **Macronutrient diets:** • Low carbohydrate diet (defined as under 130g of carbohydrates) • Very low carbohydrate (defined as under 50g of carbohydrates) **Other diets:** • Plant based diets with a calorie deficit. (Plant based diets defined as diets excluding meat and fish e.g., vegetarian, and vegan diets). • Intermittent energy restriction (patient led fasting)

	◦ Time restricted eating: ◦ Intermittent fasting (e.g., 16/8 intermittent fasting) ◦ Alternate day fasting ◦ Fasting for two days (e.g. 5:2 diet) Note: Studies providing support to participants, for example behavioural therapy (behavioural weight management advice, psychological support) and exercise alongside the diets will be included.
Comparator	**Primary comparators:** • Interventions compared to each other. • Usual care defined use of conventional/ balanced diet with calorie deficit (restriction in total energy intake) • No intervention If studies including primary comparators are not identified, studies including secondary comparators will be included: **Secondary comparators:** • Usual care as defined as: ◦ behavioural weight management advice ◦ General health promotion advice
Outcome (s)	**Primary outcomes (critical outcomes)** • Change in weight (kg) or change in BMI from baseline (including % change) • Health related quality of life measured by validated tools • Adverse events: ◦ Serious adverse events ◦ Development of eating disorders or disordered eating ◦ Hypoglycaemia ◦ Constipation ◦ Gallbladder problems ◦ Hair loss (transient alopecia) ◦ Hypotension **Secondary outcomes (important outcomes)** • Change in waist circumference (WC) • Behavioural change measured using validated tools • Adherence to intervention offered • Change in HbA1c Minimum follow-up of 12 months

1.1.3 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document.

Declarations of interest

Declarations of interest were recorded according to NICE's conflicts of interest policy.

Evidence selection

In this review, a stepped approach was planned for the search. Firstly, a search was conducted to identify systematic reviews (SRs) conducted between 2015 to 2022 and 2006 to 2014. Systematic reviews conducted between 2015 and 2022 exploring the effectiveness of different diets were prioritised and were initially sifted. If relevant SRs published between 2015 and 2022 were not identified, the next step was to search for SRs conducted between 2006 and 2014. Systematic reviews were used as a source of primary studies. If several systematic reviews were found covering the same interventions, the most recent systematic review was included. If the SR conducted a sufficiently rigorous risk of bias assessment (preferably using Cochrane risk of bias tool 2.0), this was used as the basis of our quality assessment. Evidence tables containing study characteristics were not created for RCTs identified through SRs but can be found in the original SRs.

Secondly, a sift was conducted to identify parallel RCTs and cluster RCTs published between 2015 and 2022 and 2006 and 2014. Individual parallel and cluster RCTs published between 2015 and 2022 were prioritised if gaps were identified in the evidence base. Additionally, studies would be added to the existing systematic reviews that were published after the search date. If additional gaps were identified in the evidence base, individual parallel and cluster RCTs published between 2006 and 2014 were identified for inclusion.

1.1.4 Effectiveness evidence

1.1.4.1 Included studies

In total, 40,030 records were identified from the search and 11 additional records were identified by the development team. After removing 17,538 duplicate records, 22,503 records were screened at title and abstract. Of these, 20,414 records were identified through the initial search conducted in March 2022, and a further 2,078 were identified through an updated search conducted in April 2023 to identify any new evidence published since the initial search.

A breakdown of the number of systematic reviews and primary studies is highlighted below, and a PRISMA diagram detailing the evidence selection process is provided in appendix C.

Systematic reviews

Following title and abstract screening, 174 SRs were included and ordered for full text review. 149 SRs were published from 2015 to 2022 and 25 were identified from the update search. No SRs published from 2006-2014 were included at title and abstract stage.

At full text stage, 6 of these systematic reviews matched the inclusion criteria. Included study information for these SRs is shown in Table 2. See the references in section 1.1.12 for hyperlinks to each included SR.

Primary studies

Following title and abstract screening, 343 RCTs were included and ordered for full text review. Of these, 96 were RCTs published between 2006 and 2014 and 213 were RCTs published between 2015 and 2022. A further 34 RCTs were identified from the update search.

At full text stage, 60 RCTs matched the inclusion criteria. This comprised 36 studies that had already been identified from the included SRs, 22 additional studies identified through the search and 2 studies identified from the update search. Details of the studies included from the SRs are shown in Table 3 and details of all included studies are shown in Tables 4-17.

1.1.4.2 Excluded studies

There were 451 studies excluded at full text screening (168 systematic reviews and 283 primary studies). The list of excluded studies and reasons for exclusion are provided in appendix I.

Table 2: Summary of included systematic reviews.

Author (year)	Systematic review details	Population identified	Interventions identified	Relevant outcomes identified
Astbury 2019	• 23 RCTs [3 RCTs matched our inclusion criteria] • The databases were searched from their inception to August 2018.	• Mixed population[a] • People with T2DM	• Low energy partial diet replacements	• Change in weight (kg) • Change in HbA1c
Nicholas 2021	• 15 RCTs [3 RCTs matched our inclusion criteria] • The databases were searched from their inception to July 2020	• People with T2DM	• Low energy total meal replacement	• Change in weight (kg) • Change in HbA1c
Parretti 2016	• 12 RCTs [3 RCTs matched our inclusion criteria] • The databases were searched from inception to November 2014	• Mixed population	• Very low energy total meal replacement	• Change in weight (kg) • Adverse events • Change in HbA1c
Naude 2022	• 61 RCTs [19 matched our inclusion criteria] • The databases were searched from inception to 25th June 2021	• Mixed population • People with T2DM	• Low carbohydrate diet • Very low carbohydrate diet	• Change in weight (kg) • Adverse events • Change in HbA1c
Rafiullah 2022	• 10 RCTs [4 RCTs matched our inclusion criteria] • The databases were searched from January 1st, 1980, to September 30th 2019	• People with T2DM	• Very low carbohydrate diet	• Change in weight (kg) • Change in HbA1c

Schwingshackl 2021	• 17 RCTs [4 met our inclusion criteria] • The databases were searched from inception to September 25th March 2019	• Mixed population • People with T2DM	• IER (5:2 Diet) • IER (Alternate day fast)	• Change in weight (kg) • Change in BMI • Adverse events • Change in waist circumference (WC)

[a] Mixed population refers to a sample including people living with overweight or people living with obesity.

1.1.5 Summary of studies included in the effectiveness evidence

Table 3 provides a high-level summary of the primary studies included from the SRs. Tables 4 to 17 provide a more detailed summary of all included primary studies and are presented by diet type and population.

Table 3: Summary of primary studies included from the systematic reviews

Systematic review author (year)	Primary studies included in review	Population	Intervention	Comparator	Risk of bias reported in study
Low energy meal replacement diet (Total or partial meal replacement)					
Astbury 2019[1]	Khoo 2011	T2DM population	Low energy partial meal replacement	Usual care (conventional diet)	Moderate
	Ashley 2007	Mixed population	Low energy partial meal replacement + support	Usual care (conventional diet) + support	Moderate
	Shikany 2013	Mixed population	Low energy partial meal replacement + support	Usual care (conventional diet + advice)	Low
Nicholas 2021[2]	Brown 2020	T2DM population	Low energy total meal replacement + support	Usual care (conventional diet) + support	High
	Lean 2018 (DiRECT trial)	T2DM population	Low energy total meal replacement + support	Usual care (advice)	High
	Taheri 2020 (DIADEM-I Trial)	T2DM population	Low energy total meal replacement + support	Usual care (advice)	Moderate
Very low energy meal replacement diet (Total or partial meal replacement)					
Parretti 2016[3]	Purcell 2014	Mixed population	Very low energy total meal replacement + support	Usual care (conventional diet) + support	Low
	Tuomilehto 2009 & Tuomilehto 2010	Mixed population	Very low energy total meal replacement + support	Usual care (advice)	Moderate
Low carbohydrate diet					
Naude 2022[4]	Calleja Fernandez 2012	Mixed population	Low carbohydrate diet+ support	Usual care (conventional diet) + support	High

Systematic review author (year)	Primary studies included in review	Population	Intervention	Comparator	Risk of bias reported in study
	Ebbeling 2007	Mixed population	Low carbohydrate diet+ support	Usual care (conventional diet) + support	High
	Foraker 2014	Mixed population	Low carbohydrate diet+ support	Usual care (conventional diet) + support	High
	Frisch 2009	Mixed population	Low carbohydrate diet+ support	Usual care (conventional diet) + support	High
	Klemsdal 2010	Mixed population	Low carbohydrate diet+ support	Usual care (conventional diet) + support	High
	Sacks 2009 (POUNDS LOST Trial)	Mixed population	Low carbohydrate diet+ support	Usual care (conventional diet) + support	High
	Griffin 2013	Mixed population	Low carbohydrate diet+ support	Usual care (conventional diet) + support	High
	Wycherley 2012	Mixed population	Low carbohydrate diet+ support	Usual care (conventional diet) + support	High
	Melberg 2014	Mixed population	Low carbohydrate diet+ support	Usual care (conventional diet) + support	High
	Pedersen 2014	T2DM population	Low carbohydrate diet	Usual care (conventional diet)	High
	Elhayany 2010	T2DM population	Low carbohydrate diet+ support	Usual care (conventional diet) + support	High
	Guldbrand 2012 and Guldbrand 2014	T2DM population	Low carbohydrate diet+ support	Usual care (conventional diet) + support	High
	Krebs 2012	T2DM population	Low carbohydrate diet+ support	Usual care (conventional diet) + support	Moderate
	Larsen 2011	T2DM population	Low carbohydrate diet+ support	Usual care (conventional diet) + support	
Very low carbohydrate diet					

Systematic review author (year)	Primary studies included in review	Population	Intervention	Comparator	Risk of bias reported in study
Naude 2022[4]	Bazzano 2014	Mixed population	Very low carbohydrate diet+ support	Usual care (conventional diet) + support	Moderate
	Foster 2010	Mixed population	Very low carbohydrate diet+ support	Usual care (conventional diet) + support	High
	Layman 2009	Mixed population	Very low carbohydrate diet+ support	Usual care (conventional diet) + support	High
	Lim 2010	Mixed population	Very low carbohydrate diet+ support	Usual care (conventional diet) + support	High
	Saslow 2017*	T2DM population	Very low carbohydrate diet+ support	Usual care (conventional diet) + support No intervention	High
Rafiullah 2022[5]	Goldstein 2012	T2DM population	Very low carbohydrate diet+ support	Usual care (conventional diet) + support	High
	Iqbal 2010	T2DM population	Very low carbohydrate diet+ support	Usual care (conventional diet) + support	High
	Saslow 2017*	T2DM population	Very low carbohydrate diet+ support	Usual care (conventional diet) + support	High
	Tay 2015	T2DM population	Very low carbohydrate diet+ support	Usual care (conventional diet) + support	Moderate
Intermittent energy restriction					
Schwingshackl 2021[6]	Schubel 2018 (HELENA Trial)	Mixed population	IER (5:2 Diet) + support	Usual care (advice) + support Usual care (conventional diet) + support	Moderate
	Trepanowski 2017	Mixed population	IER (Alternate day fast) + support	Usual care (conventional diet) + support No intervention	High
	Sundfor 2018	Mixed population	IER (5:2 Diet) + support	Usual care (conventional diet) + support	High
	Carter 2018	T2DM population	IER (5:2 Diet) + support	Usual care (conventional diet) + support	High

**Study picked up from two different systematic reviews.*
1. Astbury 2019- Systematic review used Cochrane Risk of Bias Tool 1. Overall rating not provided however risk of bias for each domain was presented. This was used to determine overall risk of bias.
2. Nicholas 2021 - Systematic review used Cochrane Risk of Bias Tool 1. Overall rating not provided however risk of bias for each domain was presented. This was used to determine overall risk of bias.
3. Parretti 2016 - Systematic review used Cochrane Risk of Bias Tool 1. Overall rating not provided however risk of bias for each domain was presented. This was used to determine overall risk of bias.
4. Naude 2022 - Systematic review used Cochrane Risk of Bias Tool 2. Overall rating was provided.
5. Rafiullah 2022 - Systematic review used Cochrane Risk of Bias Tool 2. Overall rating not provided however risk of bias for each domain was presented. This was used to determine overall risk of bias.
6. Schwingshackl 2021 - Systematic review used Cochrane Risk of Bias Tool 2. Overall rating not provided however risk of bias for each domain was presented. This was used to determine overall risk of bias.

Primary studies

Low energy diet - TOTAL meal replacement (TMR)

Table 4: Summary of studies looking at Low energy diet (TMR) in a mixed population

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
Low energy diet TOTAL meal replacement + support vs Usual care + support						
Ard 2019 (OPTIWIN Trial) * RCT	USA Nestlé Healthcare Nutrition	330 (12% living with type 2 diabetes (T2D))	People 18 to 70 years old with BMI of 30 to 55 kg/m² 5 private clinics and 4 academic medical centres	**Low energy total meal replacement + support:** Total MR diet using Optifast for 12-16 weeks. Medical monitoring and counselling included. Participants also had weekly 45-60-minute group behavioural sessions and received prescriptions for physical activity. Participants with BMI <45 were instructed to use five MRs per day	**Usual care (conventional diet) + support:** Modified version of the Diabetes Prevention Program (DPP) intervention. Medical monitoring and counselling included. Participants also had weekly 45- 60-minute group behavioural sessions and received prescriptions for physical activity.	• Change in weight (%) at 1 year from baseline • Serious adverse events at 1 year from baseline • Change in waist circumference (cm) at 1 year from baseline • Adherence at 1 year from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
				(800 kcal total) with 40% of calories as protein, 40% as carbohydrate, 20% as fat. Participants with BMI of 45 to 49.9 received six MRs per day (960 kcal), those with BMI≥ 50 received six MRs plus one meal daily of lean protein (3-4 ounces) and one non-starchy vegetable serving (1,100- 1,200 kcal) Participants followed their prescription for 12 to 16 weeks based on provider discretion and patient preference, after which there was gradual reintroduction of food through week 26. After week 26, participants' calories were gradually increased to achieve weight stability. During this time, participants were advised to use one to two MRs daily to facilitate weight-loss maintenance. Active intervention period: 26 weeks	During active weight loss, participants were prescribed a calorie-restricted diet emphasising lower fat intake (25%- 30% of total calories). They were advised to reduce calories by 500 to 750 kcal below estimated total energy expenditure. Active intervention period: 26 weeks	
Low energy diet TOTAL meal replacement + support vs Usual care						
Astbury 2018* & Astbury 2021*	UK Cambridge Weight Plan UK	278 (15% of total population living with T2D)	Adults living with a BMI of at least 30 kg/m² 10 primary care practices	**Low energy total meal replacement + support:** For 8 weeks, participants replaced all food with four formula food products daily (soups, shakes and bars), 750 mL of skimmed milk, 2.25 L of water or other low or no	**Usual care (advice):** Participants followed each practice's usual weight management protocol. Participants also received booklet on goal setting, monitoring, and feedback,	• Change in weight (kg) at 1 and 3 years from baseline • Change in waist circumference (cm) at 1

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
DROPLET study RCT				energy drinks, and a fibre supplement; energy intake comprised 810 kcal/day. After, there was a four-week stepwise reduction in use of the formula food products and reintroduction of conventional food-based meals. Behavioural support was provided for 8 weeks, bi-weekly for the next 4 weeks, then monthly for 3 months after which no further support was provided. During the weight maintenance phase from week 13 and 24, counsellors encouraged participants to attend monthly appointments and to consume one formula food product a day, with the remainder of the diet provided by food. Active intervention duration: 24 weeks	and advice about food types, portion control and physical activity.	and 3 years from baseline • Change in HbA1c (mmol/mol) at 1 and 3 years from baseline • Change in QoL at 1 and 3 years from baseline • Serious AEs at 1 year from baseline Outcomes in type 2 diabetes population are outlined separately.

** Denotes new primary studies identified through the search.*

Table 5: Summary of studies looking at Low energy diet (TMR) in people with type 2 diabetes

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
Low energy diet TOTAL meal replacement + support vs Usual care + support						
Brown 2020 RCT	UK Cambridge Weight Plan	90	People 18-70 years old living with type 2 diabetes and obesity (≥30kg/m²). 2 hospitals in London	**Low energy total meal replacement + support:** Participants commenced a 12-week total diet replacement using Cambridge Weight Plan. All meals were replaced with four formula low energy diet products per day (800-820 kcal/ day, 57% carbohydrate, 14% fat, 26% protein and 3% fibre) in addition to at least 2.5 litres of energy-free beverages. A fibre supplement was recommended, if required, to avoid constipation, a common side effect of using total diet replacement. This was followed by 12 weeks of structured food reintroduction and then ongoing follow-up in combination with an energy deficit diet at 3-month intervals until 12 months. Participants received counselling support by the same specialist dietician after 1 week and then monthly for the first 6 months. During the maintenance phase participants received the standard type2 diabetes healthcare profession with t face-to-face sessions from 6 months to 12 months. Participants received behavioural	**Usual care (conventional diet) + support:** Participants followed a standardized weight management program using a 600-kcal deficit for 12 months. Participants received counselling support by the same specialist dietician after 1 week and then monthly for the first 6 months. During the maintenance phase participants received the standard type2 diabetes healthcare profession with tow face-to-face sessions from 6 months to 12 months. Participants received behavioural support to aid lifestyle adherence and maintenance. Active intervention duration: 12 months	Change in weight (kg) at 1 year from baseline % Change in HbA1c at 1 year from baseline Change in waist at 1 year circumference (cm) at 1 year from baseline Change in QoL at 1 year from baseline Serious adverse events at 1 year from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
				support to aid lifestyle adherence and maintenance. Active intervention duration: 12 weeks		
Low energy diet TOTAL meal replacement + support vs Usual care						
Lean 2018 & Lean 2019* DiRECT Cluster RCT	UK	306	Adults 20-65 years old living with type 2 diabetes and a BMI of 27-45 kg/m2 49 primary care practices in Scotland/England	**Low energy total meal replacement + support:** Participants were asked to follow the Counterweight-Plus weight management programme. Weight loss was induced with a total diet replacement phase using a low energy formula diet (825- 853 kcal/day; 59% carbohydrate, 13% fat, 26% protein, 2% fibre) for 3 months (extendable up to 5 months if wished by participant), followed by structured reintroduction of 2-8 weeks (about 50% carbohydrate, 35% fat and 15% protein, and an ongoing structured programme with monthly visits for long-term weight loss maintenance. Participants were encouraged to maintain their usual physical activities. For the maintenance phase, from the end of food reintroduction up to 24 months, participants were offered monthly 30-minute appointments with the dietician or practice nurse, using tailored workbooks.	**Usual care (advice):** Participants continued with best-practice routine care with no change to dietary, medication or exercise advice. Active intervention phase: Up to 27 weeks	Change in weight (kg) at 1 and 2 years from baseline Change in HbA1c at 1 and 2 years Change in QoL at 1 and 2 years from baseline Serious adverse events at 1 and 2 years from baseline Adherence at 1 year from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
				Active intervention phase: Up to 27 weeks		
Astbury 2018* & Astbury 2021* DROPLET study RCT	UK Cambridge Weight Plan UK	278 (15% of total population living with T2D)	Adults living with a BMI of at least 30 kg/m² 10 primary care practices	**Low energy total meal replacement + support:** For 8 weeks, participants replaced all food with four formula food products daily (soups, shakes and bars), 750 mL of skimmed milk, 2.25 L of water or other low or no energy drinks, and a fibre supplement; energy intake comprised 810 kcal/day. After, there was a four-week stepwise reduction in use of the formula food products and reintroduction of conventional food-based meals. Behavioural support was provided for 8 weeks, bi-weekly for the next 4 weeks, then monthly for 3 months after which no further support was provided. During the weight maintenance phase from week 13 and 24, counsellors encouraged participants to attend monthly appointments and to consume one formula food product a day, with the remainder of the diet provided by food. Active intervention duration: 24 weeks	**Usual care (advice):** Participants followed each practice's usual weight management protocol. Participants also received booklet on goal setting, monitoring, and feedback, and advice about food types, portion control and physical activity.	• Change in weight (kg) at 1 and 3 years from baseline • Change in waist circumference (cm) at 1 and 3 years from baseline • Change in HbA1c (mmol/mol) at 1 and 3 years from baseline
Taheri 2020 DIADEM-I study	Qatar Qatar National	158	Adults 18-50 years old, with a diagnosis of type 2 diabetes	**Low energy total meal replacement + support:**	**Usual care (advice):** Participants in the control group received	Change in weight (kg) at 1 year from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
RCT	Research Fund.		within the previous 3 years and had a BMI of 27.0 kg/m² 1 primary health-care centre and 1 community health-care centre	Participants underwent a 12-week total diet replacement phase, in which they were given formula low-energy (800-820 kcal/day diet meal replacement products (57% carbohydrate, 14% fat, 26% protein and 3% fibre; Cambridge Weight Plan, Northants, UK). This was followed by a 12-week structured food reintroduction phase. When food was reintroduced, a regular meal pattern with a similar distribution of macronutrients as the meal replacement products was recommended. Participants were advised to aim for low-glycaemic index carbohydrates. Physical activity support initially focused on walking (with an aim of at least 10,000 steps per day), followed by the recommendation of increasing unsupervised activity to at least 150 min/week. Thereafter, participants managed their own energy restricted food intake and lifestyle changes for 6 months. Participants were supported by a team of trained dietitians, personal trainers, and physician. During both phases, participants were seen by dietitians and personal trainers once every 2 weeks. Thereafter, participants attended the intervention clinic once per month.	usual medical diabetes care according to clinical guidelines. Standard diet and activity advice, and diabetes education were provided. Participants were seen by a physician at baseline and then once every 3 months thereafter. Participants had access to diabetes educators and dieticians in both primary and secondary care.	Change in waist circumference (cm) at 1 year from baseline Change in QoL at 1 year from baseline Change in HbA1c at 1 year from baseline Serious adverse events at 1 year from baseline

<table>
<tr><th>Author (year) and study type</th><th>Country and funder</th><th>Sample size</th><th>Population and setting</th><th>Intervention</th><th>Comparator</th><th>Outcomes</th></tr>
<tr><td></td><td></td><td></td><td></td><td>Active intervention phase: 24 weeks</td><td></td><td></td></tr>
<tr><td colspan="7">Low energy diet TOTAL meal replacement + support vs Intermittent fasting + support</td></tr>
<tr><td>McDiarmid 2022*

MIDDAS Trial

Pilot RCT</td><td>UK

Néstle Health Science and Oviva UK Limited</td><td>79</td><td>People with overweight or obesity and type 2 diabetes, including those on insulin.

3 general practices, 2 NHS hospital trusts and a volunteer research register</td><td>Low energy total meal replacement + support:
Participants were asked to follow the Optifast low-energy diet providing about 820 kcal/ day for 8 weeks. This consisted of three sachets/day (200 kcal per sachet of shake/soup):<table><tr><th></th><th>1 Optifast sachet</th><th>1 low calorie day (3 sachets with vegetables and oil)</th></tr><tr><td>Carbs (g)</td><td>18</td><td>79</td></tr><tr><td>Protein (g)</td><td>20</td><td>69</td></tr><tr><td>Fat (g)</td><td>4.5</td><td>26</td></tr><tr><td>Calories</td><td>200</td><td>820</td></tr></table>
Participants who were unable to tolerate Optifast were offered a food-based low energy diet with a similar macronutrient profile.
This was followed by stepped food reintroduction from 1000 kcal to 1500 kcal over 4 weeks.

Group entered a continued weight loss phase (if achieved ≤ weight loss or</td><td>Intermittent energy restriction (5:2 diet) + support:
2 consecutive days per week of the Optifast LED plus 5 days of a Mediterranean diet or 1 day of food-based 800 kcal/day low energy diet plus 6 days Mediterranean diet.

Group entered a continued weight loss phase (if achieved ≤ weight loss or more than target weight loss). Continued weight loss involved a daily 25% energy restricted Mediterranean diet and 2 days/ week of food based low energy diet (800 kcal/day). This phase was for 40 weeks.

Participants were encourage to aim for 30 min of moderate intensity physical activity</td><td>Change in weight (kg) at 1 year
Change in HbA1c at 1 year
Serious adverse events at 1 year from follow up
Adherence via trial retention at 1 year from follow up</td></tr>
</table>

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
				more than target weight loss). Continued weight loss involved a daily 25% energy restricted Mediterranean diet and 2 days/ week of food based low energy diet (800 kcal/day). This phase was for 40 weeks. Participants were encouraged to aim for 30 min of moderate intensity physical activity 5 days/ week and resistance exercise. Both groups received matched behavioural support from the multi-disciplinary team (MDT), which included a diabetes specialist dietician and nurse, exercise specialist and psychologist. The dietician contacted patients weekly in weeks 1-12, fortnightly in weeks 12-28 and month in weeks 29-52. Active intervention phase: 12 weeks	5 days/ week and resistance exercise. Both groups received matched behavioural support from the multi-disciplinary team (MDT), which included a diabetes specialist dietician and nurse, exercise specialist and psychologist. The dietician contacted patients weekly in weeks 1-12, fortnightly in weeks 12-28 and month in weeks 29-52. Active intervention phase: 28 weeks	

** Denotes new primary studies identified through the search.*

Low energy diet - PARTIAL meal replacement (PMR)

Table 6: Summary of studies looking at Low energy diet (PMR) in a mixed population

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
Low energy diet PARTIAL replacement + support vs Usual care + support						

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
Ashley 2007 RCT	USA SlimFast/ Unilever	96 (T2D not detailed)	Women 25 to 50 years old with BMI of 25 to 35 kg/m² Local university community	**Low energy partial meal replacement + support:** Partial MR for 2/3 of daily meals. People were given a choice of the brand of MR drink/meal. Subjects attended classes and received instructions from a registered dietician. Diet instructions for all subjects included a low energy diet of approximately 1200 kcal/day). Each liquid meal replacement drink contained 220 kcal, 7 to 10 grams of protein, 40 to 46 grams of carbohydrate, 5 grams of dietary fibre and 1.5 to 3 grams of fat. Subjects were able to choose from the study brand of either milk-based and soy-based meal replacement drinks. The study meal replacement bars contained approximately 220 kcals, with 8 grams of protein, 22 to36 grams of carbohydrates, 2 grams of dietary fibre and 5 grams of fat. Active intervention period: 1 year	**Usual care (conventional diet) + support:** Traditional Food Group: a diet plan based on self-selection of conventional foods for meals and snacks using the USDA Food Guide Pyramid. Subjects attended classes and received instructions from a registered dietician. Diet instructions for all subjects included a low energy diet of approximately 1200 kcal/day). Intervention duration: 1 year	• Change in weight (kg) at 1 year from baseline • Change in waist circumference (cm) at 1 year from baseline
Low energy diet PARTIAL meal replacement + support vs Usual care						

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
Shikany 2013 RCT	USA Medifast Inc.	120 (none living with T2D)	Adults 19-65 years old living with a BMI of 30-50 kg/m² Recruited from the Birmingham, Alabama area	**Low energy partial meal replacement + support** The plan consisted of five portion-controlled, nutritionally balanced, low-fat meals plus one 'lean & Green' meal each day. The plan provided approximately 800 – 1,000 kcal/ day, depending on personal selections. The Lean & Green meal consisted of a lean protein source plus vegetables selected and provided by the participant from a list provided in the Quick Start Guide. The support consisted of online access to resources, including dieticians, trainers, recipes, message boards, and chat rooms, allowing participants to interact with other on the same plan. Active intervention phase was followed by a 26-week weight maintenance phase. Participants were given the option of including 0-3 Medifast meals/day to reach their energy needs. Participants were contacted during the maintenance phase either by telephone or clinic visits (until week 46) to address any concerns and ask out weight loss.	**Usual care (conventional diet + advice):** Participants provided with a 1,000 kcal/ day meal plan based on regular foods selected, procured, and prepared by the participants. Food lists, sample menus, and a portion size reference were provided. Participants were advised to take a daily multi-vitamin/ mineral supplement. Active intervention phase was followed by a 26-week weight maintenance phase. Participants remained on food based diet. Participants were contacted during the maintenance phase either by telephone or clinic visits (until week 46) to address any concerns and ask out weight loss. Active intervention duration: 26 weeks	• Change in weight (kg) at 1 year from baseline • Change in waist circumference (cm) at 1 year from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
				Active intervention duration: 26 weeks		

** Denotes new primary studies identified through the search.*

Table 7: Summary of studies looking at Low energy diet (PMR) in people with type 2 diabetes

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
Low energy diet PARTIAL meal replacement vs Usual care						
Khoo 2011 RCT	Australia National Heart Foundation Australia and Medical Benefits Foundation	31	Abdominal obesity (BMI > 30 kg/m² & WC ≥ 102 cm) Caucasian men living with type 2 diabetes. A community in Adelaide, South Australia,	**Low energy partial meal replacement:** Participants consumed two sachets daily (one at breakfast and lunch or dinner) of a liquid meal replacement, providing a maximum of 450 kcal of energy, 0.8 g/kg ideal body weight of protein, and the recommended daily allowances of minerals, vitamins, and omega-3 and omega-6 essential fatty acids, plus one other small meal, for a total of ~900 kcal/ day. All participants received a written plan with detailed diet plan, recipes, and advice on cooking and eating out.	**Usual care (conventional diet):** Participants were prescribed to reduce daily energy intake by ~600 kcal, including 300g of lean meat/ poultry/fish, and three servings/day of cereals/bread and low-fat dairy foods and two fruit and five vegetable serves per day. All participants received a written plan with detailed diet plan, recipes, and advice on cooking and eating out.	• Change in weight (kg) at 1 year from baseline • Change in waist at 1 year circumference (cm) at 1 year from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
				After 8 weeks, participants were switched to the usual care diet plan for another 44 weeks. Active intervention duration: 8 weeks	After 8 weeks, participants continued on the usual care diet plan for another 44 weeks. Active intervention duration: 52 weeks	

** Denotes new primary studies identified through the search.*

Very low energy diet – TOTAL meal replacement (TMR)

Table 8: Summary of studies looking at Very low energy diet (TMR) in a mixed population

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
Very low energy diet TOTAL meal replacement + support vs Usual care + support						
Purcell 2014 RCT	Australia Australian National Health and Medical Research Council and the Sir Edward Dunlop Medical Research	200	People 18-70 years old living with a BMI of 30-45 kg/m² Clinical Research Unit at a Melbourne metropolitan hospital.	**Very low energy total meal replacement + support:** In the rapid weight loss programme, participants consumed a commercially available very low energy diet preparation (Optifast) according to the manufacturer’s recommendation for 12 weeks. This diet contains between 450 and 800 kcal per day.	**Usual care (conventional diet) + support:** In the gradual weight loss programme, participants consumed an energy-reduced diet (400–500 kcal per day deficit), on the basis of recommendations in the Australian Guide to	Change in weight (kg) at 1, 2 and 3 years from baseline Change in waist circumference (cm) at 1 year from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
	Foundation.			Participants has appointments with the same qualified dietitian every 2 weeks (6 appointments during phase 1). Participants who achieved 12.5% weight loss or more in the allocated timeframe were eligible to enter phase 2. During this phase, the participants were instructed to follow an individualised diet for weight maintenance, based on the Australian Guide to Healthy Eating, and had individual sessions with the dietitian at weeks 4 and 12, and then every 12 weeks for 144 weeks. Active intervention period: 12 weeks	Healthy Eating (15% protein, 25–30% fat, and 55–60% carbohydrate), with one to two Optifast meal replacements every day, with the aim of 15% weight loss for 36 weeks (roughly 0·5 kg per week). Participants has appointments with the same qualified dietitian every 2 weeks (18 appointments during phase 1). Participants who achieved 12.5% weight loss or more in the allocated timeframe were eligible to enter phase 2. During this phase, the participants were instructed to follow an individualised diet for weight maintenance, based on the Australian Guide to Healthy Eating, and had individual sessions with the dietitian at weeks 4 and 12, and then every 12 weeks for 144 weeks.	

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
					Active intervention period: 36 weeks	
Seimon 2019*, Seimon 2020* and Jin 2022* TEMPO trial	Australia National Health and Medical Research Council (NHMRC)	101	Postmenopausal women living with BMI 30-40 kg/m² Charles Perkins Centre Royal Prince Alfred Clinic	**Very low energy total meal replacement + support:** Participants used total meal replacement diet (KicStart meal replacement shakes and soups from Prima Health Solutions) supplemented with a whey protein isolate (Beneprotein; Nestlé HealthCare Nutrition) to achieve the prescribed protein target. Severe intervention involved a severe restriction of 65% to 75% relative to estimated energy expenditure for 4 months (16 weeks) or until a body mass index of no lower than 20 was reached, whichever came first. This was followed by moderate energy restriction (ie, the moderate intervention) for the remaining period to 12 months (52 weeks). Participants attended individual dietary appointments with the trial dietitian approximately every 2 weeks for the first 26 weeks of the intervention and then approximately every month until 52 weeks.	**Usual care (advice +conventional diet) + support:** Moderate energy restriction of 25% to 35% relative to estimated energy expenditure for a total of 12 months (52 weeks). This was achieved using a food-based diet, with recommendations based on the Australian Guide to Healthy Eating. The guide provides recommendations on the average number of standard servings of the 5 core food groups (ie, vegetables, fruits, grains and cereals, meat and meat alternatives, and reduced fat dairy) that an individual should consume to meet nutritional requirements based on age and sex. Participants attended individual dietary appointments with the trial dietitian approximately every 2 weeks for the first 26 weeks of the	Change in weight (kg) at 1 year and 3 years Change in waist circumference (cm) at 1 year Serious adverse events at 1 year

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
				Active intervention period: 16 weeks	intervention and then approximately every month until 52 weeks. Active intervention period: 1 year	
Very low energy diet TOTAL meal replacement + support vs Usual care						
Tuomilehto 2009 & Tuomilehto 2010 RCT	Finland Supported by the Kuopio University hospital, Juho Vainio Foundation, Yrjo Jahnsson Foundation, Jalmari and Rauha Ahokkaan Foundation, Finnish Anti-Tuberculosis Foundation	81 (including some participants (8% in intervention arm and 11% in the control arm) taking "diabetes medication")	People 18-65 years old living with a BMI of 28-40 kg/m² and apnea–hypopnea index (AHI), 5–15 events/hour. Clinics of Otorhinolaryngology and Respiratory Medicine of the Kuopio University Hospital	**Very low energy total meal replacement + support:** Participants were provided with a group-based very low-calorie diet (VLCD) of 600- 800 kcal/day (Nutrilett [Nycomed Pharma, Oslo, Norway], Modifast [Novartis, Basel, Switzerland], Nutrifast [Leiras, Helsinki, Finland], or Naturdiet [Vitamex, Norrköping, Sweden]) for 12 weeks. In addition to VLCD products, the patients were allowed to have calorie-free drinks and vegetables in accordance with our outpatient clinic's weight reduction program. During the VLCD period, follow-up visits were arranged every second week and the sessions were supervised by the nutritionist. The clinical nutritionist provided dietary and lifestyle counselling	**Usual care (advice):** The subjects in the control group were given general oral and written information about diet and exercise at baseline, at the 3-month visit, and at the 1-year visit by the study nurse and physician, but no specific individualized programs were offered to them. Active intervention period: 1 year	Change in weight (kg) at 1 and 2 years from baseline Serious adverse events at 1 year and 2 years from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
				at each visit, with the emphasis placed on diet, exercise, and modification of lifestyle in general, specifically focusing on eating behaviour. After the VLCD, a physiotherapist supervised two of the group meetings, which focused on circuit-type resistance exercise to improve functional capacity. The lifestyle intervention lasted for 1 year and consisted of 14 visits with the study nutritionist. Active intervention period: 12 weeks		

** Denotes new primary studies identified through the search.*

Low carbohydrate diet

Table 9: Summary of studies looking at Low carbohydrate diet in a mixed population

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
Low carbohydrate diet + support vs Usual care (conventional diet) + support						
Calleja Fernandez 2012 RCT	Spain No funding	40	People 18-70 years old living with a BMI between 28 and 35 kg/m²	Low carbohydrate diet+ support: Diet providing 40% carbohydrate, 30% protein and 30% fat. The	Usual care (conventional diet) + support: Control diet providing 55% carbohydrate, 15% protein and 30% fat. The	BMI at 1 year

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
			Outpatient university endocrinology and nutrition complex in León	total caloric requirement minus 1000 kcal. The dietitian was responsible for providing individual counselling and written material to the participants on the initial visit, and then the patients were instructed to record their food intake in a daily food diary and to discuss it with the dietitian on each visit at every 2 weeks for 16 weeks at the beginning of the trial and on each 3 monthly visit for 1 year. Active intervention duration: 1 year	total caloric requirement minus 1000 kcal. The dietitian was responsible for providing individual counselling and written material to the participants on the initial visit, and then the patients were instructed to record their food intake in a daily food diary and to discuss it with the dietitian on each visit at every 2 weeks for 16 weeks at the beginning of the trial and on each 3 monthly visit for 1 year. Active intervention duration: 1 year	
Ebbeling 2007 RCT	USA National Institute of Diabetes and Digestive and Kidney Diseases, Charles H. Hood Foundation and the National	73	People 18-35 years old with a BMI ≥30 kg/m² Outpatient hospital in Boston	Low carbohydrate diet + support: Low-glycaemic load diet providing 40% carbohydrate, 35% fat, 25% protein. Physical activity recommendations. No energy restriction. Participants were equipped with food-choice lists that delineated products into low–, moderate–, and high–glycaemic load categories. Registered dietitians provided information during cooking demonstrations to	Usual care (conventional diet) + support: Low fat diet providing 55% carbohydrate, 20% fat, 25% protein. Physical activity recommendations. No energy restriction. Participants were equipped with food-choice lists that delineated products into low-, moderate-, and high-fat categories. Registered dietitians provided information during cooking	Change in weight (kg) at 74 weeks from baseline Partially applicable due to no calorie deficit for comparator

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
	Center for Research			encourage consumption of low–glycaemic load foods and led interactive activities using food models to define appropriate serving sizes of high–glycaemic load foods (eg, refined grain products, sweets) Active intervention duration: 6 months	demonstrations to encourage consumption of low-fat foods and led interactive activities using food models to define appropriate serving sizes of high-fat foods (eg, butter) and sweets Active intervention duration: 6 months	
Foraker 2014 (LEAF Study) RCT	USA Breast Cancer Research Foundation and the National Center for Advancing Translational Sciences	79	Postmenopausal women aged 30 and above living with a BMI of 25-34 kg/m² Outpatient general clinical research centre in Columbus	Low carbohydrate diet + support: Low-carbohydrate diet providing 40% of total calories from carbohydrates, 30% from protein 30% from fat. Exercise (10,000 steps a day). Each participant provided with a calorie goal based on the Harris-Benedict equation and counselling / support from a dietician. Active intervention duration: 1 year	Usual care (conventional diet) + support: Low fat diet providing 60% of total calories from carbohydrates, 20% from protein 20% from fat. Exercise (10,000 steps a day). Each participant provided with a calorie goal based on the Harris-Benedict equation and counselling / support from a dietician. Active intervention duration: 1 year	Weight (kg) at 1 year
Frisch 2009 RCT	Germany Various German	200	Adults 18-70 years old living with a BMI over 27 kg/m²	Low carbohydrate diet + support:	Usual care (conventional diet) + support:	Change in weight (kg) at 1 year from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
	health insurances and the Institute for Applied Telemedicine at Ruhr University Bochum		Outpatient heart centre in Bad Oeynhausen	Low carbohydrate diet providing <40% if the total energy intake from carbohydrates, >35% from fat and 25% from protein. 500 kcal/day energy reduction advised. Weekly calls with a nutritionist for 6 months. Active intervention duration: 1 year	The group received a conventional low-fat diet The target macronutrient composition in the group was a diet providing >55% energy from carbohydrates, <30% from fat and 15% from protein. 500 kcal/day energy reduction advised. Weekly calls with a nutritionist for 6 months. Active intervention duration: 1 year	Change in waist circumference (cm) at 1 year from baseline % Change in HbA1c at 1 year from baseline
Klemsdal 2010 RCT	Norway Norwegian National Research Council grant	202	Adults 30-65 years old living with a BMI between 28 and 40 kg/m² and at least one criterion of metabolic syndrome Outpatient hospital clinic in Oslo	Low carbohydrate diet + support: Low glycaemic load diet providing 35%- 40% of energy from fat, 25-30% from protein and 30-35% from carbohydrate. A 500 kcal/d deficit recommended. 2 individual and 5 group sessions with a dietician. Active intervention duration: 1 year	Usual care (conventional diet) + support: Low fat diet aimed to achieve the intake of a diet with <30% of energy from fat, about 15% from protein, 55-60% from carbohydrates. A 500 kcal/d deficit recommended. 2 individual and 5 group sessions with a dietician. Active intervention duration: 1 year	Change in weight (kg) at 1 year from baseline Change in waist circumference (cm) at 1 year from baseline
Melberg 2014	Sweden A number of public sector	70	Postmenopausal women who live with a BMI ≥ 27	Low carbohydrate diet + support: Palaeolithic diet: providing 30% of energy intake from protein,	Usual care (conventional diet) + support:	Change in BMI at 2 years from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
RCT	Swedish bodies		kg/m² and do not smoke. Outpatient clinical research centre at a university hospital in Umeå	40% from fat and 30% from carbohydrates. 12 group sessions with a dietician in 24 month period. Active intervention duration: 2 years	Nordic Nutrition Recommendations providing 55% of energy intake from carbohydrates, 15% from protein, 30% from fat. 12 group sessions with a dietician in 24 month period Active intervention duration: 2 years	Partially applicable due to no calorie deficit for comparator
Griffin 2013 RCT	Australia Grant from Meat and Livestock Australia.	71	Healthy women aged 18 to 25 years with BMI > 27.5 kg/ m2. Setting: Likely Australia based on authors and funder. Further information not provided in papers	Low carbohydrate diet + support: High protein diet provided 32% protein (107 g/day), 41% carbohydrate (138 g/day) and 25% fat (38 g/day) All participants received detailed meal plans, an identical behaviour modification program and attended weekly until 3 months, fortnightly between 3 and 6 months then monthly until 12 months. Active intervention duration: 1 year	Usual care (conventional diet) + support: Higher carbohydrate diet provided 20% protein (67 g/day), 58% carbohydrate (191 g/day) and 21% fat (32 g/day) All participants received detailed meal plans, an identical behaviour modification program and attended weekly until 3 months, fortnightly between 3 and 6 months then monthly until 12 months. Active intervention duration: 1 year	Change in weight (kg) at 1 year from baseline Change in waist circumference (cm) at 1 year from baseline Partially applicable due to no calorie deficit for comparator

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
Sacks 2009 RCT RC POUNDS LOST	USA Grants from the National Heart, Lung, and Blood Institute and the General Clinical Research Center, National Institutes of Health	811	People 30-70 years old living with a BMI 25-40 kg/m² Outpatient university hospital in Boston and outpatient biomedical research centre in Baton Rouge	Low carbohydrate diet + support: Diet providing 35% carbohydrates 40% fat, 25% protein. 90 minutes of moderate physical exercise. Caloric deficit of 750 kcal per day. Regular sessions with dieticians and behavioural counsellors. The goal for physical activity was 90 minutes of moderate exercise per week.	Usual care (conventional diet) + support: Diet providing 65% carbohydrates 20% fat, 15% protein. 90 minutes of moderate physical exercise. Caloric deficit of 750 kcal per day. Regular sessions with dieticians and behavioural counsellors. The goal for physical activity was 90 minutes of moderate exercise per week.	Change in weight (kg) at 2 years
Wycherley 2012 RCT	Australia Meat and Livestock Australia through a project grant	123	Men living with a BMI at least 27 and less than 40 kg/m². Aged <20 or >65 years, had diabetes or uncontrolled hypertension, a history of gastrointestinal, renal, coronary, metabolic or hepatic disease or a malignancy; were taking hypoglycaemic medication or drugs which affect insulin sensitivity, or were smokers.	Low carbohydrate diet + support: High protein diet providing 40% carbohydrates, 25% fat, 35% protein. Energy prescription of 7000 kJ per day. Regular contact with dietician during first 12 weeks. Active intervention duration: 1 year	Usual care (conventional diet) + support: High carbohydrate diet providing 58% carbohydrates, 25% fat, 17% protein. Energy prescription of 7000 kJ per day. Regular contact with dietician during first 12 weeks. Active intervention duration: 1 year	Change in weight (kg) at 1 year Change in waist circumference (cm) at 1 year

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
			Outpatient research clinic in Adelaide			

** Denotes new primary studies identified through the search.*

Table 10: Summary of studies looking at Low carbohydrate diet in people with type 2 diabetes

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
Low carbohydrate diet vs Usual care (conventional diet)						
Pedersen 2014 RCT	Australia Funding not reported	76	Adults aged 18-75 years living with type 2 diabetes and a BMI of at least 27 kg/m² Setting not reported	Low carbohydrate diet: High-protein diet providing 40% carbohydrate, 30% fat, 30% protein. Energy limited to 6000 kJ/day. Active intervention duration: 1 year	Usual care: Standard protein diet providing 50% carbohydrate, 30% fat, 20% protein. Energy limited to 6000 kJ/day. Active intervention duration: 1 year	Weight (kg) at 1 year from baseline % Change in HbA1c at 1 year
Low carbohydrate diet + support vs Usual care (conventional diet) + support						
Elhayany 2010 RCT	Israel Not reported	259	People diagnosed with type 2 diabetes who are 30-65 years old and living with a BMI 27-34 kg/m²	Low carbohydrate diet + support: Low-carbohydrate Mediterranean diet: 35% carbohydrates, 45% fat, 20% protein. Physical activity three times a week for 30 to 45 min.	Usual care (conventional diet) + support: Traditional Mediterranean diet: 50% carbohydrates, 30% fat, 20% protein. Physical activity three times a week for 30 to 45	Change in weight (kg) at 1 year from baseline Change in waist circumference (cm) at 1 year from baseline % Change in HbA1c at 1 year from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
			10 urban outpatient primary care clinics in the central district	Calories prescribed as 20/kg body weight. Patients were followed up by the same dietitian every 2 weeks for 1 year. Active intervention duration: 1 year	min. Calories prescribed as 20/kg body weight. Patients were followed up by the same dietitian every 2 weeks for 1 year. Active intervention duration: 1 year	
Guldbrand 2012 & Guldbrand 2014	Sweden University Hospital of Linköping Research Funds	61	People diagnosed with type 2 diabetes Note: There were no weight or age exclusion criteria however baseline data showed that mean BMI in intervention arm was 33.8 and 31.6 in the control arm. Outpatient primary healthcare centres in Motala and Borensberg	Low carbohydrate diet + support: Low carbohydrate diet: 20% of energy from carbohydrates, 30% from protein, 50% from fat. Energy content of 6694 kJ/day for women or 7531 kJ/day for men. Dietitian provided recipes and a menu for one week. Two different physicians conducted the group session where participants learnt which foods to choose from. Active intervention duration: 2 years	Usual care (conventional diet) + support: Low fat diet: 55% energy from carbohydrates, 15% from protein, 30% from fat. Energy content of 6694 kJ/day for women or 7531 kJ/day for men. Dietitian provided recipes and a menu for one week. Two different physicians conducted the group session where participants learnt which foods to choose from. Active intervention duration: 2 years	Change in weight (kg) at 1 and 2 years from baseline Change in waist circumference (cm) at 1 and 2 years from baseline % Change in HbA1c at 1 and 2 years from baseline Change in Quality of life at 1 and 2 years from baseline
Krebs 2012 RCT	New Zealand	419	Adults 30-76 years old diagnosed with type 2 diabetes and living with a BMI ≥ 27 kg/m²	Low carbohydrate diet + support: Low-fat high-protein diet: 40% of energy from carbohydrate, 30% from protein, and 30% from fat.	Usual care (conventional diet) + support: Low-fat high-carbohydrate diet: 55% of energy from carbohydrate, 15% from	Change in weight (kg) at 1 and 2 years Change in waist circumference (cm) at 1 and 2 years from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
DEWL Trial	Health Research Council of New Zealand		Outpatient clinical centres in Wellington, Auckland and Christchurch	Reduce total energy intake by 2000 kJ/day. At the beginning of the study, individualised dietary prescription based on estimation of energy requirements were discussed on a one-to-one basis with each participant. Participants mainly had group sessions thereafter which were 1 hour long consisting of diet-specific information and education and were conducted every 2 weeks for the first 6 months, then every month for the second 6 months. No further dietary advice was offered by the dietitians after 12 months. Participants were then asked to continue following their prescribed diets on their own in the second year. Active intervention duration: 1 year	protein, and 30% from fat. Reduce total energy intake by 2000 kJ/day. At the beginning of the study, individualised dietary prescription based on estimation of energy requirements were discussed on a one-to-one basis with each participant. Participants mainly had group sessions thereafter which were 1 hour long consisting of diet-specific information and education and were conducted every 2 weeks for the first 6 months, then every month for the second 6 months. No further dietary advice was offered by the dietitians after 12 months. Participants were then asked to continue following their prescribed diets on their own in the second year. Active intervention duration: 1 year	% Change in HbA1c at 1 and 2 years from baseline Change in Quality of life at 1 and 2 years from baseline
Larsen 2011 RCT	Australia	108	Adults 30-75 years old living with type	Low carbohydrate diet + support:	Usual care (conventional diet) + support:	Change in weight (kg) at 1 year from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
	Meat and Livestock Australia nutritional research grant		2 diabetes and a BMI o 27-40 kg/m² Outpatient heart and diabetes institute in Melbourne	High protein diet: 40% of energy from carbohydrate, 30% from protein, 30% from fat. Energy prescription of ~6400 kJ/day or 30% energy restriction for three months followed by energy balance for nine months. 4 individual dietician appointments and 3 monthly group sessions. Active intervention duration: 1 year	High carbohydrate diet: 55% from carbohydrate, 15% from protein, 30% from fat. Energy prescription of ~6400 kJ/day or 30% energy restriction for three months followed by energy balance for nine months. 4 individual dietician appointments and 3 monthly group sessions. Active intervention duration: 1 year	Change in waist circumference (cm) at 1 from baseline % change in HbA1c at 1 year from baseline

** Denotes new primary studies identified through the search.*

Very low carbohydrate diet

Table 11: Summary of studies looking at Very low carbohydrate diet in a mixed population

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
Very low carbohydrate diet + support vs Usual care (diet) + support						
Bazzano 2014 RCT	USA Tulane University Hypertensio	148 family background :	Adults 22-75 years old living with a BMI Of 30-45 kg/m²	Very low carbohydrate diet + support: Instructed to maintain an intake of digestible carbohydrate (total carbohydrate minus total fibre) of less than 40	Usual care (diet) + support: Those assigned to the low-fat diet were instructed to maintain less than 30% of their daily energy intake from total fat (with < 7%	<u>All</u> Change in weight (kg) at 1 year from baseline Change in waist circumference at 1 year from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
	n and Renal Centre of Excellence	Black: n=77 White: n=76	Tulane University Hypertension and Renal Centre of Excellence	g/d. A specific calorie/ energy goal was not set. Participants met with a dietitian in weekly individual counselling sessions for the first 4 weeks, followed by small group counselling sessions every other week for the next 5 months (a total of 10 sessions) and monthly for the last 6 months of the intervention period. Individual and group counselling with a dietitian. Active intervention duration: 1 year	from saturated fat) and 55% from carbohydrate, based on National Cholesterol Education Program guidelines. A specific calorie/ energy goal was not set. Participants met with a dietitian in weekly individual counselling sessions for the first 4 weeks, followed by small group counselling sessions every other week for the next 5 months (a total of 10 sessions) and monthly for the last 6 months of the intervention period. Active intervention duration: 1 year	Adverse events: constipation at 1 year Serious adverse events at 1 year White family background Change in weight (kg) at 1 year from baseline Change in waist circumference at 1 year from baseline Black family background Change in weight (kg) at 1 year from baseline Change in waist circumference at 1 year from baseline Partially applicable due to no calorie deficit for comparator
Brinkworth 2009* +Brinkworth 2016 A*	Australia National Health and Medical Research Council of Australia	118	Adults living with abdominal obesity ages 24 to 64 y with abdominal obesity (waist circumference: ≥94 cm in men, ≥80 cm in women) and at least one additional metabolic syndrome risk factor.	Very low carbohydrate diet + support: Very low carbohydrate diet (4% of total energy as carbohydrate [<20g], 35% protein, and 61% fat. Diet designed to be isocaloric with moderate energy restriction. After 8 weeks, participants in group were provided with the option of a 20 g carbohydrate exchange (i.e., a carbohydrate prescription of <40g).	Usual care (diet) + support: Low fat diet- 46% of total energy as carbohydrate, 24% protein, and 30% fat [<8% saturated fat]. Diet designed to be isocaloric with moderate energy restriction. On a fortnightly basis for the first 8 weeks, and monthly thereafter, participants also met individually with a	Change in weight (kg) at 1 year from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
			Conducted in CSIRO Clinical Research Unit (Adelaide)	On a fortnightly basis for the first 8 weeks, and monthly thereafter, participants also met individually with a qualified dietitian who provided detailed dietary advice, meal plans, and recipe information pertaining to each diet. Active intervention duration: 1 year	qualified dietitian who provided detailed dietary advice, meal plans, and recipe information pertaining to each diet. Active intervention duration: 1 year	
Foster 2010 RCT	USA National Institutes of Health	307	Adults 18-65 years old living with a BMI 30-40 kg/m² University of Colorado Denver, Washington University, University of Pennsylvania.	**Very low carbohydrate diet + support:** Limited carbohydrate intake but allowed unrestricted consumption of fat and protein. Limit carbohydrate intake to 20 g per day for 12 weeks. Then gradually increased carbohydrate intake (5 g/d per week). Comprehensive, in-person group behavioural treatment weekly for 20 weeks, every other week for 20 weeks, and then every other month for the remainder of the study. Active intervention duration: 1 year	**Usual care (diet) + support:** Low-fat diet, which consisted of limiting energy intake to 1200 to 1500 kcal/d for women and 1500 to 1800 kcal/d for men, with approximately 55% of calories from carbohydrate, 30% from fat, and 15% from protein. Comprehensive, in-person group behavioural treatment weekly for 20 weeks, every other week for 20 weeks, and then every other month for the remainder of the study. Active intervention duration: 1 year	Change in weight (kg) at 1 and 2 years from baseline Adverse events: constipation at 1 and 2 years Adverse events: hair loss at 1 and 2 years Serious adverse events at 1 and 2 years
Hu 2015*	USA	148	People 22-75 years old living	**Very low carbohydrate diet + support:** Net carbohydrate	**Usual care (diet) + support:** Low-fat diet which	Change in weight (kg) at 1 year from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
RCT	National Institutes of Health and the Tulane University Hypertensio n and Renal Center of Excellence		with a BMI 30-45 kg/m² Tulane University Health Sciences Center in New Orleans, Louisiana.	intake was restricted to <40 grams/day. Regular individual and group counselling sessions with a dietician. Regular meetings with dieticians scheduled over the 12 months. An optional daily low-carbohydrate meal replacement (bar or shake) was provided to participants for the duration of the intervention. Active intervention duration: 1 year	restricted total fat to <30% of daily energy, with <7% from saturated fat. Regular individual and group counselling sessions with a dietician. Regular meetings with dieticians scheduled over the 12 months. An optional daily low-fat meal replacement (bar or shake) was provided to participants for the duration of the intervention. Active intervention duration: 1 year	Partially applicable due to no calorie deficit for comparator
Layman 2009 RCT	USA National Cattlemen's Beef Association, Beef Checkoff, and Kraft Foods	130	People 40-56 years old living with a BMI of at least 26 kg/m². University of Illinois and The Pennsylvania State University	**Very low carbohydrate diet + support:** Diet provided dietary protein at1.6 g kg-1 d-1 (~30% of energy intake) with a carbohydrate:protein ratio <1.5 and dietary lipids ~30% energy intake. Throughout the 12-mo study, participants were required to attend a 1-h meeting each week at the weight management research facility. Active intervention duration: 1 year	**Usual care (diet) + support:** Diet provided dietary protein equal to 0.8 g kg-1 d-1 (~15% of energy intake) with a carbohydrate:protein ratio >3.2 and total fat ~30% of energy intake. Throughout the 12-mo study, participants were required to attend a 1-h meeting each week at the weight management research facility. Active intervention duration: 1 year	Change in weight (kg) at 1 year from baseline Partially applicable due to no calorie deficit for comparator

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
Lim 2010 RCT	Australia National Heart Foundation and CSIRO Health Sciences and Nutrition	104	People 20-65 years old with at least one risk factor for CVD (other than obesity) and a BMI 25-40 kg/m² Outpatient clinic in Adelaide	**Very low carbohydrate diet + support:** Diet provided 35% of energy as protein, 60% fat, 20% saturated fat, 4% carbohydrate. Participants were provided with prescriptive meal plans and foods contributing to 65% energy of the meal plans. They also received individual dietary counselling every 2 weeks from a qualified dietitian to monitor compliance to their assigned diets. Following the intensive phase, subjects were advised to maintain their allocated energy-restricted diet for an additional 12 months. Active intervention duration: 15 months	**Usual care (diet) + support:** High unsaturated fat diet - 20% energy as protein, 30% fat, 6% saturated fat, 8% polyunsaturated fat, 50% carbohydrate). Participants were provided with prescriptive meal plans and foods contributing to 65% energy of the meal plans. They also received individual dietary counselling every 2 weeks from a qualified dietitian to monitor compliance to their assigned diets. Following the intensive phase, subjects were advised to maintain their allocated energy-restricted diet for an additional 12 months. Active intervention duration: 15 months	Change in weight (kg) at 15 months from baseline Partially applicable due to no calorie deficit for comparator

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
Moreno 2014* & Moreno 2016* RCT	Spain Protein Supplies, S.L.	79 (no people receiving insulin therapy)	People 18-65 years old living with a BMI ≥ 30 and stable weight for 3 months Obesity Unit at the Hospital Gregorio Maranon, Madrid	**Very low carbohydrate diet + support:** The group followed a very low-calorie-ketogenic diet via a commercial weight loss program (Pronokal method). Each protein preparation contained 15 g protein, 4 g carbohydrates, and 3 g fat, and provided 90–100 kcal. It begins with 600–800 kcal/day through 5 preparations that are low in carbohydrates (<50 g). The diet lasted 45–60 days in total. Then followed a low-calorie diet initiated for the remainder of the trial. 9 group meetings and 3 individual support meetings occurred with reinforcement phone calls. Active intervention duration: 1 year	**Usual care (diet) + support:** The standard low calorie diet was an equilibrated diet that had a caloric value 10% below the total metabolic expenditure of each individual. The calories provided to this group ranged between 1400 and 1800 kcal/day. The ration of macronutrients provided was 45–55 % carbohydrates, 15–25 % proteins, and 25–35 % fat. 9 group meetings and 3 individual support meetings occurred with reinforcement phone calls. Active intervention duration: 1 year	Change in weight (kg) at 1 year from baseline % Change in HbA1c at 1 year from baseline Adverse events: constipation at 1 year Adverse events: hair loss at 1 year
Very low carbohydrate diet + support vs no intervention						
Lim 2010 RCT	Australia National Heart Foundation and CSIRO Health	104	People 20-65 years old with at least one risk factor for CVD (other than obesity) and a BMI 25-40 kg/m²	**Very low carbohydrate diet + support:** Diet provided 35% of energy as protein, 60% fat, 20% saturated fat, 4% carbohydrate. Participants were provided with prescriptive meal plans and foods contributing to 65%	**No intervention:** The control group attended the clinic at baseline and 15 months for measurements as described for the diet groups, but they received no dietary intervention for the duration of the study	Change in weight (kg) at 15 months from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
	Sciences and Nutrition		Outpatient clinic in Adelaide	energy of the meal plans. They also received individual dietary counselling every 2 weeks from a qualified dietitian to monitor compliance to their assigned diets. Following the intensive phase, subjects were advised to maintain their allocated energy-restricted diet for an additional 12 months. Active intervention duration: 15 months		

** Denotes new primary studies identified through the search.*

Table 12: Summary of studies looking at Very low carbohydrate diet in people with type 2 diabetes

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
Very low carbohydrate diet + support vs Usual care (diet) + support						
Tay 2015A, Tay 2018*, Brinkworth 2016B* & Kakoschke 2021*	Australia National Health and Medical Research Council of Australia & Agency for Science,	115	Adults living with overweight and obese [BMI (in kg/m^2): 26–45; age: 35– 68 y] with T2D (HbA1c ≥7.0% or taking a diabetes medication)	**Very low carbohydrate diet + support:** Very low carbohydrate diet, 14% of total energy from carbohydrate (<50 g/d),), 28% as protein and 58% as fat. Moderate (500–1000-kcal/d deficit) energy restriction diet. Participants met	**Usual care (diet) + support**: Participants in the high carbohydrate diet, the prescribed dietary profile was 53% of total energy as carbohydrate, 17% as protein and <30% as total fat. Moderately energy restricted.	Change in weight (kg) at 1 and 2 years Change in HbA1c at 1 and 2 years Change in waist circumference at 1 year Quality of life at 1 year and 2 years from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
	Technology and Research, Singapore		Commonwealth Scientific and Industrial Research Organisation Clinical Research Unit (Adelaide, Australia)	individually with a dietitian (every 2 weeks for 12 weeks and monthly thereafter). They undertook 1 hour professionally supervised exercise classes 3 days per week. Active intervention duration: 2 years	Regular dietician appointments and multicomponent exercise programme. Active intervention duration: 2 years	Adherence at 1 and 2 years
Goldstein 2011	Israel No funding	52 (not receiving insulin)	People 35-75 years olds with BMI 30-39.9 kg/m² HbA1c > 7% and not receiving insulin. University hospital clinic	**Very low carbohydrate diet + support:** 4-week DASH (The Dietary Approach to Stop Hypertension) diet followed by modified Akins diet for 12 months. Very low carbohydrate diet containing up to 25 g per day for the first 6 weeks. Increasing to a ceiling of 40 g daily. Nutritional counselling during initial 12-week period following randomization received weekly Active intervention duration: 1 year	**Usual care (diet) + support:** 4-week DASH diet followed by an American Diabetes Association diet for 12 months. Calorie-restricted regime: men were allowed up to 1500 kcal/day and women, 1200 kcal/day. Active intervention duration: 1 year	Change in weight (kg) at 1 year Change in HbA1c at 1 year
Iqbal 2010	USA Grant support: VA Merit Review	144	Adults living with type 2 diabetes and a BMI > 30 kg/m² Clinics at the Philadelphia	**Very low carbohydrate diet + support:** Target of 30 g carbohydrate intake per day using an electronic calorie counter. Provided very general handouts that were specific to their dietary intervention.	**Usual care (diet) + support:** People given an individualized “fat budget” and a calorie goal, which were based on the participant’s height, weight, and target calorie intake	Change in HbA1c at 1 and 2 years from baseline Serious adverse events at 2 years

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
	Entry Program		Veterans Affairs Medical Center	Active intervention duration: 2 years	(500 kcal deficit) using an electronic calorie counter. Provided with very general handouts that were specific to their dietary intervention. Active intervention duration: 2 years	
Saslow 2017	USA William K. Bowes, Jr. Foundation and the Mount Zion Health Fund	34	Adults living with type 2 diabetes or prediabetes with an HbA1c over 6% and a BMI ≥ 25. San Francisco, California (UCSF)	**Very low carbohydrate diet + support:** Very low carbohydrate, high fat, non calorie-restricted diet. 20–50 g of carbohydrates per day. 13 2-hour classes covering diet, sleep, exercise and a focus learning skills to support behaviour change. This included psychological skills was led by a psychologist with experience teaching mindfulness and health behaviour change. Active intervention duration: 1 year	**Usual care (diet) + support:** Medium carbohydrate (165 g per day), low fat, calorie-restricted (-500 k/cal), carbohydrate counting diet. 13 2-hour classes covering diet, sleep, exercise and a focus learning skills to support behaviour change. This included psychological skills was led by a psychologist with experience teaching mindfulness and health behaviour change. Active intervention duration: 1 year	Weight (kg) at 1 year HbA1c at 1 year

** Denotes new primary studies identified through the search.*

Intermittent energy restriction – 5:2 Diet

Table 13: Summary of studies looking at Intermittent energy restriction (5:2 diet) in a mixed population

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
Intermittent energy restriction (5:2 diet) vs Usual care (advice)						
Hajek 2021* RCT	UK Medical Research Council	200	Adults BMI ≥30 kg/m² (or ≥28 kg/m², with co-morbidities) who wanted to lose weight. Weight Management Clinic run by the Health and Lifestyle Research Unit, Queen Mary University of London	Intermittent energy restriction (5:2 diet): Leaflet on restricting caloric intake to 500 kcal for women and 600 kcal for men on two non-consecutive days a week. Active intervention period: 1 year	Usual care (advice): Standard Brief Advice: British Heart Foundation guides 'Facts Not Fads' and 'Get Active, Stay Active' plus the NHS 'Change 4 Life' series of booklets and a leaflet listing local resources for exercise. Active intervention period: 1 year	Change in weight (kg) at 1 year from baseline Adherence via at 1 year
Intermittent energy restriction (5:2 diet) + support vs Usual care (advice)						
Hajek 2021* RCT	UK Medical Research Council	200	Adults BMI ≥30 kg/m² (or ≥28 kg/m², with co-morbidities) who wanted to lose weight. Weight Management Clinic run by the Health and	Intermittent energy restriction (5:2 diet) + support: Leaflet on restricting caloric intake to 500 kcal for women and 600 kcal for men on two non-consecutive days a week. In addition, the participants were invited to attend six group support sessions (in weeks 1–6), each lasting one hour. Sessions	Usual care (advice): Standard Brief Advice: British Heart Foundation guides 'Facts Not Fads' and 'Get Active, Stay Active' plus the NHS 'Change 4 Life' series of booklets and a leaflet listing local resources for exercise.	Change in weight (kg) at 1 year from baseline Adherence via at 1 year

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
			Lifestyle Research Unit, Queen Mary University of London	were moderated by advisors. Participants were weighed and reported on their experience over the past week, whether they managed to adhere to the plan, whether they cook or use pre-prepared food on the fasting days, how they cope with hunger, etc. Active intervention period: 1 year	Active intervention period: 1 year	
Intermittent energy restriction (5:2 diet) + support vs Usual care (advice)+ support						
Schubel 2018 HELENA Trial RCT	Germany Helmholtz Association of German Research Centers	100	Adults 35-65 years old living with a BMI ≥ 25 to <40 kg/m² HELENA Trial at the German Cancer Research Center, Heidelberg	Intermittent energy restriction (5:2 diet) + support: Group were advised to restrict their energy intake on 2 self-selected non-consecutive days per week to 25% of the individual energy requirement. The remaining 5 d of the week were based on a eucaloric balanced diet [according to the guidelines of the German Society for Nutrition]. Thus, the weekly average calorie intake corresponded to ~80% of the normal energy requirement. Participants in all groups were informed about the guidelines of the German Nutrition Society for a healthy balanced diet by the dietitians and advised to maintain	Usual care (advice)+ support: Informed about the guidelines of the German Nutrition Society for a healthy balanced diet by a dietitian and advised to maintain habitual physical activity levels. The number of personal contacts and counselling sessions was the same for all study participants overall, but individuals in the 5:2 diet and continuous energy restriction arms received longer and more comprehensive counselling sessions.	Change in weight (kg) at 1 year from baseline Change in waist circumference (cm) at 1 year baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
				habitual physical activity levels throughout the study. The number of personal contacts and counselling sessions was the same for all study participants overall, but individuals in the 5:2 diet and continuous energy restriction arms received longer and more comprehensive counselling sessions with personalized dietary plans, specific for the regimens. At the end of this intervention phase, participants returned to the study centre for examinations and were motivated by the dietitians to continue with the prescribed regimen during the maintenance phase (weeks 13 to 24), but no further dietary counselling followed throughout the remaining weeks of the study, neither in person nor on the phone. Active intervention period: 12 weeks	At the end of this intervention phase, participants returned to the study centre for examinations and were motivated by the dietitians to continue with the prescribed regimen during the maintenance phase (weeks 13 to 24), but no further dietary counselling followed throughout the remaining weeks of the study, neither in person nor on the phone. Active intervention period: 12 weeks	
Intermittent energy restriction (5:2 diet) + support vs Usual care (diet)+ support						
Schubel 2018 + Pannen 2021*	Germany	100	Adults 35-65 years old living with a BMI ≥ 25 to <40 kg/m²	Intermittent energy restriction (5:2 diet) + support: Group were advised to restrict their energy intake on 2 self-	Usual care (diet)+ support: Continuous energy restriction- group were advised to restrict energy	Change in weight (kg) at 1 and 2 years

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
HELENA Trial RCT	Helmholtz Association of German Research Centers		HELENA Trial at the German Cancer Research Center, Heidelberg	selected non-consecutive days per week to 25% of the individual energy requirement. The remaining 5 d of the week were based on a eucaloric balanced diet [according to the guidelines of the German Society for Nutrition]. Thus, the weekly average calorie intake corresponded to ~80% of the normal energy requirement. Participants in all groups were informed about the guidelines of the German Nutrition Society for a healthy balanced diet by the dietitians and advised to maintain habitual physical activity levels throughout the study. The number of personal contacts and counselling sessions was the same for all study participants overall, but individuals in the 5:2 diet and continuous energy restriction arms received longer and more comprehensive counselling sessions with personalized dietary plans, specific for the regimens. At the end of this intervention phase, participants returned to the study centre for examinations	intake to 80% of the individual energy requirement. Personalized diet plans aiming at implementing the recommendations of the German Society for Nutrition and to reduce energy-dense foods were provided by the dietitians. Participants in all groups were informed about the guidelines of the German Nutrition Society for a healthy balanced diet by the dietitians and advised to maintain habitual physical activity levels throughout the study. The number of personal contacts and counselling sessions was the same for all study participants overall, but individuals in the 5:2 diet and continuous energy restriction arms received longer and more comprehensive counselling sessions with personalized dietary plans, specific for the regimens.	Change in waist circumference (cm) at 1 year

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
				and were motivated by the dietitians to continue with the prescribed regimen during the maintenance phase (weeks 13 to 24), but no further dietary counselling followed throughout the remaining weeks of the study, neither in person nor on the phone. Active intervention period: 12 weeks	At the end of this intervention phase, participants returned to the study centre for examinations and were motivated by the dietitians to continue with the prescribed regimen during the maintenance phase (weeks 13 to 24), but no further dietary counselling followed throughout the remaining weeks of the study, neither in person nor on the phone. Active intervention period: 12 weeks	
Sundfor 2018 RCT	Norway Financial via a three-year doctoral fellowship from the Norwegian Health Association	112	Adults 21-70 years old living with abdominal obesity. BMI 30-45.0 kg/m², waist circumference ≥94/≥80 cm (men/women), ≥1 additional metabolic syndrome component	Intermittent energy restriction (5:2 diet) + support: Intermittent ER (6 months) group were limited to 400 kcal/day for females and 600 kcal/day for males for two non-consecutive per week while eating as usual the remaining five days a week. Menus were provided to increase satiety on near-fasting days. To improve compliance all participants received	Usual care (diet)+ support: Participants in the continuous energy restriction group were advised to reduce energy intake evenly on all seven days a week. The daily energy intake for participants in the group was based on the calculated caloric restriction two “fasting” days a week equals when the calorie	Change in weight (kg) at 1 year from baseline Change in waist circumference (cm) at 1 year from baseline Serious adverse events at 1 year

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
			Oslo University Hospital, Department of endocrinology, morbid obesity and Preventive medicine	individualized dietary plans, including educational materials and individual counselling in cognitive behavioural methods. A 6-month weight-loss phase including 10 visits with dieticians was followed by a 6-month maintenance phase without additional face-to-face counselling. Active intervention period: 6 months	restriction is evenly distributed on all 7 days of the week. They received individualised menus. To improve compliance all participants received individualized dietary plans including educational materials and individual counselling in cognitive behavioural methods. A 6-month weight-loss phase including 10 visits with dieticians was followed by a 6-month maintenance phase without additional face-to-face counselling. Active intervention period: 6 months	

** Denotes new primary studies identified through the search.*

Table 14: Summary of studies looking at Intermittent energy restriction (5:2 diet) in people with type 2 diabetes

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
Intermittent energy restriction (5:2 diet) + support vs Usual care (diet)+ support						

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
Carter 2018, Carter 2019* RCT	Australia Authors supported by public sector grants/fellowship	63	Adults living with type 2 diabetes and a BMI ≥27 kg/m² University of South Australia, Adelaide	Intermittent energy restriction (5:2 diet) + support: 2100 to 2500 kJ/day (500–600 kcal/day) for 2 days of the week and followed their usual diet for the other 5 days. Both groups received written dietary information booklets with portion advice and sample menus; no food or meal replacements were provided. Dietary counselling was provided by a dietitian (S.C.) and occurred every 2 weeks for the first 3 months and every 2 to 3 months for the final 9 months. Active intervention period: 1 year	Usual care (diet)+ support: Participants in the continuous energy restriction group followed a diet of 5000 to 6300 kJ/day (1200–1500 kcal/day) (45% carbohydrate, 30% protein and 25% fat). Both groups received written dietary information booklets with portion advice and sample menus; no food or meal replacements were provided. Dietary counselling was provided by a dietitian (S.C.) and occurred every 2 weeks for the first 3 months and every 2 to 3 months for the final 9 months. Active intervention period: 1 year	Change in weight (kg) at 1 and 2 years from baseline Change in HbA1c at 1 and 2-years baseline
Intermittent energy restriction (5:2 diet) + support vs Low energy TOTAL meal replacement diet						
McDiarmid 2022* MIDDAS Trial Pilot RCT	UK Néstle Health Science and Oviva UK Limited	79	People with overweight or obesity and type 2 diabetes, including those on insulin.	Intermittent energy restriction (5:2 diet) + support: 2 consecutive days per week of the Optifast LED plus 5 days of a Mediterranean diet or 1 day of food-based 800	Low energy total meal replacement + support: Participants were asked to follow the Optifast low-energy diet providing about 820 kcal/ day for 8 weeks. This consisted of three sachets/day (200 kcal per sachet of shake/soup):	Change in weight (kg) at 1 year Change in HbA1c at 1 year Serious adverse events at 1 year from follow up

<table>
<tr><th>Author (year) and study type</th><th>Country and funder</th><th>Sample size</th><th>Population and setting</th><th>Intervention</th><th>Comparator</th><th>Outcomes</th></tr>
<tr><td></td><td></td><td></td><td>3 general practices, 2 NHS hospital trusts and a volunteer research register</td><td>kcal/day low energy diet plus 6 days Mediterranean diet.

Group entered a continued weight loss phase (if achieved ≤15% weight loss or more than target weight loss). Continued weight loss involved a daily 25% energy restricted Mediterranean diet and 2 days/ week of food based low energy diet (800 kcal/day). This phase was for 40 weeks.

Participants were encouraged to aim for 30 min of moderate intensity physical activity 5 days/ week and resistance exercise. Both groups received matched behavioural support from the multi-disciplinary team (MDT), which included a diabetes specialist dietician and nurse, exercise specialist and psychologist. The dietician contacted patients weekly in weeks 1-12, fortnightly in weeks 12-28 and month in weeks 29-52.</td><td><table>
<tr><th></th><th>1 Optifast sachet</th><th>1 low calorie day (3 sachets with vegetables and oil)</th></tr>
<tr><td>Carbs (g)</td><td>18</td><td>79</td></tr>
<tr><td>Protein (g)</td><td>20</td><td>69</td></tr>
<tr><td>Fat (g)</td><td>4.5</td><td>26</td></tr>
<tr><td>Calories</td><td>200</td><td>820</td></tr>
</table>
Participants who were unable to tolerate Optifast were offered a food-based low energy diet with a similar macronutrient profile.
This was followed by stepped food reintroduction from 1000 kcal to 1500 kcal over 4 weeks.

Group entered a continued weight loss phase (if achieved ≤15% weight loss or more than target weight loss). Continued weight loss involved a daily 25% energy restricted Mediterranean diet and 2 days/ week of food based low energy diet (800 kcal/day). This phase was for 40 weeks.

Participants were encouraged to aim for 30 min of moderate intensity physical activity 5 days/ week and</td><td>Adherence via trial retention at 1 year from follow up</td></tr>
</table>

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
				Active intervention phase: 28 weeks	resistance exercise. Both groups received matched behavioural support from the multi-disciplinary team (MDT), which included a diabetes specialist dietician and nurse, exercise specialist and psychologist. The dietician contacted patients weekly in weeks 1-12, fortnightly in weeks 12-28 and month in weeks 29-52. Active intervention phase: 12 weeks	

** Denotes new primary studies identified through the search.*

Intermittent energy restriction – Alternate day fasting (ADF)

Table 15: Summary of studies looking at Intermittent energy restriction (ADF) in a mixed population

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
Intermittent energy restriction (Alternate day fasting) + support vs Usual care (diet) + support						
Trepanowski 2017 RCT	USA National Institutes of Health/National Heart, Lung, and Blood, Diabetes and Digestive and	69	Adults 18-65 years old with a BMI between 25 and 39.9 kg/m² University of Illinois at Chicago	Intermittent energy restriction (Alternate- day fasting) + support: During the 6-month weight-loss phase, the intervention groups were instructed to reduce their energy intake by a mean of 25% per day.	Usual care (diet) + support: During the 6-month weight-loss phase, the intervention groups were instructed to reduce their energy intake by a mean of 25% per day. The group were instructed to consume 75% of	% Change in weight at 1 year from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
	Kidney Diseases.			The group consumed 25% of baseline energy intake as a lunch (between 12 PM and 2 PM) on fast days and 125% of baseline energy intake split between 3 meals on alternating feast days. Meals provided for the first 3 months and received dietary counselling thereafter. From months 4 to 6, when food was no longer provided, intervention participants met individually with a dietician or nutritionist weekly to learn how to continue with their diets on their own. Active intervention period: 6 months	baseline energy intake split between 3 meals every day. Meals provided for the first 3 months and received dietary counselling thereafter. Meals provided for the first 3 months and received dietary counselling thereafter. From months 4 to 6, when food was no longer provided, intervention participants met individually with a dietician or nutritionist weekly to learn how to continue with their diets on their own Active intervention period: 6 months	
Oustric 2021*	UK European Society for Clinical Nutrition and Metabolism (ESPEN)	46	Women 18-55 years old living with a BMI of 25.0–34.9 kg/m² University of Leeds and surrounding area	Intermittent energy restriction (Alternate- day fasting) + support: Ad libitum day alternating with 75% energy restriction day with LighterLife (UK) total diet replacement products. Until ≥5% weight loss or up to 12 weeks. Participants met weekly with a dietitian to monitor weight loss	Usual care (diet) + support: Continuous energy restriction (25% daily energy restriction with all foods provided) to ≥5% weight loss or up to 12 weeks. Participants met weekly with a dietitian to monitor weight loss and were	% Change in weight at 1 year from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
				and were provided with pre-portioned food that required minimal preparation. Active intervention period: 12 weeks	provided with pre-portioned food that required minimal preparation. Active intervention period: 12 weeks	
Intermittent energy restriction (Alternate day fasting) + support vs No intervention						
Trepanowski 2017 RCT	USA National Institutes of Health/National Heart, Lung, and Blood, Diabetes and Digestive and Kidney Diseases.	69	Adults 18-65 years old with a BMI between 25 and 39.9 kg/m² University of Illinois at Chicago	Intermittent energy restriction (Alternate- day fasting) + support: During the 6-month weight-loss phase, the intervention groups were instructed to reduce their energy intake by a mean of 25% per day. The group consumed 25% of baseline energy intake as a lunch (between 12 PM and 2 PM) on fast days and 125% of baseline energy intake split between 3 meals on alternating feast days. Meals provided for the first 3 months and received dietary counselling thereafter. From	No intervention: During the 6-month weight-loss phase, the intervention groups were instructed to reduce their energy intake by a mean of 25% per day. Control Group were instructed to maintain their weight throughout the trial and not to change their eating or physical activity habits. Controls received no food or dietary counselling.	% Change in weight at 1 year from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
				months 4 to 6, when food was no longer provided, intervention participants met individually with a dietician or nutritionist weekly to learn how to continue with their diets on their own. Active intervention period: 6 months		

** Denotes new primary studies identified through the search.*

Intermittent energy restriction – Time restricted eating (TRE)

Table 16: Summary of studies looking at Intermittent energy restriction (TRE) in a mixed population

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
Intermittent energy restriction (Time restricted eating) vs Usual care (diet)						
Byrne 2018* RCT MATADOR study	Australia Australian National Health and Medical Research Council (NHMRC)	51	Men 25-54 years old living with a BMI 30-45 kg/m² Single centre in Queensland	Intermittent energy restriction (Time restricted eating) + support: 8 × 2-week blocks of energy restriction (ER) interspersed with 7 × 2-week blocks of energy balance. Designed to provide a 33% reduction in energy intake. Participants were provided with all main meals and morning and afternoon snacks for the duration	Usual care (diet): Continuous energy restriction -16 weeks of energy restriction. Designed to provide a 33% reduction in energy intake. Participants were provided with all main meals and morning and afternoon snacks for the duration of the study. Meals were	Change in weight (kg) at 1 year from end of baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
				of the study. Meals were prepared by a commercial kitchen under the direction of a dietician and delivered to the participants' homes each week. Active intervention period: 30 weeks	prepared by a commercial kitchen under the direction of a dietician and delivered to the participants' homes each week. Active intervention period: 16 weeks	
Keogh 2014* RCT	Australia Australian National Health and Medical Research Council (NHMRC)	36	Adult women living with overweight and obesity (BMI ≥27kg/m² A research centre	Intermittent energy restriction – alternate week ER. Participants followed an energy restricted diet based on the 'Total Wellbeing Diet' portion and recipe system from the Commonwealth Scientific and Industrial Research Organisation (CSIRO). Intervention group followed a 5500-kJ energy restriction diet for 1 week, followed by 1 week of their usual diet. Participants attended the research centre every 2 weeks for 8 weeks and for a follow-up visit at 52 weeks. Participants were instructed to continue their allocated IER strategy from week 8 to week 52 but did not attend the research centre during that time.	Usual care (diet): continuous energy restriction. Participants followed an energy restricted diet based on the 'Total Wellbeing Diet' portion and recipe system from the Commonwealth Scientific and Industrial Research Organisation (CSIRO). Control group participants followed a 5500-kJ energy restriction diet continuously for the duration of the study. Participants attended the research centre every 2 weeks for 8 weeks and for a follow-up visit at 52 weeks. Participants were instructed to continue their allocated CER strategy from week 8 to week 52 but did not attend the research centre during that time.	Change in weight (kg) 1 year from baseline Change in waist circumference (cm) 1 year from baseline

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
				Active intervention period: 8 weeks	Active intervention period: 8 weeks	

** Denotes new primary studies identified through the search.*

Intermittent energy restriction: intermittent fasting

Table 17: Summary of studies looking at Intermittent energy restriction (intermittent fasting) in a mixed population

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
Intermittent energy restriction: intermittent fasting vs Usual care (advice)						
Teong 2023* RCT	Australia National Health and Medical Research Council Project Grant Australian Government Research Training Program Scholarship from The	209	Adults age 58 ± 10 years, BMI 34.8 ± 4.7 kg/m² at risk of type2 diabetes University of Adelaide	Intermittent time restricted eating (30% energy requirements between 0800 and 1200 hours and followed by a 20-h fasting period on three non-consecutive days per week, and ad libitum eating on other days Active intervention period: 6 months	Standard care (weight loss booklet) *(Study did contain a calorie restriction CR arm but this has been excluded due to non-specific criteria for calorie restriction which didn't match our protocol)*	HbA1c % change from baseline to 18 months Body weight kg – change from baseline to 18-months Number of serious adverse events Number of adverse events Constipation

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
	University of Adelaide. Diabetes Australia Research Program Grant				Active intervention period: 6 months	
Intermittent energy restriction: intermittent fasting vs habitual meal timing						
Wei 2023* RCT	China Grants from the National Key Research and Development Project, Joint Funds of the National Natural Science Foundation of China, National Natural Science Foundation of China (81970736), and Key-Area Clinical Research	88	Adults aged 18-75, BMI between 28.0 and 45.0 kg/m² Diagnosed with NAFLD Nanfang Hospital in Guangzhou,	All participants were instructed to follow a diet of 1500 to 1800 kcal/d for men and 1200 to 1500 kcal/d for women. The diets were composed of 40% to 55% carbohydrate, 15% to 20% protein, and 20% to 30% fat. Participants assigned to the TRE group were instructed to consume the prescribed calories from 8:00 am to 4:00 pm every day, and only noncaloric beverages were permitted outside of the daily eating window.	All participants were instructed to follow a diet of 1500 to 1800 kcal/d for men and 1200 to 1500 kcal/d for women. The diets were composed of 40% to 55% carbohydrate, 15% to 20% protein, and 20% to 30% fat. Participants in the DCR group had no eating time restriction during the 12-month study period.	Weight change from baseline to 12 months kg Waist circumference cm Constipation

Author (year) and study type	Country and funder	Sample size	Population and setting	Intervention	Comparator	Outcomes
	Program of Southern Medical University (LC2019ZD010 and 2019CR022)					

** Denotes new primary studies identified through the search.*

See appendix D for full evidence tables.

1.1.6 Summary of the effectiveness evidence

Low energy diet TOTAL meal replacement

Table 18: Mixed population

No of studies	Design	No of participants: Low energy TOTAL MR	No of participants: Usual care	Effect (95% CI)	Quality	Interpretation
Low energy TOTAL MR + support vs Usual care (conventional diet) + support						
% Change in weight at 1 year from baseline. MID = 5% (follow-up 12 months; Better indicated by lower values)						
1[(a)]	RCT	135	138	MD: -5.0 (-5.14 to -4.86)	VERY LOW	**Favours low energy TOTAL MR**
Change in waist circumference (WC; cm) at 1 year from baseline. MID = 4.65 (follow-up 12 months; Better indicated by lower values)						
1[(a)]	RCT	135	138	MD: -4.7 (-7.26 to -2.14)	VERY LOW	**Favours low energy TOTAL MR**
Serious adverse events at 1 year from baseline. MID 0.8 to 1.25 (follow-up 12 months). Better indicated by lower values						
1[(a)]	RCT	7/155 (4.5%)	3/150 (2%)	RR: 2.26 (0.59 to 8.57)	VERY LOW	Could not differentiate between interventions
Adherence at 1 year from baseline. MID 0.8 to 1.25 (follow-up 12 months). Better indicated by higher values						
1[(a)]	RCT	95/135 (70.4%)	94/138 (68.1%)	RR: 1.03 (0.88 to 1.21)	LOW	Could not differentiate between interventions
Low energy TOTAL MR + support vs Usual care (advice)						
Change in weight (kg) at 1 year from baseline. MID = 3.5 (follow-up 12 months; Better indicated by lower values)						
1[(b)]	RCT	104	95	MD: -7.6 (-9.92 to -5.28)	MODERATE	**Favours low energy TOTAL MR**
Change in WC (cm) at 1 year from baseline. MID = 3.25 (follow-up 12 months; Better indicated by lower values)						
1[(b)]	RCT	99	91	MD: - 5.0 (-7.24 to -2.76)	LOW	**Favours low energy TOTAL MR**
Change in HbA1c (mmol/mol) at 1 year from baseline. MID = 5 mmol/mol (follow-up 12 months; Better indicated by lower values)						
1[(b)]	RCT	91	75	MD: -2.2 (-4.71 to 0.31)	MODERATE	Could not differentiate between interventions

No of studies	Design	No of participants		Effect (95% CI)	Quality	Interpretation
		Low energy TOTAL MR	Usual care			
Change in Quality of life (QoL; EQ-5D Index) at year 1 from baseline. MID = 0.07 (follow-up 12 months; Better indicated by higher values)						
1[(b)]	RCT	100	93	MD: 0.02 (-0.02 to 0.06)	MODERATE	Could not differentiate between interventions
Change in QoL (EQ-5D VAS) at year 1 from baseline. MID = 8.5 (Better indicated by higher values)						
1[(b)]	RCT	101	96	MD: 3.8 (-1.19 to 8.79)	LOW	Could not differentiate between interventions
Change in QoL (OWL-QOL) at year 1 from baseline. MID = 8.35 (follow-up 12 months; Better indicated by higher values)						
1[(b)]	RCT	99	94	MD: 3.0 (-2.32 to 8.32)	MODERATE	Could not differentiate between interventions
Serious adverse events at 1 year from baseline. MID 0.8 to 1.25 (follow-up 12 months). Better indicated by lower values						
1[(b)]	RCT	15/138 (10.9%)	17/140 (12.1%)	RR: 0.9 (0.47 to 1.72)	VERY LOW	Could not differentiate between interventions
Adverse event: constipation at 1 year from baseline. MID 0.8 to 1.25 (follow-up 12 months). Better indicated by lower values						
1[(b)]	RCT	20/138 (14.5%)	0/140 (0%)	RR: 41.59 (2.54 to 680.93)	MODERATE	**Favours usual care**
Change in weight (kg) at 3 years from baseline. MID = 3.85 (follow-up 3 years; Better indicated by lower values)						
1[(b)]	RCT	96	83	MD: -3.6 (-6.06 to -1.14)	LOW	**Favours low energy TOTAL MR**
Change in WC (cm) at 3 years from baseline. MID = 3.65 (follow-up 3 years; Better indicated by lower values)						
1[(b)]	RCT	77	70	MD: -5.0 (-7.66 to -2.34)	LOW	**Favours low energy TOTAL MR**
Change in HbA1c (mmol/mol) at 3 years from baseline. MID = 5 mmol/mol (follow-up 3 years; Better indicated by lower values)						
1[(b)]	RCT	71	61	MD: 3.9 (1.11 to 6.69)	LOW	**Favours low energy USUAL CARE**
Change in QoL (EQ-5D index) at 3 years from baseline. MID = 0.008 (follow-up 3 years; Better indicated by higher values)						
1[(c)]	RCT	67	70	MD: 0.02 (-0.02 to 0.06)	VERY LOW	Could not differentiate between interventions
Change in QoL at 3 years (EQ-5D VAS). MID = 57.55 (follow-up 3 years; Better indicated by higher values)						

No of studies	Design	No of participants		Effect (95% CI)	Quality	Interpretation
		Low energy TOTAL MR	Usual care			
1(c)	RCT	79	70	MD: -16.0 (-43.32 to 11.32)	MODERATE	Could not differentiate between interventions
Change in QoL at 3 years (OWL-QOL). MID = 7.35 (follow-up 3 years; Better indicated by higher values)						
1(c)	RCT	77	70	MD: 1.4 (-3.6 to 6.4)	MODERATE	Could not differentiate between interventions

(a) Ard 2019
(b) Astbury 2018 (DROPLET)
(c) Astbury 2021 (DROPLET)

Table 19: In people with Type 2 diabetes

No of studies	Design	No of participants		Effect (95% CI)	Quality	Interpretation
		Low energy TOTAL MR	Usual care			
Low energy TOTAL MR + support vs Usual care (advice)						
Change in weight (kg) at 1 year from baseline. MID= 2.65 (follow-up 12 months; Better indicated by lower values)						
3(a)	RCT	225	242	MD: -8.67 (-9.91 to -7.42)	LOW	**Favours low energy TOTAL MR**
Change in WC (cm) at 1 year from baseline. MID = 2.92 (follow-up 12 months; Better indicated by lower values)						
2(b)	RCT	86	94	MD: -7.19 (-9.61 to -4.77)	MODERATE	**Favours low energy TOTAL MR**
Change in HbA1c (mmol/mol) at 1 year from baseline. MID = 5 mmol/mol (follow-up 12 months; Better indicated by lower values)						
3(a)	RCT	346	365	MD: -7.98 (-10.28 to -5.69)	VERY LOW	**Favours low energy TOTAL MR**
Change in QoL (EQ-5D VAS) at 1 year from baseline. MID = 8 (follow-up 12 months; Better indicated by higher values)						
2(c)	RCT	208	225	MD: 6.06 (2.86 to 9.25)	VERY LOW	**Favours low energy TOTAL MR**
Change in QoL (EQ-5D Health utility score) at 1 year from baseline. MID= 0.101 (follow-up 12 months; Better indicated by higher values)						
1(d)	RCT	138	148	MD: 0.03 (-0.02 to 0.07)	LOW	Could not differentiate between interventions

No of studies	Design	No of participants		Effect (95% CI)	Quality	Interpretation
		Low energy TOTAL MR	Usual care			
Serious adverse events at 1 year from baseline. MID 0.8 to 1.25 (follow-up 12 months). Better indicated by lower values						
2[(c)]	RCT	7/227 (3.1%)	6/226 (2.7%)	RR: 1.16 (0.40 to 3.36)	VERY LOW	Could not differentiate between interventions
Adherence at 1 year from baseline. MID 0.8 to 1.25 (follow-up 12 months). Better indicated by higher values						
1[(d)]	RCT	117/143 (81.8%)	115/115 (100%)	RR: 0.82 (0.76 to 0.89)	VERY LOW	**Favours Low energy USUAL CARE**
Change in weight (kg) at 2 years from baseline. MID= 2.6 (follow-up 2 years; Better indicated by lower values)						
1[(e)]	RCT	129	143	MD: -5.43 (-6.87 to -3.99)	LOW	**Favours Low energy TOTAL MR**
Change in HbA1c (mmol/mol) at 2 years from baseline. MID = 5 mmol/mol (follow-up 2 years; Better indicated by lower values)						
1[(e)]	RCT	129	143	MD: -4.82 (-8.28 to -1.36)	VERY LOW	**Favours Low energy TOTAL MR**
Change in QoL (EQ-5D VAS) at 2 years from baseline. MID = 7.55 (follow-up 2 years; Better indicated by higher values)						
1[(e)]	RCT	129	143	MD: 4.64 (0.39 to 8.89)	VERY LOW	**Favours Low energy TOTAL MR**
Change in QoL (EQ-5D Health utility score) at 2 years from baseline. MID = 0.097 (follow-up 2 years; Better indicated by higher values)						
1[(e)]	RCT	129	143	MD: 0.02 (-0.02 to 0.07)	LOW	Could not differentiate between interventions
Serious adverse events at 2 years from baseline. MID 0.8 to 1.25 (follow-up 2 years). Better indicated by lower values						
1[(e)]	RCT	11/157 (7%)	19/149 (12.8%)	RR: 0.55 (0.27 to 1.12)	VERY LOW	Could not differentiate between interventions
Change in weight (kg) at 3 years from baseline. MID = 2.55 (follow-up 3 years; Better indicated by lower values)						
1[(f)]	RCT	19	17	MD: -3.5 (-8.65 to 1.65)	LOW	Could not differentiate between interventions
Change in WC (cm) at 3 years from baseline. MID = 3.75 (follow-up 3 years; Better indicated by lower values)						
1[(f)]	RCT	15	14	MD: -3.8 (-10.86 to 3.26)	LOW	Could not differentiate between interventions
Change in HbA1c (mmol/mol) at 3 years from baseline. MID = 5mmol/mol (follow-up 3 years; Better indicated by lower values)						

No of studies	Design	No of participants		Effect (95% CI)	Quality	Interpretation
		Low energy TOTAL MR	Usual care			
1(f)	RCT	16	17	MD: 8.3 (-0.47 to 17.07)	LOW	Could not differentiate between interventions
Low energy TOTAL MR + support vs Usual care + support						
Change in weight (kg) at 1 year from baseline. MID = 3.05 (follow-up 12 months; Better indicated by lower values)						
1(g)	RCT	45	45	MD: -4.2 (-6.49 to -1.91)	VERY LOW	**Favours Low energy TOTAL MR**
Change in WC at 1 year from baseline. MID = 7.0 (follow-up 12 months; Better indicated by lower values)						
1(g)	RCT	45	45	MD: -10.4 (-15.65 to -5.15)	VERY LOW	**Favours Low energy TOTAL MR**
% change in HbA1c at 1 year from baseline. MID = 5% (follow-up 12 months; Better indicated by lower values)						
1(g)	RCT	45	45	MD: -0.34 (-0.9 to 0.22)	LOW	Could not differentiate between interventions
Change in QoL at 1 year from baseline (EQ-5D). MID = 9.7 (follow-up 12 months; Better indicated by higher values)						
1(g)	RCT	45	45	MD: 10.39 (1.86 to 18.92)	VERY LOW	**Favours Low energy TOTAL MR**
Serious adverse events at 1 year from baseline. MID 0.8 to 1.25 (follow-up 12 months). Better indicated by lower values						
1(g)	RCT	5/45 (11.1%)	9/45 (20%)	RR: 0.56 (0.2 to 1.53)	VERY LOW	Could not differentiate between interventions
Low energy TOTAL MR + support vs IER (5:2 diet) + support						
Change in weight (kg) at 1 year from baseline. MID = 3.1 (follow-up 12 months; Better indicated by lower values)						
1(h)	RCT	40	39	MD: -1.1 (-3.77 to 1.57)	LOW	Could not differentiate between interventions
Change in HbA1c at 1 year from baseline. MID = 5 mmol/mol (follow-up 12 months; Better indicated by lower values)						
1(h)	RCT	40	39	MD: -0.6 (-5.46 to 4.26)	LOW	Could not differentiate between interventions
Serious adverse events at 1 year from baseline. MID 0.8 to 1.25 (follow-up 12 months). Better indicated by lower values						
1(h)	RCT	4/40 (10%)	4/39 (10.3%)	RR: 0.98 (0.26 to 3.63)	VERY LOW	Could not differentiate between interventions

No of studies	Design	No of participants		Effect (95% CI)	Quality	Interpretation
		Low energy TOTAL MR	Usual care			
Adherence at 1 year from baseline (follow-up 12 months) Better indicated by higher values						
1[h]	RCT	30/40 (75%)	27/39 (69.2%)	RR: 1.08 (0.82 to 1.43)	LOW	Could not differentiate between interventions

(a) Astbury 2018 (DROPLET); Lean 2018 (DIRECT); Taheri 2020
(b) Astbury 2018 (DROPLET); Taheri 2020
(c) Lean 2018 (DIRECT); Taheri 2020
(d) Lean 2018 (DIRECT)
(e) Lean 2019 (DIRECT)
(f) Astbury 2018 (DROPLET)
(g) Brown 2020
(h) McDiarmid 2022

Low energy diet PARTIAL meal replacement

Table 20: Mixed population

No of studies	Design	No of participants		Effect (95% CI)	Quality	Interpretation
		Low energy PARTIAL MR	Usual care			
Low energy PARTIAL MR + support vs Usual care (conventional diet) + support						
Change in weight (kg) at 1 year from baseline. MID = 3.35 (follow-up 12 months; Better indicated by lower values)						
1[a]	RCT	35	35	MD: 1.1 (-1.65 to 3.85)	LOW	Could not differentiate between interventions
Change in WC (cm) at 1 year from baseline. MID = 3.5 (follow-up 12 months; Better indicated by lower values)						
1[a]	RCT	35	35	MD: 1.2 (-1.57 to 3.97)	LOW	Could not differentiate between interventions
Low energy PARTIAL MR + support vs Usual care (advice/diet)						
Change in weight (kg) at 1 year from baseline. MID = 3.5 (follow-up 12 months; Better indicated by lower values)						
1[b]	RCT	57	56	MD: -2.8 (-5.38 to -0.22)	MODERATE	**Favours Low energy PARTIAL MR**
Change in WC (cm) at 1 year from baseline. MID = 2.6 (follow-up 12 months; Better indicated by lower values)						

No of studies	Design	No of participants		Effect (95% CI)	Quality	Interpretation
		Low energy PARTIAL MR	Usual care			
1[b]	RCT	57	56	MD: -1.4 (-3.3 to 0.5)	MODERATE	Could not differentiate between interventions

(a) Ashley 2007
(b) Shikany 2013

Table 21: In people with type 2 diabetes

No of studies	Design	No of participants		Effect (95% CI)	Quality	Interpretation
		Low energy PARTIAL MR	Usual care			
Low energy PARTIAL MR vs Usual care						
Change in weight (kg) at 1 year from baseline. MID = 2.6 (follow-up 12 months; Better indicated by lower values)						
1[a]	RCT	19	12	MD: -0.6 (-4.06 to 2.86)	VERY LOW	Could not differentiate between interventions
Change in WC at 1 year from baseline. MID = 1.84 (follow-up 12 months; Better indicated by lower values)						
1[a]	RCT	19	12	MD: -3.4 (-5.88 to -0.92)	LOW	**Favours Low energy PARTIAL MR**

(a) Khoo 2011

Very low energy diet TOTAL meal replacement

Table 22: Mixed population

No of studies	Design	No of participants		Effect (95% CI)	Quality	Interpretation
		Very low energy TOTAL MR	Usual care			
Very low energy TOTAL MR + support vs Usual care (advice/conventional diet) + support (Pooled result for all groups)						
Change in weight at 1 year from baseline. MID = 3.39 (follow-up 12 months; Better indicated by lower values)						
2[a]	RCT	143	142	MD: -2.45 (-10.75 to 5.85)	VERY LOW	Could not differentiate between interventions

No of studies	Design	No of participants Very low energy TOTAL MR	 Usual care	Effect (95% CI)	Quality	Interpretation
Change in weight at 1 year from baseline - Mixed population (Males and females). MID = 2.15 (follow-up 12 months; Better indicated by lower values) (Male and female subgroup)						
1[(b)]	RCT	97	103	MD: 1.58 (0.15 to 3.01)	MODERATE	**Favours Usual care**
Change in weight at 1 year from baseline - Only females. MID = 4.6 (follow-up 12 months; Better indicated by lower values) (Female only subgroup)						
1[(c)]	RCT	46	39	MD: -6.9 (-10.88 to -2.92)	LOW	**Favours very low energy TOTAL MR**
Change in WC at 1 year from baseline. MID = 4.9 (follow-up 12 months; Better indicated by lower values)						
1[(c)]	RCT	46	38	MD: -7.4 (-11.65 to -3.15)	LOW	**Favours very low energy TOTAL MR**
Change in weight at 2 years from baseline. MID = 3.7 (follow-up 2 years; Better indicated by lower values)						
2[(a)]	RCT	142	134	MD: -1.73 (-3.19 to -0.27)	MODERATE	**Favours very low energy TOTAL MR**
Change in weight at 2 years from baseline - Mixed population (Males and females). MID = 2.35 (follow-up 2 years; Better indicated by lower values)						
1[(b)]	RCT	97	103	MD: -1.5 (-3.03 to 0.03)	MODERATE	Could not differentiate between interventions
Change in weight at 2 years from baseline - Only females. MID = 5 (follow-up 2 years; Better indicated by lower values)						
1[(c)]	RCT	45	31	MD: -4.0 (-8.79 to 0.79)	LOW	Could not differentiate between interventions
Change in WC at 2 years from baseline. MID = 5 (follow-up 2 years; Better indicated by lower values)						
1[(c)]	RCT	45	31	MD: -4.3 (-9.09 to 0.49)	LOW	Could not differentiate between interventions
Change in weight at 3 years from baseline. MID = 4.35 (follow-up 3 years; Better indicated by lower values)						
2[(a)]	RCT	102	74	MD: -0.51 (-2.96 to 1.93)	HIGH	Could not differentiate between interventions
Change in weight at 3 years from baseline - Mixed population (Males and females). MID = 3.25 (follow-up 3 years; Better indicated by lower values)						

No of studies	Design	No of participants		Effect (95% CI)	Quality	Interpretation
		Very low energy TOTAL MR	Usual care			
1(b)	RCT	61	43	MD: 0.2 (-2.56 to 2.96)	HIGH	Could not differentiate between interventions
Change in weight at 3 years from baseline - Only females. MID = 5.05 (follow-up 3 years; Better indicated by lower values)						
1(c)	RCT	41	31	MD: -3.1 (-8.35 to 2.15)	LOW	Could not differentiate between interventions
Change in WC at 3 years from baseline. MID = 4.7 (follow-up 3 years; Better indicated by lower values)						
2(a)	RCT	102	74	MD: -1.13 (-3.81 to 1.55)	HIGH	Could not differentiate between interventions
Change in WC at 3 years from baseline - Mixed population (Males and females). MID = 4.22 (follow-up 3 years; Better indicated by lower values)						
1(b)	RCT	61	43	MD: -0.3 (-3.5 to 2.9)	HIGH	Could not differentiate between interventions
Change in WC at 3 years from baseline - Only females. MID = 5.15 (follow-up 3 years; Better indicated by lower values)						
1(c)	RCT	41	31	MD: -3.1 (-8.02 to 1.82)	LOW	Could not differentiate between interventions
Very low energy TOTAL MR + support vs Usual care (advice)						
Change in weight at 1 year from baseline. MID = 2.8 (follow-up 12 months; Better indicated by lower values)						
1(d)	RCT	35	37	MD: -8.3 (-11.11 to -5.49)	MODERATE	**Favours Very low energy TOTAL MR**
Change in WC at 1 year from baseline. MID = 3 (follow-up 12 months; Better indicated by lower values)						
1(d)	RCT	35	37	MD: -8.6 (-11.52 to -5.68)	MODERATE	**Favours Very low energy TOTAL MR**
Change in weight at 2 years from baseline. MID = 3.75 (follow-up 2 years; Better indicated by lower values)						
1(e)	RCT	35	36	MD: -4.4 (-7.66 to -1.14)	LOW	**Favours Very low energy TOTAL MR**
Change in WC at 2 years from baseline. MID = 3.65 (follow-up 2 years; Better indicated by lower values)						
1(e)	RCT	35	36	MD: -4.2 (-7.46 to -0.94)	LOW	**Favours Very low energy TOTAL MR**

(a) Purcell 2014; Seimon 2019 (TEMPO)
(b) Purcell 2014

(c) Seimon 2019 (TEMPO)
(d) Tuomilehto 2009
(e) Tuomilehto 2010

Low carbohydrate diet

Table 23: Mixed population

No of studies	Design	No of participants: Low carbohydrate diet	No of participants: Usual care	Effect (95% CI)	Quality	Interpretation
Low carb diet + support vs Usual care + support						
Change in weight (kg) at 1 year from baseline. MID = 6.1 (follow-up 12 months; Better indicated by lower values)						
6[(a)]	RCT	336	349	MD: -0.81 (-1.77 to 0.15)	LOW	Could not differentiate between interventions
Change in weight (kg) at 1 year from baseline - Mixed population (males and females). MID = 2.55 (follow-up 12 months; Better indicated by lower values)						
3[(b)]	RCT	236	239	MD: -0.65 (-1.69 to 0.4)	LOW	Could not differentiate between interventions
Change in weight (kg) at 1 year from baseline - Only females. MID = 2.8 (follow-up 12 months; Better indicated by lower values)						
2[(c)]	RCT	43	49	MD: -1.79 (-4.8 to 1.22)	VERY LOW	Could not differentiate between interventions
Change in weight (kg) at 1 year from baseline - Only males. MID = 5.45 (follow-up 12 months; Better indicated by lower values)						
1[(d)]	RCT	57	61	MD: -1.4 (-5.28 to 2.48)	LOW	Could not differentiate between interventions
Change in weight (kg) at 2 years from baseline. MID = 3.35 (follow-up 2 years; Better indicated by lower values)						
1[(e)]	RCT	201	204	MD: 0.6 (-0.77 to 1.97)	LOW	Could not differentiate between interventions
Change in BMI at 1 year from baseline. MID = 1.2 (follow-up 12 months; Better indicated by lower values)						
1[(f)]	RCT	21	19	MD: -0.23 (-1.8 to 1.34)	VERY LOW	Could not differentiate between interventions
Change in BMI at 2 years from baseline. MID = 0.8 (follow-up 2 years; Better indicated by lower values)						

No of studies	Design	No of participants		Effect (95% CI)	Quality	Interpretation
		Low carbohydrate diet	Usual care			
1[(g)]	RCT	27	22	MD: -1.0 (-2.04 to 0.04)	VERY LOW	Could not differentiate between interventions
Change in WC (cm) at 1 year from baseline. MID = 4.5 (follow-up 12 months; Better indicated by lower values)						
4[(h)]	RCT	293	298	MD: -1.37 (-3.36 to 0.61)	VERY LOW	Could not differentiate between interventions
Change in WC (cm) at 1 year from baseline - Mixed population (males and females). MID = 5.01 (follow-up 12 months; Better indicated by lower values)						
2[(i)]	RCT	200	202	MD: -0.3 (-4.31 to 3.7)	VERY LOW	Could not differentiate between interventions
Change in WC (cm) at 1 year from baseline - Only males. MID = 3.5 (follow-up 12 months; Better indicated by lower values)						
1[(d)]	RCT	57	61	MD: -1.3 (-3.72 to 1.12)	VERY LOW	Could not differentiate between interventions
Change in WC (cm) at 1 year from baseline - Only females. MID = 1.9 (follow-up 12 months; Better indicated by lower values)						
1[(j)]	RCT	36	35	MD: -3.5 (-6.39 to -0.61)	VERY LOW	**Favours Low carb diet**
% Change in HbA1c at 1 year from baseline. MID = 5% (follow-up 12 months; Better indicated by lower values)						
1[(k)]	RCT	100	100	MD: 0.0 (-0.06 to 0.06)	LOW	Could not differentiate between interventions

(a) Ebbeling 2007; Frisch 2009; Klemsdal 2010; Foraker 2014; Griffin 2013; Wycherley 2012
(b) Ebbeling 2007; Frisch 2009; Klemsdal 2010
(c) Foraker 2014; Griffin 2013
(d) Wycherley 2012
(e) Sacks 2009
(f) Calleja-Fernandez 2012 (in people with insulin resistance) and Calleja-Fernandez 2012 (in people without insulin resistance)
(g) Mellberg 2014
(h) Frisch 2009; Klemsdal 2010; Wycherley 2012; Griffin 2013
(i) Frisch 2009; Klemsdal 2010
(j) Griffin 2013
(k) Frisch 2009

Table 24: In people with type 2 diabetes

No of studies	Design	No of participants: Low carbohydrate diet	No of participants: Usual care	Effect (95% CI)	Quality	Interpretation
Low carb diet vs Usual care						
Weight (kg) at 1 year from baseline. MID = 9.2 (follow-up 12 months; Better indicated by lower values)						
1[(a)]	RCT	31	33	MD: -2.3 (-11.59 to 6.99)	VERY LOW	Could not differentiate between interventions
% Change in HbA1c at 1 year from baseline. MID = 5% (follow-up 12 months; Better indicated by lower values)						
1[(a)]	RCT	21	24	MD: -0.1 (-2.91 to 2.71)	LOW	Could not differentiate between interventions
Low carb diet + support vs Usual care + support						
Change in weight (kg) at 1 year from baseline. MID = 10.2 (follow-up 12 months; Better indicated by lower values)						
4[(b)]	RCT	351	352	MD: -0.27 (-1.65 to 1.1)	LOW	Could not differentiate between interventions
Change in weight (kg) at 2 years from baseline. MID = 9.9 (follow-up 2 years; Better indicated by lower values)						
2[(c)]	RCT	237	243	MD: 1.97 (-1.41 to 5.36)	MODERATE	Could not differentiate between interventions
Change in WC (cm) at 1 year from baseline. MID = 5.06 (follow-up 12 months; Better indicated by lower values)						
4[(b)]	RCT	351	352	MD: -0.19 (-1.55 to 1.17)	LOW	Could not differentiate between interventions
Change in WC (cm) at 2 years from baseline. MID = 6.85 (follow-up 2 years; Better indicated by lower values)						
2[(c)]	RCT	237	243	MD: 1.89 (-0.55 to 4.32)	MODERATE	Could not differentiate between interventions
% Change in HbA1c at 1 year from baseline. MID = 5% (follow-up 12 months; Better indicated by lower values)						
4[(b)]	RCT	352	352	MD: 0.03 (-0.16 to 0.21)	LOW	Could not differentiate between interventions
% Change in HbA1c at 2 years from baseline. MID = 5% (follow-up 2 years; Better indicated by lower values)						

No of studies	Design	No of participants		Effect (95% CI)	Quality	Interpretation
		Low carbohydrate diet	Usual care			
2[(c)]	RCT	237	243	MD: 0.0 (-0.26 to 0.26)	MODERATE	Could not differentiate between interventions
Change in QoL (SF-36 Physical component score (PCS) at 1 year from baseline. MID = 4.76 (follow-up 12 months; Better indicated by higher values)						
2[(c)]	RCT	237	243	MD: 1.02 (-0.67 to 2.72)	MODERATE	Could not differentiate between interventions
Change in QoL (SF-36 Physical component score (PCS) at 2 years from baseline. MID = 4.9 (follow-up 2 years; Better indicated by higher values)						
2[(c)]	RCT	237	243	MD: -1.91 (-3.64 to -0.18)	MODERATE	**Favours Usual care**
Change in QoL (SF-36 Mental component score (MCS) at 1 year from baseline. MID = 4.7 (follow-up 12 months; Better indicated by higher values)						
2[(c)]	RCT	237	243	MD: 1.22 (-0.43 to 2.88)	MODERATE	Could not differentiate between interventions
Change in QoL (SF-36 Mental component score (MCS) at 2 years from baseline. MID = 4.97 (follow-up 2 years; Better indicated by higher values)						
2[(c)]	RCT	237	243	MD: 1.02 (-0.71 to 2.74)	MODERATE	Could not differentiate between interventions

(a) Pedersen 2014
(b) Elhayany 2010; Guldbrand 2012; Krebs 2012; Larsen 2011
(c) Guldbrand 2012; Krebs 2012

Very low carbohydrate diet

Table 25: Mixed population

No of studies	Design	No of participants: Very low carbohydrate diet	No of participants: Usual care	Effect (95% CI)	Quality	Interpretation
Very low carb diet + support vs Usual care + support						
Change in weight (kg) at 1 year from baseline - Mixed population (Mixed family backgrounds). MID = 3.21 (follow-up 12 months; Better indicated by lower values)						
7[(a)]	RCT	431	395	MD: -2.38 (-4.22 to -0.55)	VERY LOW	**Favours very low carb diet**
Change in weight (kg) at 1 year from baseline - Black family background. MID = 2.9 (follow-up 12 months; Better indicated by lower values)						
1[(b)]	RCT	40	36	MD: -3.3 (-5.97 to 0.63)	VERY LOW	**Favours very low carb diet**
Change in weight (kg) at 1 year from baseline - White family background. MID = 3.5 (follow-up 12 months; Better indicated by lower values)						
1[(b)]	RCT	34	33	MD: -3.9 (-7.3 to -0.5)	VERY LOW	**Favours very low carb diet**
Change in WC (cm) at 1 year from baseline - Mixed population (Mixed family backgrounds). MID = 3.85 (follow-up 12 months; Better indicated by lower values)						
1[(b)]	RCT	75	73	MD: -1.7 (-4.2 to 0.8)	VERY LOW	Could not differentiate between interventions
Change in WC (cm) at 1 year from baseline - Black family background. MID = 3.8 (follow-up 12 months; Better indicated by lower values)						
1[(b)]	RCT	40	36	MD: -2.9 (-6.39 to 0.59)	VERY LOW	Could not differentiate between interventions
Change in WC (cm) at 1 year from baseline - White family background. MID = 3.9 (follow-up 12 months; Better indicated by lower values)						
1[(b)]	RCT	34	33	MD: -0.2 (-4.01 to 3.61)	VERY LOW	Could not differentiate between interventions
% Change in HbA1c at 1 year from baseline. MID = 5% (Better indicated by lower values)						
1[(c)]	RCT	27	26	MD: -0.38 (-0.66 to -0.1)	LOW	**Favours very low carb diet**
Adverse event: Hair loss at 1 year. MID = 0.8 to 1.25 (Better indicated by lower values)						

No of studies	Design	No of participants		Effect (95% CI)	Quality	Interpretation
		Very low carbohydrate diet	Usual care			
2[d]	RCT	31/179 (17.3%)	19/181 (10.5%)	RR: 1.63 (0.97 to 2.75)	VERY LOW	Could not differentiate between interventions
Adverse event: Constipation at 1 year. MID = 0.8 to 1.25 (Better indicated by lower values)						
3[e]	RCT	69/255 (27.1%)	53/253 (20.9%)	RR: 1.16 (0.58 to 2.31)	VERY LOW	Could not differentiate between interventions
Change in weight (kg) at 2 years from baseline. MID = 5.4 (follow-up 2 years; Better indicated by lower values)						
1[f]	RCT	153	154	MD: 1.03 (-1.39 to 3.45)	LOW	Could not differentiate between interventions
Adverse event: Hair loss at 2 years (follow-up 2 years). MID = 0.8 to 1.25 (Better indicated by lower values)						
1[f]	RCT	23/153 (15%)	15/154 (9.7%)	RR: 1.54 (0.84 to 2.84)	VERY LOW	Could not differentiate between interventions
Adverse event: Constipation at 2 years (follow-up 2 years). MID = 0.8 to 1.25 (Better indicated by lower values)						
1[f]	RCT	39/153 (25.5%)	17/154 (11%)	Risk difference: 0.14 (0.06 to 0.23)	LOW	**Favours Usual care**
Very low carb diet + support vs No intervention						
Change in weight (kg) at 15 months from baseline. MID = 2.5 (follow-up 15 months; Better indicated by lower values)						
1[g]	RCT	17	19	MD: -3.7 (-6.94 to 0.46)	VERY LOW	**Favours Very low carb diet**

(a) Bazzano 2014; Brinkworth 2016a; Foster 2010; Hu 2015; Layman 2009; Lim 2010; Moreno 2014
(b) Bazzano 2014
(c) Moreno 2014
(d) Foster 2010; Moreno 2014
(e) Moreno 2014; Foster 2010; Bazzano 2014
(f) Foster 2010
(g) Lim 2010

Table 26: In people with type 2 diabetes

No of studies	Design	No of participants: Very low carbohydrate diet	No of participants: Usual care	Effect (95% CI)	Quality	Interpretation
Very low carb diet + support vs Usual care + support						
Change in weight (kg) at 1 year from baseline. MID = 2.85 (follow-up 12 months; Better indicated by lower values)						
3[(a)]	RCT	70	67	MD: 0.83 (-1.24 to 2.89)	VERY LOW	Could not differentiate between interventions
% Change HbA1c at 1 year from baseline. MID = 5% (follow-up 12 months; Better indicated by lower values)						
4[(b)]	RCT	98	107	MD: 0.1 (-0.18 to 0.37)	LOW	Could not differentiate between interventions
Change in WC (cm) at 1 year from baseline. MID = 3.1 (follow-up 12 months; Better indicated by lower values)						
1[(c)]	RCT	41	37	MD: -0.7 (-3.58 to 2.18)	LOW	Could not differentiate between interventions
Adherence at 1 year (follow-up 12 months)						
1[(c)]	RCT	41/58 (70.7%)	37/57 (64.9%)	RR: 1.09 (0.85 to 1.4)	VERY LOW	Could not differentiate between interventions
Serious adverse events at 1 year (follow-up 12 months)						
1[(d)]	RCT	2/28 (7.1%)	3/40 (7.5%)	RR: 0.95 (0.17 to 5.33)	VERY LOW	Could not differentiate between interventions
Change in weight (kg) at 2 years from baseline. MID = 2.8 (follow-up 2 years; Better indicated by lower values)						
1[(e)]	RCT	33	28	MD: -0.2 (-3.05 to 2.65)	LOW	Could not differentiate between interventions
% Change HbA1c at 2 years from baseline. MID = 5% (follow-up 2 years; Better indicated by lower values)						
2[(f)]	RCT	61	68	MD: 0.25 (-0.1 to 0.6)	MODERATE	Could not differentiate between interventions
Adherence at 2 years (follow-up 2 years)						
1[(e)]	RCT	33/57 (57.9%)	28/58 (48.3%)	RR: 1.2 (0.85 to 1.7)	VERY LOW	Could not differentiate between interventions
QoL (PAID questionnaire) Higher scores indicate higher distress at 1 year. MID = 0.95 (follow-up 12 months; Better indicated by higher values)						

No of studies	Design	No of participants		Effect (95% CI)	Quality	Interpretation
		Very low carbohydrate diet	Usual care			
1(g)	RCT	41	37	MD: 3.1 (2.28 to 3.92)	LOW	**Favours usual care**
QoL (Diabetes-39 (Diabetes control)) Higher scores indicate greater impact on QoL at 1 year. MID = 1.4 (follow-up 12 months; Better indicated by higher values)						
1(g)	RCT	41	37	MD: 2.7 (1.46 to 3.94)	LOW	**Favours usual care**
QoL (Diabetes-39 (Anxiety and worry)) Higher scores indicate greater impact on QoL at 1 year. MID = 1.95 (follow-up 12 months; Better indicated by higher values)						
1(g)	RCT	41	37	MD: 9.4 (7.69 to 11.11)	LOW	**Favours usual care**
QoL (Diabetes-39 (Social burden)) Higher scores indicate greater impact on QoL at 1 year. MID = 1.15 (follow-up 12 months; Better indicated by higher values)						
1(g)	RCT	41	37	MD: 2.7 (1.68 to 3.72)	LOW	**Favours Usual care**
QoL (Diabetes-39 (Energy and Mobility) Higher scores indicate greater impact on QoL at 1 year. MID = 1.15 (follow-up 12 months; Better indicated by higher values)						
1(g)	RCT	41	37	MD: 6.8 (5.78 to 7.82)	LOW	**Favours Usual care**
QoL (PAID questionnaire) Higher scores indicate higher distress at 2 years. MID = 1.07 (follow-up 2 years; Better indicated by lower values)						
1(h)	RCT	33	28	MD: -0.32 (-1.38 to 0.74)	LOW	Could not differentiate between interventions
QoL (Diabetes-39 (Diabetes control)) Higher scores indicate greater impact on QoL at 2 years. MID = 1.4 (follow-up 2 years; Better indicated by lower values)						
1(h)	RCT	33	28	MD: 4.36 (2.99 to 5.73)	MODERATE	**Favours Usual care**
QoL (Diabetes-39 (Anxiety and worry)) Higher scores indicate greater impact on QoL at 2 years. MID = 1.86 (follow-up 2 years; Better indicated by lower values)						
1(h)	RCT	33	28	MD: 9.7 (7.86 to 11.54)	MODERATE	**Favours Usual care**

No of studies	Design	No of participants: Very low carbohydrate diet	No of participants: Usual care	Effect (95% CI)	Quality	Interpretation
QoL (Diabetes-39 (Social burden)) Higher scores indicate greater impact on QoL at 2 years. MID = 1.15 (follow-up 2 years; Better indicated by lower values)						
1[h]	RCT	33	28	MD: 1.99 (0.86 to 3.12)	LOW	**Favours Usual care**
QoL (Diabetes-39 (Energy and Mobility)) Higher scores indicate greater impact on QoL at 2 years. MID = 1.28 (follow-up 2 years; Better indicated by lower values)						
1[g]	RCT	41	37	MD: 1.38 (0.27 to 2.49)	VERY LOW	**Favours Usual care**

(a) Goldstein 2011; Saslow 2017; Tay 2015
(b) Goldstein 2011; Iqbal 2010; Saslow 2017; Tay 2015
(c) Tay 2015
(d) Iqbal 2010
(e) Tay 2018
(f) Iqbal 2010; Tay 2018
(g) Brinkworth 2016b
(h) Kakoschke 2021

Intermittent energy restriction (IER) – 5:2 Diet

Table 27: Mixed population

No of studies	Design	No of participants: IER (5:2 diet)	No of participants: Usual care	Effect (95% CI)	Quality	Interpretation
Intermittent energy restriction (5:2 diet) vs Usual care (advice)						
Change in weight (kg) at 1 year from baseline. MID = 2.85 (follow-up 12 months; Better indicated by lower values)						
1[a]	RCT	100	100	MD: -0.1 (-1.57 to 1.37)	HIGH	Could not differentiate between interventions
Adherence at 1 year (follow-up 12 months)						
1[a]	RCT	56/100 (56%)	48/100 (48%)	RR: 1.17 (0.89 to 1.53)	LOW	Could not differentiate between interventions

No of studies	Design	No of participants		Effect (95% CI)	Quality	Interpretation
		IER (5:2 diet)	Usual care			
Intermittent energy restriction (5:2 diet) + support vs Usual care (advice)						
Change in weight (kg) at 1 year from baseline. MID = 2.85 (follow-up 12 months; Better indicated by lower values)						
1[(a)]	RCT	100	100	MD: -0.8 (-2.24 to 0.64)	HIGH	Could not differentiate between interventions
Adherence at 1 year (follow-up 12 months)						
1[(a)]	RCT	45/100 (45%)	48/100 (48%)	RR: 0.94 (0.7 to 1.26)	LOW	Could not differentiate between interventions
Intermittent energy restriction (5:2 diet) + support vs Usual care (advice) + support						
Change in weight (kg) at 1 year from baseline. MID = 6.86 (follow-up 12 months; Better indicated by lower values)						
1[(b)]	RCT	49	52	MD: -2.9 (-8.83 to 3.03)	LOW	Could not differentiate between interventions
Change in WC (cm) at 1 year from baseline. MID = 5.5 (follow-up 12 months; Better indicated by lower values)						
1[(b)]	RCT	49	52	MD: -2.0 (-6.72 to 2.72)	LOW	Could not differentiate between interventions
Intermittent energy restriction (5:2 diet) + support vs Usual care (diet) + support						
Change in weight (kg) at 1 year from baseline. MID = 5.5 (follow-up 12 months; Better indicated by lower values)						
2[(c)]	RCT	103	107	MD: 0.89 (-1.45 to 3.22)	LOW	Could not differentiate between interventions
Change in weight (kg) at 2 years from baseline. MID = 0.6 (follow-up 2 years; Better indicated by lower values)						
1[(d)]	RCT	32	38	MD: -0.7 (-6.5 to 5.1)	VERY LOW	Could not differentiate between interventions
Change in WC (cm) at 1 year from baseline. MID = 4.6 (follow-up 12 months; Better indicated by lower values)						
2[(c)]	RCT	103	110	MD: 0.81 (-1.24 to 2.86)	LOW	Could not differentiate between interventions

(a) Hajek 2021
(b) Schubel 2018 (HELENA trial)
(c) Schubel 2018 (HELENA trial); Sundfor 2018
(d) Pannen 2021 (HELENA trial)

Table 28: In people with type 2 diabetes

No of studies	Design	No of participants IER (5:2 diet)	Usual care	Effect (95% CI)	Quality	Interpretation
Intermittent energy restriction (5:2 diet) + support vs Usual care (diet) + support						
Change in weight (kg) at 1 year from baseline. MID = 3.28 (follow-up 12 months; Better indicated by lower values)						
1[(a)]	RCT	70	67	MD: -1.8 (-4.09 to 0.49)	VERY LOW	Could not differentiate between interventions
Change in weight (kg) at 2 years from baseline. MID = 4.5 (follow-up 2 years; Better indicated by lower values)						
1[(b)]	RCT	70	67	MD: 0.0 (-2.99 to 2.99)	LOW	Could not differentiate between interventions
% change in HbA1c at 1 year from baseline. MID = 5% (follow-up 12 months; Better indicated by lower values)						
1[(a)]	RCT	70	67	MD: -0.2 (-0.62 to 0.22)	LOW	Could not differentiate between interventions
% change in HbA1c at 2 years from baseline. MID = 5% (follow-up 2 years; Better indicated by lower values)						
1[(b)]	RCT	70	67	MD: -0.3 (-1.01 to 0.41)	LOW	Could not differentiate between interventions
Intermittent energy restriction (5:2 diet) + support vs Low energy TOTAL MR + support						
Change in weight (kg) at 1 year from baseline. MID = 2.9 (follow-up 12 months; Better indicated by lower values)						
1[(c)]	RCT	39	40	MD: 1.1 (-1.57 to 3.77)	LOW	Could not differentiate between interventions
Change in HbA1c at 1 year from baseline. MID = 5 mmol/mol (follow-up 12 months; Better indicated by lower values)						
1[(c)]	RCT	39	40	MD: 0.6 (-4.26 to 5.46)	LOW	Could not differentiate between interventions
Serious adverse events at 1 year from baseline (follow-up 12 months)						
1[(c)]	RCT	4/39 (10.3%)	4/40 (10%)	RR: 1.03 (0.28 to 3.82)	VERY LOW	Could not differentiate between interventions
Adherence at 1 year from baseline (follow-up 12 months)						
1[(c)]	RCT	27/39 (69.2%)	30/40 (75%)	RR: 0.92 (0.7 to 1.22)	LOW	Could not differentiate between interventions

(a) Carter 2018
(b) Carter 2019
(c) McDiamid 2022

Intermittent energy restriction (IER) – Alternate day fasting (ADF) Diet

Table 29: Mixed population

No of studies	Design	No of participants: Alternate day fasting	No of participants: Usual care	Effect (95% CI)	Quality	Interpretation
Intermittent energy restriction (ADF diet) + support vs Usual care (diet) + support						
% Change in weight from baseline at 1 year. MID = 5% (follow-up 12 months; Better indicated by lower values)						
2[(a)]	RCT	46	49	MD: -0.06 (-0.78 to 0.65)	LOW	Could not differentiate between interventions
% Change in weight from baseline at 1 year - Mixed population (males + females). MID = 5% (follow-up 12 months; Better indicated by lower values)						
1[(b)]	RCT	34	31	MD: -0.7 (-3.1 to 1.7)	LOW	Could not differentiate between interventions
% Change in weight from baseline at 1 year - Females only. MID = 5% (follow-up 12 months; Better indicated by lower values)						
1[(c)]	RCT	12	18	MD: 0.0 (-0.75 to 0.75)	LOW	Could not differentiate between interventions
Intermittent energy restriction (ADF diet) + support vs No intervention						
% Change in weight from baseline at 1 year. MID = 5% (follow-up 12 months; Better indicated by lower values)						
1[(b)]	RCT	-	-	MD: -6.0 (-8.5 to -3.5)	VERY LOW	**Favours ADF diet**

(a) Trepanowski 2017; Oustric 2021
(b) Trepanowski 2017
(c) Oustric 2021

Intermittent energy restriction – Time restricted eating (TRE)

Table 30: Mixed population

No of studies	Design	No of participants: Time restricted eating (TRE)	No of participants: Usual care	Effect (95% CI)	Quality	Interpretation
Intermittent energy restriction (TRE) + support vs Usual care (diet) + support						

No of studies	Design	No of participants		Effect (95% CI)	Quality	Interpretation
		Time restricted eating (TRE)	Usual care			
Change in weight (kg) from end of baseline. MID = 2.5 (follow-up 12 months; Better indicated by lower values)						
2[(a)]	RCT	34	30	MD: -1.33 (-3.91 to 1.25)	VERY LOW	Could not differentiate between interventions
Change in weight (kg) from end of baseline - Males only. MID = 2.2 (follow-up 12 months; Better indicated by lower values)						
1[(b)]	RCT	15	13	MD: -8.1 (-12.54 to -3.66)	LOW	**Favours TRE**
Change in weight (kg) from end of baseline - Females only. MID = 2.8 (follow-up 12 months; Better indicated by lower values)						
1[(c)]	RCT	19	17	MD: 2.1 (-1.06 to 5.26)	VERY LOW	Could not differentiate between interventions
Change in waist circumference (cm) from end of baseline to 1 year - Females only. MID = 2.8 (follow-up 12 months; Better indicated by lower values)						
1[(c)]	RCT	19	17	MD: -0.4 (-3.61 to 2.81)	VERY LOW	Could not differentiate between interventions

(a) Byrne 2018; Keogh 2014
(b) Byrne 2018
(c) Keogh 2014

Intermittent energy restriction (IER) – Intermittent fasting

Table 31: Mixed population

No of studies	Design	No of participants: Intermittent energy restriction (iTRE): intermittent fasting	No of participants: Standard care (weight loss booklet)	Effect (95% CI)	Quality	Interpretation
Intermittent energy restriction (iTRE): intermittent fasting vs Usual care (advice)						
HbA1c % change from baseline – 18 months. MID = 0.13 (Better indicated by lower values)						
1[(a)]	RCT	85	41	MD -0.06 lower (-0.15 lower to 0.03 higher)	MODERATE	Could not differentiate between interventions
Body weight (kg) change from baseline – 18 months. MID = 4 (Better indicated by lower values)						
1[(a)]	RCT	85	41	MD -1.72 lower (-4.79 lower to 1.35 higher)	LOW	Could not differentiate between interventions
Number with at least one serious adverse event. MID = 0.8 to 1.25 (18 month follow up)						
1[(a)]	RCT	2/85 (2.4%)	0/41 (0%)	RR 2.44 (0.12, 49.73)	VERY LOW	Could not differentiate between interventions
Number with at least one adverse event. MID = 0.8 to 1.25 (18 month follow up)						
1[(a)]	RCT	31/85 (36%)	6/41 (14.6%)	RR 2.49 (1.13, 5.50)	LOW	**Favours standard care (weight loss booklet)**
Constipation. MID = 0.8 to 1.25 (18 month follow up)						
1[(a)]	RCT	6/85 (7.1%)	3/41 (7.3%)	RR 0.96 (0.25, 3.67)	VERY LOW	Could not differentiate between interventions
Intermittent energy restriction: intermittent fasting vs Usual care (diet)						
Weight change from baseline to 12 months (kg) MID = 3 (Better indicated by lower values)						
1[(b)]	RCT	45	43	MD -0.60 -3.21 lower to 2.01 higher)	MODERATE	Could not differentiate between interventions
Waist circumference from baseline to 12 months (cm) MID = 3.2 (Better indicated by lower values)						

No of studies	Design	No of participants		Effect (95% CI)	Quality	Interpretation
		Intermittent energy restriction (iTRE): intermittent fasting)	Standard care (weight loss booklet)			
1[(b)]	RCT	45	43	MD -1.10 (-3.92 lower to 1.72 higher)	MODERATE	Could not differentiate between interventions
Constipation at 18 months. MID = 0.8 – 1.25						
1[(b)]	RCT	2/45 (4.4%)	0/43 (0%)	RR 4.78 (0.24-96.84)	LOW	Could not differentiate between interventions

[(a)] Teong 2023
[(b)] Wei 2023

See appendix E for forest plots and appendix F for full GRADE tables

1.1.7 Economic evidence

A single search was performed to identify published economic evaluations of relevance to this review question in this guideline update (see Appendix B). The search retrieved 1,280 results and after removing duplicates, 1,043 were screened. 1,038 studies were excluded after the title and abstract screening, and an additional 3 studies were excluded following the full-text review.

See also the health economic study selection flow chart in Appendix G.

1.1.7.1 Included studies

Three health economic studies were included in this review. This is summarised in the health economic profile (Table 1 and Table 2) below and the health economic evidence table in Appendix H.

1.1.7.2 Excluded studies

Three economic studies were excluded at full-text screening. The list of excluded studies and reasons for exclusions are provided in Appendix I.

1.1.8 Summary of included economic evidence

Table 1: Total diet replacement (mixed population)

Applicability & limitations	Other comments	Intervention	Absolute		Incremental			Uncertainty
			Cost	Effects	Cost	Effects	ICER	
Kent et al. (2019)								
Directly applicable with potentially serious limitations(Appendix H)	**Approach to analysis:** A cost-utility analysis based on 1-year data from the DROPLET trial. Data from the DROPLET trial was incorporated into an adapted version of the PRIMEtime Cost-Effectiveness Obesity model. PRIMEtime is a population-based, proportional multistate life table model which links BMI to mortality and related diseases. **BMI related complications considered:** Type 2 diabetes, coronary heart disease, stroke, and cancers of the breast, colon, liver, kidney, and pancreas. **Perspective:** UK NHS health care perspective **Time horizon:** lifetime	**Lifetime time horizon**						**Deterministic:** Scenario analyses were performed for different combinations of the rate of weight regain, total diet replacement program costs, discount rates, adding further health care costs, modelling a direct effect on weight loss EQ-5D utility values, and applying the treatment to the general UK population. Total diet replacement remained cost-effective in all the above scenarios if we value a QALY at £20,000 **Probabilistic:** Performed with 95% confidence intervals reported. The 95% CI for the ICER ranged from £8,082 to £17,827 per QALY gained.
		Nurse-led behavioural support program	£7,425	23.19 QALYs	-	-	-	
		Total diet replacement	£8,090	23.26 QALYs	£665	0.065	£12,955 per QALY	

-

NICE model								
Directly applicable with minor limitations	**Approach to analysis:** A cost-utility analysis based on the 2-year results from DROPLET trial. PRIMEtime model was adapted for NICE economic evaluations and diseases' prevalence was adjusted to reflect the population of interest. Published and academic-in-confidence data from DIRECT was used to extrapolate long-term weight regain using a Weibull function. **BMI related complications considered:** Type 2 diabetes, coronary heart disease, stroke, and cancers of the breast, colon, liver, kidney, and pancreas. **Perspective:** UK NHS health care perspective **Time horizon:** lifetime	People living with overweight or obesity (BMI>25)	-	-	£739	0.032	£22,742 per QALY	**Deterministic:** A scenario analysis assuming a more rapid linear weight regain was conducted. Whit this alternative weight regain assumption, the intervention ceased being cost-effective in people living with obesity. A further scenario analysis with a linear weight regain and a discount rate of 1.5% for both costs and outcomes found the intervention cost-effective in both populations. **Probabilistic:** A probabilistic analysis using Monte Carlo simulation was conducted. The intervention was found to be cost-effective in 79% of the simulation in people living with obesity, but only 24% in people living with overweight and obesity
		People living with obesity (BMI>30)	-	-	£718	0.044	£16,456per QALY	

Table 2: Total diet replacement (people with diabetes)

Applicability & limitations	Other comments	Intervention	Absolute		Incremental			Uncertainty
			Cost	Effects	Cost	Effects	ICER	
Xin et al. (2020)								
Directly applicable with potentially serious limitations (Appendix H)	**Approach to analysis:** The cost-effectiveness analysis was a within-trial analysis based on the 2 years follow-up data DiRECT trial using intervention costs and healthcare resource use measured during the time of the study. The cost-utility analysis was a lifetime analysis developed by predicting time to relapse among those in remission at 2 years and applying mean management costs of diabetes. **BMI related complications considered:** Diabetes **Perspective:** UK NHS health care perspective	**2-year time horizon**						**Deterministic:** Several scenario analyses with different assumptions on relapses, time-horizon, remission rates, QoL reduction, mortality and long-term costs. Moreover, the model was run for men and women separately. In all scenarios, the intervention remained dominant in the lifetime time horizon analysis. **Probabilistic:** Performed with 95% Cis reported. For the two-year time horizon, the 95% CI was counterweight-plus being dominant to a cost of £4,212 per remission. For a lifetime horizon counterweight-plus was dominant at both the lower end and higher end of its 95% CI.
		Standard care	£2,420	3.4%, proportion of diabetes remission	-	-	-	
		Total diet replacement (Counterweight-Plus intervention)	£3,036	35.6%, proportion of diabetes remission	£616	32.3	£1,907 per remission	
		Lifetime time horizon						
		Standard care	£34,283	11.22 QALYs	-	-	-	
		Total diet replacement (Counterweight-Plus intervention)	£32,947	11.27 QALYs	-£1,337	0.06	Dominant	
NICE model								
Directly applicable with minor limitations	**Approach to analysis:** A cost-utility analysis based on the meta-analysis conducted for the systematic review and including DROPLET, DIRECT and DIADEM-I trials. PRIMEtime model was adapted for NICE economic	People living with overweight or obesity (BMI>25)	-	-	£1,217	0.193	£6,317 per QALY	**Deterministic:** Two different scenarios were tested, one with a more rapid linear weight regain and one using a discount rate of 1.5% for both costs and discounts. The intervention remained cost-effective in both scenarios

	evaluations and diseases' prevalence was adjusted to reflect the population of interest. Published and academic-in-confidence long-term data from DIRECT was used to extrapolate weight regain using a Weibull function. **BMI related complications considered:** Type 2 diabetes, coronary heart disease, stroke, and cancers of the breast, colon, liver, kidney, and pancreas. **Perspective:** UK NHS health care perspective **Time horizon:** lifetime	People living with obesity (BMI>30)	-	-	£1,212	0.192	£6,318 per QALT	**Probabilistic:** A probabilistic analysis using Monte Carlo simulation was conducted. The intervention was found to be cost-effective in 100% of the simulations in both populations included

1.1.9 Economic model

A health economic model was utilised to assess the cost-effectiveness of diet interventions. The full economic report is available in the appendix.

PRIMEtime, a model developed by the Nuffield Department of Population Health at Oxford University and linking change in lifestyle (such as BMI) to the incidence of non-communicable diseases (NCD) was adapted for NICE economic evaluations. In particular the following parameters were altered:

- BMI distribution in the UK population as well as gender split and average age were collected from the most recent Health Survey for England (HSE) 2019, which is a survey conducted each year covering a range of characteristics including socio-economic, demographic and health indicators.
- The prevalence several diseases in people with BMI > 25 kg/m^2 and BMI > 30 kg/m^2 was adjusted using data from HSE 2016-2019. These were: diabetes type 2, ischemic heart disease (IHD), stroke and cirrhosis
- EQ-5D-3L utility score in the general population was estimated using the ALDVMM model described in the latest NICE DSU report
- The cost of each disease was updated using the methodology described by Cobiac et al. 2022{Cobiac, 2022 #4}
- Incidence, prevalence and case fatality were updated to the most recent data using the Burden of Disease database

The model uses change in BMI following an intervention and simulates weight regain over time, which was modelled in the base case using a Weibull function fitted to the longest longitudinal data available from DIRECT trial. Changes in BMI are then translated into changes in disease incidence, which are used to estimate improvement in health, measured as quality-adjusted life years (QALYs), and saving in healthcare costs. The analysis is based on the following assumptions:

1. BMI affects people’s health and NHS healthcare costs only through the channel of BMI-related diseases. Direct impacts of a high BMI on health, for instance mental health or mobility, are not included.

2. All disease included in the models are chronic. This means they cause a healthcare cost, higher mortality and a loss in utility for the entire lifetime of the person. Different costs and quality of life are applied in the first cycles for some diseases when appropriate i.e. when the disease has a higher impact during its acute phase

3. Remission, i.e. transition from a disease to a healthy state, is allowed only for diabetes and only in the subgroup of people reflecting DIRECT trial population. This conclusion is drawn from the data obtained from the DIRECT trial study, which showed that the intervention increased the probability of diabetes remission among those who lost weight. All individuals who achieved remission are assumed to experience a relapse in the long term, as their weight returns to pre-intervention levels.

For further details, see the full economic report for evidence review F.

In the base case scenario, weight regain was modelled through a Weibull function and a discount rate of 3.5% for costs and health outcomes was applied. Although the model was built to assess the cost-effectiveness of any interventions, only total diet replacement (TDR) low-energy diet interventions were explored, as these were the only diets showing promising medium-term results in the clinical review. The model was run separately for people who have diabetes and for a mixed population with and without diabetes. Further subgroup analyses were conducted for those with a BMI above 25 kg/m^2 and those with a BMI above

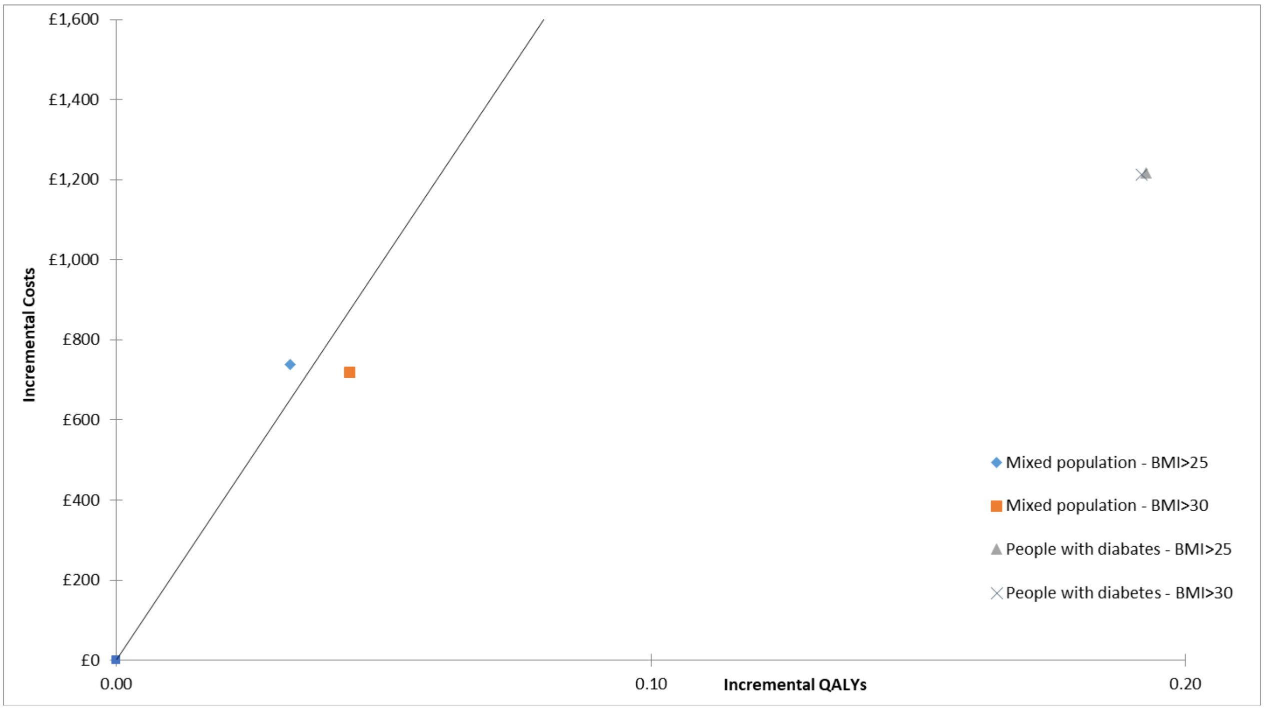
30 kg/m^2. The model was run probabilistically using 5,000 simulations and the results of the lifetime horizon analysis are illustrated in Table 3 and Figure 1.

Table 3: TDR low-energy diet versus standard care – probabilistic base case* results

Disease	Incremental cost per person	Incremental QALYs per person	Cost per QALY	Probability of being cost-effective (£20k/QALY)
Mixed population, overweight and obesity (BMI>25)	£739 (697 to 768)	0.032 (0.22 to 0.046)	**£22,742**	24%
Mixed population, obesity (BMI>30)	£718 (661 to 757)	0.044 (0.029 to 0.062)	**£16,456**	79%
People with diabetes, overweight and obesity (BMI > 25)	£1,217 (1,085 to 1,317)	0.193 (0.161 to 0.230)	**£6,317**	100%
People with diabetes and obesity (BMI > 30)	£1,212 (1,082 to 1,307)	0.192 (0.169 to 0.219)	**£6,318**	100%

** Weibull weight regain and 3.5% discounting rate on both outcomes and costs*
Note: The mixed population includes people with and without diabetes

Figure 1: Cost-effectiveness plane: TDR low-energy diet versus standard care – probabilistic base case* results



** Weibull weight regain and 3.5% discounting rate on both outcomes and costs*
Notes: The mixed population includes people with and without diabetes. The diagonal line represents NICE threshold of £20k/QALY

The scenario analysis on the mixed population showed that the results were sensitive to the assumption on weight regain. Whereas in the base case scenario weight regain was assumed to follow a Weibull curve, a further scenario with a faster weight regain modelled using a linear curve converging to 0 after 5 years was explored. In this scenario, the intervention ceased to be cost-effective in a mixed population living with obesity (BMI > 30 kg/m^2).

In conclusion, the PRIMEtime model developed by the Nuffield Department of Population Health at Oxford University was adapted for this guideline and used to assess the cost-effectiveness of low-energy diet interventions. In a mixed population, a TDR low-energy diet was found to be cost-effective compared to standard care only for those with a BMI above 30 kg/m^2. The results were sensitive to the assumption on weight regain as, when a more conservative linear regain was used, the cost per QALY became higher than £20,000 (£22,742 per QALY). In people with diabetes, the intervention was cost-effective irrespective of individuals' overweight or obesity status and regardless of any assumptions regarding weight regain. This is because cost-effectiveness in this population is mainly driven by diabetes remissions, which were observed in the included DIRECT trial.

1.1.10 The committee's discussion and interpretation of the evidence

1.1.10.1. The outcomes that matter most

During the review protocol stage, a number of critical and important outcomes were identified. The committee highlighted that the most important outcomes were change in weight or change in BMI from baseline to demonstrate a direct impact of the interventions. Quality of life and adverse events such as serious adverse events and development of eating disorders were also considered critical outcomes for decision making. Change in waist circumference was considered an important rather than critical outcome because it is less commonly reported in trials relative to change in weight or BMI which are usually the primary outcome, and it is less commonly used in clinical practice.

The committee noted that outcomes such as change in HbA1c were important when considering change in weight in people with type 2 diabetes. This is because reduction in weight can result in change in HbA1c which can lead to diabetes remission, which is when the blood sugar levels are below the diabetes range, usually without the need for any diabetes medication. The committee therefore agreed that change in HbA1c was an important outcome.

1.1.10.2 The quality of the evidence

During the development of this review, a stepped approach was utilised in which recent systematic reviews (those published between 2015 and 2022) were initially prioritised for inclusion. Through this approach, 6 systematic reviews were included which were deemed to be fully applicable. The overall risk of bias of the included systematic reviews ranged from low to high. All included systematic reviews provided risk of bias for the individual RCTs they included. This information was used in this review to determine the overall quality of the evidence.

Overall, 60 RCTs were included in this review. Thirty-six of the included RCTs were identified through the included systematic reviews and 24 additional RCTs were identified which provided new evidence on the different diets. The quality of the evidence ranged from high to very-low quality, with only a small number of findings rated high quality and most being rated as low or very low. Evidence was mainly downgraded for risk of bias due to issues around sequence generation, allocation concealment, blinding of participants and personnel, and missing data.

In the review protocol, a number of different comparators were identified. These included interventions compared to each other, no intervention, or usual care which could include the use of a conventional or balanced diet or could include the use of behavioural weight management advice. Several studies were identified which compared different diets to usual care, which either included the use of a conventional diet or advice. However, the committee noted that advice could not be considered an active comparator. They noted that in the DROPLET and DiRECT trials, the comparator arm received usual care in the form of standard weight management or diabetes advice which was considered to be general or basic advice. While the committee agreed it was appropriate not to downgrade this evidence for indirectness, they took these factors into account when considering the strength of the recommendations.

The review protocol also stated that where studies compared diets to usual care in the form of conventional diet, that conventional diet should be accompanied by a calorie deficit. While the majority of the studies included a calorie deficit in the control arm, 6 studies (Melberg 2014, Ebbeling 2007, Griffin 2013, Bazzano 2014, Hu 2015 and Lim 2010) did not include a calorie deficit in the control arm. These studies explored the effectiveness of low carbohydrate and very-low carbohydrate diets. These studies were downgraded for indirectness.

Additionally, the target population in the review protocol is adults aged 18 years and over living with overweight or obesity. While most studies included matched this population inclusion criteria, the committee noted that several studies included more selective populations. For example, the DiRECT trial included people aged between 20 and 65 years, who had been diagnosed with type 2 diabetes within the previous 6 years. While the trial authors selected diabetes duration based on the trade-off between achieving remission and benefiting the largest number of people, the committee noted that in practice you typically see people with different diabetes duration. They considered the potential need to downgrade this evidence for indirectness but agreed that the population was still directly applicable to the target population for the review because it comprised adults living with overweight or obesity.

1.1.10.3 Benefits and harms

Approaches to dietary interventions

The 2014 NICE guideline on obesity identification, assessment and management (CG189) recommended that in children, young people and adults, dietary changes and interventions should be tailored to food preferences and allow for a flexible and individual approach to reduce calorie intake. The committee agreed that this approach was crucial when it came to making dietary changes but noted that the 2014 recommendation did not detail the key factors that need to be taken into account when tailoring dietary interventions.

There was a lack evidence for subgroups such as people from ethnic minority family backgrounds and lower socioeconomic groups and a lack of evidence on adherence to different diets, so it was not possible to use evidence to inform recommendations on how to tailor dietary interventions. However, based on their expertise, the committee updated the existing recommendations to highlight that it was important to take into consideration food preferences, including cultural food preferences and personal circumstances such as home environment and financial circumstances when tailoring dietary interventions as these factors can have an impact on the effectiveness and adherence to dietary interventions.

The committee further noted that some people may have co-morbidities such as type 1 diabetes, inflammatory bowel disease or non-alcoholic fatty liver disease (NAFLD) that need to be considered when tailoring dietary interventions, as these conditions can limit the types of food groups people can eat. For example, a low-fat diet may be required for people with NAFLD, or carbohydrate intake may need to be controlled in people with type 1 diabetes. The committee further noted that it is important to consider if a person has an eating disorder or disordered eating as this can have an impact on the appropriateness of dietary interventions in this population. While this evidence review focused on the adult population, the committee agreed that the principles of the recommendation in the section on dietary advice are applicable to all age groups and therefore drafted the recommendation to cover all ages.

The 2014 guideline also recommended that restrictive and nutritionally unbalanced diets should not be used because they are ineffective in the long-term and can be harmful. The 2014 guidance also recommended that people should be encouraged to improve their diet even if they do not lose weight, because there can be other health benefits and that people should be encouraged to eat a nutritionally balanced diet in the long term, consistent with other health eating advice. The evidence reviewed did not contradict these recommendations so the committee agreed to retain them, but also used their expertise to add that people should be encouraged to improve their dietary intake even if they do not lose weight because there can be other health benefits such as improvement in lipid profile and reduction in the risk of type 2 diabetes and cardiovascular disease.

General principles of dietary interventions

The 2014 NICE guideline on obesity identification, assessment and management (CG189) recommended that the main requirement of a dietary approach to weight loss is that total energy intake should be less than energy expenditure. Additionally, diets that have a 600 kcal/day deficit or that reduce calories by lowering fat content (low-fat diets), in combination with expert support and intensive follow up were recommended for sustainable weight loss.

The committee agreed that achieving and maintaining an energy deficit is a key feature of dietary interventions which can be achieved by lowering specific macronutrient content, however they queried the evidence base around applying a 600 kcal/day deficit. In this review, the effectiveness of a number of different diets was evaluated, including macronutrient diets such as low- and very-low carbohydrate diets. Studies focusing on low-carbohydrate diets typically compared the diet to a conventional diet, which in several studies was a low-fat diet. These diets were also typically provided with support usually in the form of appointments with a dietitian. The majority of these diets were also accompanied with a calorie deficit which were either individualised for each participant or a 500 -800 kcal/ day deficit was recommended. Evidence on low-carbohydrate diets demonstrated that for almost all outcomes, the diet did not result in improvements in weight, BMI, waist circumference, or HbA1c, relative to conventional (usually low-fat) diets, apart from a small improvement in waist circumference for females (Tables 23 and 24). Evidence on very-low carbohydrate diets did show a reduction in weight at 1 year, but this was not sustained at 2 years and there was no improvement in quality of life for people with type 2 diabetes following a very-low carbohydrate diet (Tables 25 and 26).

While evidence on macronutrient diets (low carbohydrate, very low carbohydrate, or low-fat diets) did not demonstrate an improvement in a number of outcomes including change in weight, in practice, variations of these diets are commonly used and have shown to be effective. Based on the evidence and their expertise, the committee amended existing recommendations to remove reference to a 600 kcal/day deficit because they felt this was an arbitrarily specific number and instead stated that dietary approaches to support weight loss should maintain an energy deficit and this can be achieved by lowering specific macronutrient content. They also stressed that any dietary approaches that have an energy deficit are offered with adequate support, for example by an appropriately trained healthcare professional, such as a registered dietitian or registered nutritionist, and should include sufficient follow up to help people maintain any weight loss in the long term.

Low energy diets (total and partial meal replacement)

The 2014 NICE guideline on obesity identification, assessment and management (CG189) recommended that low-calorie diets (which contain between 800-1600 calories/ day) could be considered but it was highlighted that these diets were less likely to be nutritionally complete.

In the current review, low-calorie diets were referred to as low-energy diets and were defined as diets containing 800-1200 calories per day. The committee noted that further guidance around the use of low-energy diets were required as these diets are being used in practice and at the time of this update being piloted by NHS England to treat obesity and type 2 diabetes. The NHS Type 2 Diabetes Path to Remission Programme was being offered to people aged between 18-65years, who had a diagnosis of type 2 diabetes within the last 6 years and had a BMI over 27kg/m^2 in people from White ethnic family backgrounds or over 25 kg/m^2 in people from Black, Asian or other ethnic family backgrounds.

In this review, evidence was identified on the effectiveness of low energy diets provided as total meal replacements and partial meal replacements. This evidence indicated that in a mixed population, low energy total meal replacements plus support demonstrated a greater reduction in percentage weight and waist circumference (WC) at 1 year when compared with usual care (conventional diet) plus support (Table 18). When this diet was compared with usual care which was in the form of advice, evidence showed that there was a greater reduction in weight and WC at 1 and 3 years follow up (Table 18).

In people with type 2 diabetes, low energy total meal replacements plus support demonstrated a reduction in weight, WC, HbA1c and improvement in quality of life at 1 and 2 years when compared with usual care alone (Table 19). Low energy total meal replacement diets plus support also resulted in reduction in weight, WC, percentage HbA1c and improvement in quality of life when compared to usual care plus support (Table 19). However, 1 study (DiRECT Trial) demonstrated that adherence was better in the usual care arm when compared with low-energy diet plus support (Table 19).

The evidence showed similar findings when low energy diets were provided as partial meal replacements: for a mixed population there was a significant reduction in weight compared to usual care in the form of diet and advice (Table 20), and for people with type 2 diabetes there was a significant reduction in waist circumference (Table 21).

Based on the clinical and cost effectiveness evidence (see section 1.1.10.4) and the quality of the evidence, the committee agreed that low-energy diets could be considered as a diet approach to weight loss with long term support. As evidence was identified in people living with overweight and obesity, as well as those with type 2 diabetes, the committee agreed that low-energy diets should be considered in people living with obesity, irrespective of type 2 diabetes diagnosis and should also be considered in people living with overweight with a type 2 diabetes diagnosis.

The committee also noted that the NHS pilot of low-energy diets was limited to people who have had a diagnosis of type 2 diabetes in the last 6 years. While the pilot was based on the DiRECT and DROPLET trials, the DiRECT trial specifically included people with diabetes duration up to 6 years. Correspondence with the trial authors highlighted that a 6 year cut-off was utilised in the trial as this was seen as a compromise between the most likely duration for achieving remission and duration which would potentially benefit the largest number of people. The DIADEM-I trial included in this review also included a cut-off for people with diagnosis of type 2 diabetes within the previous 3 years.

The committee noted that they were not aware of wider evidence on the relationship between the duration of type 2 diabetes and the likelihood of remission with weight loss. They also noted that as weight loss in people with type 2 diabetes could potentially lead to diabetes remission, there could be an improvement in quality of life, which has been supported by evidence identified in this review. Based on this understanding, the committee agreed that low-energy diets should be considered in people living with overweight with type 2 diabetes irrespective of diabetes duration. They also agreed that further research is required on the effectiveness of low energy diets in people living with overweight and obesity with different durations of type 2 diabetes, so they drafted a research recommendation about this (see Appendix J).

The committee focused on the intervention design of individual studies to identify further information about the diets. In the DROPLET trial, participants received nutritionally complete meals that were given for a period of 8 weeks. In the DiRECT trial, participants received nutritionally complete meals for 12 weeks. Other trials included in the evidence such as the OPTIWIN trial, participants followed the diet for 12 to 16 weeks while in Brown 2020, participants followed the diet for 12 weeks. Based on this information, the committee recommended that low-energy diets should be nutritionally complete and should be followed for a maximum of 12 weeks.

While the new recommendations state that low-energy diets should be followed for a maximum of 12 weeks, the committee noted that it was important to state that these should not be considered as long-term weight management strategies due to the restrictive nature of these diets. Based on this understanding, the committee recommended that low-energy diets should not be used as a long-term strategy to manage obesity.

Furthermore, it was noted that all the studies included as part of the evidence for low-energy total meal replacement diets offered support to participants. For example, in the DIADEM-I trial, participants were supported by a team of trained dietitians, personal trainers and a physician. In the DiRECT trial, participants were offered long-term support by dietician or practice nurse. Due to the restrictive nature of these diets and to help people maintain their weight following low-energy diets, it was vital that support was provided as part of a multicomponent strategy. They also stated that the diet should be accompanied with ongoing clinical support and supervision including advice on food re-introduction. They also stated that an appropriately trained registered dietitians and registered nutritionists should also be involved. Based on the evidence and their expertise, the committee further highlighted that low-energy diets should only be considered as part of a multicomponent overweight and obesity management strategy with long term support which is offered within specialist overweight and obesity management services. The committee further highlighted that other services such as the type 2 diabetes management services can also provide support. They acknowledged that providing this support may create additional challenges related to resource allocation, training, and accessibility, but integration of dietary support services within existing healthcare structures and use of telehealth or support websites/apps may be helpful.

Very low energy diets (total meal replacement)

The 2014 NICE guideline on obesity identification, assessment and management (CG189) recommended that very-low-calorie-diets should not routinely be used to manage obesity. The guideline also recommended that very-low-calorie diets should only be considered as part of a multicomponent weight management strategy, for people who are living with obesity and who have a clinically assessed need to rapidly lose weight (for example, people who need joint replacement surgery or who are seeking fertility services). Furthermore, these diets should be nutritionally complete, should be followed for a maximum of 12 weeks either continuously or intermittently and the person following the diet is given ongoing clinical support.

In the current review, very-low-calorie diets were referred to as very-low-energy diets and were defined as diets containing less than 800 calories per day. Evidence was only identified on the use of very-low-energy total meal replacements in a mixed population. No studies were identified on the use of this diet in people with type 2 diabetes. Studies included in the review also provided very-low-energy-diets continuously, and no evidence was identified on these diets being used intermittently. Due to this lack of evidence, the committee opted to remove the reference to these diets being used intermittently, but they retained the rest of the recommendation. In the included studies, the committee noted that very-low-energy diets were given for a period of 12 to 16 weeks and support was also offered alongside the diet which was usually in the form of appointments with a dietitian. In terms of the evidence, the use of very-low-energy total meal replacement diets did result in reduction in waist circumference at 1 year when compared with usual care (advice/ conventional diet) with support, and a reduction in weight at 1 year but this was for females only (Table 22). The evidence also showed that the very-low-energy total meal replacement diet resulted in a reduction in weight and WC at 1 and 2 years when compared to usual care (advice) (Table 22).

While evidence suggested promising results, the committee highlighted that very-low-energy-diets are very restrictive in nature and it is important to consider the adverse events associated with the use of the diet, for which no evidence was identified. However, the committee noted that in practice, very-low-energy diets are being used and side effects such as constipation, fatigue and hair loss are quite common, therefore it is important to include further guidance on the use of these diets.

Due to the restrictive nature of the diet, the committee retained an existing recommendation to state that very-low-energy diets should not be used as a long-term strategy to manage obesity. They also further stated that very-low-energy diets should only be considered as part of a multicomponent overweight and obesity management strategy offered within specialist overweight and obesity management services and should be followed for a maximum of 12 weeks, with ongoing clinical support and supervision including advice on food re-introduction. They also stated that appropriately trained registered dietitians and registered nutritionists should be involved.

Similar to the 2014 recommendations, the committee agreed that the very-low-energy diets can be considered in people with a clinically assessed need to rapidly lose weight, although they were not aware of evidence that demonstrated that people who need to lose weight in order to access other services would necessarily have better outcomes from those services. Additionally, studies included in this review did not limit the participants to people who needed to rapidly lose weight. It was also noted that requiring people to lose weight before receiving other treatment may not only delay people from receiving treatment that can improve their quality of life but can also be stigmatising to people living with overweight and obesity. The consequence of this weight stigma can include low self-esteem, negative body image, depression and anxiety.

The committee noted that for some procedures, weight loss can make the procedure safer and more technically feasible. For example, obesity can make some procedures as part of the fertility treatment, such as egg collection, challenging. Weight loss before such a treatment may make the procedure more technically feasible. Based on this understanding, the committee agreed that it was important to highlight the importance of surgical feasibility and safety as a reason to rapidly lose weight rather than access to other services. Furthermore, the committee drafted an additional research recommendation for further research into the effectiveness of low-energy and very-low-energy diets in people who need to lose weight in order to access treatment for other conditions (see Appendix J).

Discussions about low-energy and very-low-energy diets

The 2014 NICE guideline stated that before starting someone on a very-low-calorie diet as part of a multicomponent weight management strategy, counselling and assessment for eating disorders and other psychopathology should be considered to make sure the diet is appropriate for the person. The risk and benefits of the diet should also be discussed with people, and they should be informed that a very-low-calorie diet is not a long-term weight management strategy, and that regaining weight may happen and is not because of their own or their clinician's failure. Lastly, reintroduction of food following a liquid diet should also be discussed. The committee agreed with the sentiments of this recommendation, but amended it based on the evidence and their expertise. They also highlighted that discussions should occur upfront for both low and very-low energy diets, so that a shared decision can be reached about treatment options.

The committee noted that while evidence was identified that supported the use of low and very-low-energy diets, due to the restrictive nature of these diets, adverse events are possible. In this review, some evidence was identified on adverse events. For most outcomes relating to adverse events, studies could not differentiate between different dietary interventions and the control, although moderate quality evidence from one study showed participants following a low energy total meal replacement diet reported significantly higher rates of constipation than control participants. The committee noted that in practice, adverse events such as constipation, fatigue and hair loss are commonly seen. Additionally, due to the restrictive nature of these diets, weight loss can happen rapidly, but once a person is reintroduced to food, weight regain is possible, which is a risk associated with these diets.

Based on this understanding, the committee recommended that before starting someone on low or very low-energy diets, people should be made aware of the restrictive nature of these diets, particularly very-low-energy diets which are used for very specific goals and should not be considered a long-term overweight and obesity management strategy. Additionally, the health benefits (such as improvement in diabetes) should be discussed alongside the risks associated with the diets. This can include adverse events, weight regain and weight cycling, which is the continual cycle of losing weight and regaining weight. The committee also stated that as part of the discussion people should be made aware of the fact that weight regain can happen and if it does it is not because of the person or the healthcare professional’s failure.

Furthermore, while no evidence was identified on the development of eating disorders or disordered eating, the committee raised concerns on the psychological impact of these diets. Based on this understanding, the committee highlighted that it was important that as part of the discussions, healthcare professionals consider assessment and counselling for eating disorders and other psychopathology.

Additionally, due to the limited evidence identified on adverse events, the committee drafted an additional research recommendation to further explore the adverse events, including development of eating disorders or disordered eating, associated with these diets (see Appendix J).

The committee also noted that a key feature of these diets is that these require reintroduction to foods following the diet. For example, in the DROPLET trial, participants replaced all food with four formula food products daily (soups, shakes and bars) and after 8 weeks, there was a four week stepwise reduction in use of the formula food products and the reintroduction of conventional food based meals. During this process, the participants were supported by counsellors. A similar approach was also utilised in the DiRECT trial where the total diet replacement phase was followed by a structured food reintroduction phase and an ongoing structured programme with monthly visits for long-term weight loss maintenance.

The committee noted that support was critical with these diets, not only because people need to be supported while they are reintroduced to foods, but also because weight regain may happen and can be challenging for people to navigate and understand, so people will require support in order to understand long-term weight maintenance options. Based on this understanding, the committee recommended that reintroduction of food following the diet should also be discussed with the person as well as the long-term weight maintenance support or therapy options available to the person if weight regain does happen. This can include nutritional, physical activity, pharmacological or surgical support.

The committee also stated that people who may receive low and very-low energy diets may have comorbidities that require medication. Starting someone on these diets may require medication dosage to be changed. Based on this understanding, the committee also recommended that healthcare professionals should review any existing medication and discuss any changes that may need to be made to medication regime.

1.1.10.4 Cost effectiveness and resource use

Based on the clinical review, the committee agreed that the low energy total replacement diet (TDR) interventions show the most promising clinical results in terms of initial weight loss and long-term weight maintenance. Two studies on the cost-effectiveness of low energy TDR were included in the review. Kent et al. 2019 assessed the cost-effectiveness of Cambridge plan TDR based on the UK trial, DROPLET, and found the intervention to be cost-effective among a mixed population with BMI higher than 30 kg/m ^{2}. However, the analysis was based on the first year of the trial results and relied on conservative weight regain assumption in the long term. Moreover, the base case scenario was not in line with the NICE reference case as it used a lower discount rate of 1.5% for both costs and health outcomes. Xin et al. 2020 assessed the cost-effectiveness of a TDR intervention among people who were overweight (BMI over 27kg/m^2) and live with T2DM, based on another UK trial DiRECT. They also found the intervention to be cost-effective, however, the analysis focused on diabetic events only and did not include all obesity-related outcomes. In addition, they extrapolated lifetime consequences based solely on the two-year results from the trial, which were insufficient to accurately estimate long-term weight regain and lifetime risk of diabetes relapse and remission rates.

As the follow-up data for both DiRECT and DROPLET are now available (either publicly or academic-in-confidence), we decided to conduct a cost-utility analysis using an adaptation of the PRIMEtime model. The original PRIMEtime model was developed by a group of researchers from the Nuffield Department of Population Health at University of Oxford, in order to estimate changes in health outcomes and costs related to population changes in diet and physical activity. The model was originally developed for interventions targeting the entire UK population, so it was adapted for NICE economic analyses focusing on four specific populations: people with diabetes who are living with overweight or obesity, people with diabetes who are living with obesity, a mixed population who is living with overweight or obesity and mixed population who is living with obesity. As the committee acknowledged that weight regain is a crucial aspect, two scenarios were tested: a first scenario used academic-in-confidence data from the DiRECT trial to estimate a gradual regain over a long-term; a second scenario assumed a more rapid increase occurring in 5 years, as done already in the literature

The TDR was found to be cost-effective in people with T2DM regardless of whether they are overweight (cost per QALY = £6,317 , % cost-effective = 100%) or live with obesity (cost per QALY = £6,318, % cost-effective = 100%). The results remained robust across all scenarios in the sensitivity analyses. In a mixed population, TDR was found to be cost-effective in people who live with obesity (cost per QALY = £16,456, % cost-effective = 79%) but only marginally cost-effective among those who are overweight (cost per QALY = ££22,742, % cost-effective = 24%). When assuming a linear weight regain to the pre-intervention level after 5 years in the sensitivity analyses, TDR was not even cost-effective in those who live with obesity (cost per QALY = £26,327, % cost-effective = 10%). The difference in results between the mixed population and people with T2DM is mainly due to the clinical benefits in diabetes remission after the TDR, leading to an increase in quality of life and a reduction in diabetes-related healthcare costs.

In addition, we conducted a health inequality impact assessment for the TDR interventions using a prototype tool developed by the University of York. The tool calculates the net health effects of the interventions across index of multiple deprivation (IMD) quintiles in England. Due to higher prevalence and uptake of weight management services among the most deprived groups total health benefits at the population level were highest for these groups. However, at the individual level the average per person QALYs gain for these groups was smaller than expected due to lower completion rates of weight management interventions in these groups. The findings help us to identify the key drivers of inequality and point out the need for more research on the facilitators and barriers to weight management services among people from more deprived groups. Full details can be found in the inequalities analysis report (Evidence review F-B).

Based on the findings of the economic model and inequality impact assessment, the committee agreed that the TDR is likely to be cost-effective among people with T2DM, no matter whether they are living with overweight or obesity. For people without T2DM, TDR appears be cost-effective among people who live with obesity while the evidence for people who are living with overweight is less convincing. Therefore, the committee agreed to make a weak (consider) recommendation for the low-energy TDR among people living with obesity, or who are living with overweight and with T2DM. Although the evidence provided by published studies and the original economic evaluation suggested that TDR was very likely to be cost-effective in these two populations, the committee were aware that, sometimes, weight regain could occur rapidly and be harmful if people experience weight cycling. Therefore, a weak recommendation was preferred to a stronger one as, in certain cases, a low-energy TDR might not be the most appropriate intervention.

Both TDR interventions in DROPLET and DiRECT trials included a long-term support component in weight maintenance that was proven to be successful in reducing weight regain over the long-term (3-5 years). The committee highlighted the importance of including support to people who are receiving TDR and updated the original recommendation to include a discussion on long-term weight maintenance support options, including physical activity, surgical interventions and so on. Although this recommendation could potentially increase pressure on weight management services, it is expected to increase the number of people receiving support by health professionals while on a TD diet, which will increase the likelihood they maintain a healthy weight and reduce the risk of harmful weight regain.

The committee also noted that, currently, TDR interventions might entail financial burdens for patients if they are required to pay out-of-pocket for the associated products. However, the recommendation is expected to increase NHS funding for TDR interventions to provide them free-of-charge for the eligible population. Although this could lead to an increase of NHS spending in the short-term, it is expected to reduce future spending linked to obesity-related diseases. This is confirmed by the evidence and the original economic model that found the intervention cost-effective in the long-term.

The committee highlighted the NHS Type 2 Diabetes Path to Remission Programme which already provides free-of-charge a low calorie, total diet replacement treatment in selected areas for people with type 2 diabetes who are living with obesity or overweight. Results from this will help to build knowledge and understanding about the use of these interventions and the impact they might have on the treatment of people with type 2 diabetes.

1.1.10.5 Other factors the committee took into account

Other diets

No evidence was identified on the effectiveness of plant-based diets and the committee did not draft any recommendations or research recommendations for plant base diets. The committee noted that in plant-based diets are typically used to improve general wellbeing or due to sustainability or ethical issues, rather than for weight loss.

Some evidence was identified on intermittent energy restriction. This evidence demonstrated that alternate day fasting (ADF) resulted in a greater reduction in percentage change in weight when compared with no intervention, however the evidence could not differentiate between ADF diet with support compared to usual care (diet) with support for all outcomes (Table 29). Time restricted eating with support also resulted in change in weight when compared with usual care (diet) with support, but the evidence could not differentiate between the 5:2 diet and usual care (advice) (Table 27). One study (Teong 2023) also demonstrated that fewer adverse events occurred in the usual care arm when compared with intermittent fasting. However, evidence could not differentiate between various intermittent energy restriction diets and control for other outcomes such as WC or change in HbA1c. The evidence on this dietary approach was also largely of low to very low quality and mainly came from only 1 or 2 trials per comparison. Due to these limitations, the committee did not draft specific recommendations on the use of these diets but noted that in practice intermittent energy restriction is now being used more commonly in practice, and therefore it would be useful to have further research on these diets. Based on this, the committee drafted a research recommendation to explore the effectiveness of these diets (see Appendix J).

1.1.11 Recommendations supported by this evidence review

This evidence review supports recommendations 1.16.1 to 1.16.12 and the research recommendations outlined in appendix K on: the effectiveness of low-energy diets in people living with overweight and obesity with different durations of type 2 diabetes; the effectiveness and cost-effectiveness of low-energy and very-low-energy diets in achieving and maintaining weight loss in adults who are required to lose weight before receiving treatment for other health conditions because they are living with overweight or obesity; the adverse events associated with different dietary approaches to losing weight in people living with overweight and obesity; and the effectiveness and cost-effectiveness of intermittent fasting in achieving and maintaining weight loss in adults living with overweight or obesity.

1.1.12 References – included studies

1.1.12.1 Effectiveness evidence – systematic reviews

Astbury, N.M., Piernas, C., Hartmann-Boyce, J. et al. (2019) A systematic review and meta-analysis of the effectiveness of meal replacements for weight loss. Obesity Reviews 20(4): 569-587

Naude, Celeste E, Brand, Amanda, Schoonees, Anel et al. (2022) Low-carbohydrate versus balanced-carbohydrate diets for reducing weight and cardiovascular risk. The Cochrane database of systematic reviews 1: cd013334

Nicholas, A.P., Soto-Mota, A., Lambert, H. et al. (2021) Restricting carbohydrates and calories in the treatment of type 2 diabetes: A systematic review of the effectiveness of 'low-carbohydrate' interventions with differing energy levels. Journal of Nutritional Science 10: e76

Parretti, H.M., Jebb, S.A., Johns, D.J. et al. (2016) Clinical effectiveness of very-low-energy diets in the management of weight loss: A systematic review and meta-analysis of randomized controlled trials. Obesity Reviews 17(3): 225-234

Rafiullah, M.; Musambil, M.; David, S.K. (2022) Effect of a very low-carbohydrate ketogenic diet vs recommended diets in patients with type 2 diabetes: A meta-analysis. Nutrition Reviews 80(3): 488-502

Schwingshackl, L., Zahringer, J., Nitschke, K. et al. (2021) Impact of intermittent energy restriction on anthropometric outcomes and intermediate disease markers in patients with overweight and obesity: systematic review and meta-analyses. Critical reviews in food science and nutrition 61(8): 1293-1304

1.1.12.2 Effectiveness evidence – primary studies

Ard, J.D., Lewis, K.H., Rothberg, A. et al. (2019) Effectiveness of a Total Meal Replacement Program (OPTIFAST Program) on Weight Loss: Results from the OPTIWIN Study. Obesity 27(1): 22-29

Ashley, Judith M., Herzog, Holly, Clodfelter, Sharon et al. (2007) Nutrient adequacy during weight loss interventions: a randomized study in women comparing the dietary intake in a meal replacement group with a traditional food group. Nutrition Journal 6(1): 12

Astbury, N.M., Aveyard, P., Nickless, A. et al. (2018) Doctor Referral of Overweight People to Low Energy total diet replacement Treatment (DROPLET): Pragmatic randomised controlled trial. BMJ (Online) 362: k3760

Astbury, N.M., Edwards, R.M., Ghebretinsea, F. et al. (2021) Extended follow-up of a short total diet replacement programme: results of the Doctor Referral of Overweight People to Low Energy total diet replacement Treatment (DROPLET) randomised controlled trial at 3 years. International Journal of Obesity 45(11): 2432-2438

Bazzano, L.A., Hu, T., Reynolds, K. et al. (2014) Effects of low-carbohydrate and low-fat diets: A randomized trial. Annals of Internal Medicine 161(5): 309-318

Brinkworth, G.D., Luscombe-Marsh, N.D., Thompson, C.H. et al. (2016) Long-term effects of very low-carbohydrate and high-carbohydrate weight-loss diets on psychological health in obese adults with type 2 diabetes: randomized controlled trial. Journal of Internal Medicine 280(4): 388-397

Brinkworth, G.D., Noakes, M., Buckley, J.D. et al. (2009) Long-term effects of a very-low-carbohydrate weight loss diet compared with an isocaloric low-fat diet after 12 mo. American Journal of Clinical Nutrition 90(1): 23-32

Brinkworth, G.D., Wycherley, T.P., Noakes, M. et al. (2016) Long-term effects of a very-low-carbohydrate weight-loss diet and an isocaloric low-fat diet on bone health in obese adults. Nutrition 32(9): 1033-1036

Brown, A., Dornhorst, A., McGowan, B. et al. (2020) Low-energy total diet replacement intervention in patients with type 2 diabetes mellitus and obesity treated with insulin: A randomized trial. BMJ Open Diabetes Research and Care 8(1): e001012

Byrne, N M, Sainsbury, A, King, N A et al. (2018) Intermittent energy restriction improves weight loss efficiency in obese men: the MATADOR study. International journal of obesity (2005) 42(2): 129-138

Calleja Fernandez, A., Vidal Casariego, A., Cano Rodriguez, I. et al. (2012) One-year effectiveness of two hypocaloric diets with different protein/carbohydrate ratios in weight loss and insulin resistance. Nutricion hospitalaria 27(6): 2093-2101

Carter, S.; Clifton, P.M.; Keogh, J.B. (2018) Effect of Intermittent Compared With Continuous Energy Restricted Diet on Glycemic Control in Patients With Type 2 Diabetes: A Randomized Noninferiority Trial. JAMA network open 1(3): e180756

Carter, S.; Clifton, P.M.; Keogh, J.B. (2019) The effect of intermittent compared with continuous energy restriction on glycaemic control in patients with type 2 diabetes: 24-month follow-up of a randomised noninferiority trial. Diabetes Research and Clinical Practice 151: 11-19

Ebbeling, C.B., Leidig, M.M., Feldman, H.A. et al. (2007) Effects of a low-glycemic load vs low-fat diet in obese young adults: A randomized trial. Journal of the American Medical Association 297(19): 2092-2102

Elhayany, A., Lustman, A., Abel, R. et al. (2010) A low carbohydrate Mediterranean diet improves cardiovascular risk factors and diabetes control among overweight patients with type 2 diabetes mellitus: A 1-year prospective randomized intervention study. Diabetes, Obesity and Metabolism 12(3): 204-209

Foraker, R.E., Pennell, M., Sprangers, P. et al. (2014) Effect of a low-fat or low-carbohydrate weight-loss diet on markers of cardiovascular risk among premenopausal women: A randomized trial. Journal of Women's Health 23(8): 675-680

Foster, G.D., Wyatt, H.R., Hill, J.O. et al. (2010) Weight and metabolic outcomes after 2 years on a low-carbohydrate versus low-fat diet: A randomized trial. Annals of Internal Medicine 153(3): 147-157

Frisch, S., Zittermann, A., Berthold, H.K. et al. (2009) A randomized controlled trial on the efficacy of carbohydrate-reduced or fat-reduced diets in patients attending a telemedically guided weight loss program. Cardiovascular Diabetology 8: 36

Goldstein, T., Kark, J.D., Berry, E.M. et al. (2011) The effect of a low carbohydrate energy-unrestricted diet on weight loss in obese type 2 diabetes patients - A randomized controlled trial. e-SPEN 6(4): e178-e186

Griffin, H J, Cheng, H L, O'Connor, H T et al. (2013) Higher protein diet for weight management in young overweight women: a 12-month randomized controlled trial. Diabetes, obesity & metabolism 15(6): 572-5

Guldbrand, H., Dizdar, B., Bunjaku, B. et al. (2012) In type 2 diabetes, randomisation to advice to follow a low-carbohydrate diet transiently improves glycaemic control compared with advice to follow a low-fat diet producing a similar weight loss. Diabetologia 55(8): 2118-2127

Guldbrand, H., Lindstrom, T., Dizdar, B. et al. (2014) Randomization to a low-carbohydrate diet advice improves health related quality of life compared with a low-fat diet at similar weight-loss in Type 2 diabetes mellitus. Diabetes Research and Clinical Practice 106(2): 221-227

Hajek, P., Przulj, D., Pesola, F. et al. (2021) A randomised controlled trial of the 5:2 diet. PLoS ONE 16(11november): e0258853

Hu, T., Yao, L., Reynolds, K. et al. (2015) The effects of a low-carbohydrate diet vs. a low-fat diet on novel cardiovascular risk factors: A randomized controlled trial. Nutrients 7(9): 7978-7994

Iqbal, N., Vetter, M.L., Moore, R.H. et al. (2010) Effects of a low-intensity intervention that prescribed a low-carbohydrate vs. a low-fat diet in obese, diabetic participants. Obesity 18(9): 1733-1738

Jin, X., Gibson, A.A., Salis, Z. et al. (2022) Effect of severe versus moderate energy restriction on physical activity among postmenopausal female adults with obesity: a pre-specified secondary analysis of the TEMPO Diet randomized controlled Trial. The American journal of clinical nutrition

Kakoschke, N., Zajac, I.T., Tay, J. et al. (2021) Effects of very low-carbohydrate vs. high-carbohydrate weight loss diets on psychological health in adults with obesity and type 2 diabetes: a 2-year randomized controlled trial. European Journal of Nutrition 60(8): 4251-4262

Keogh, J.B., Pedersen, E., Petersen, K.S. et al. (2014) Effects of intermittent compared to continuous energy restriction on short-term weight loss and long-term weight loss maintenance. Clinical Obesity 4(3): 150-156

Khoo, Joan, Piantadosi, Cynthia, Duncan, Rae et al. (2011) Comparing effects of a low-energy diet and a high-protein low-fat diet on sexual and endothelial function, urinary tract symptoms, and inflammation in obese diabetic men. The journal of sexual medicine 8(10): 2868-75

Klemsdal, T.O., Holme, I., Nerland, H. et al. (2010) Effects of a low glycemic load diet versus a low-fat diet in subjects with and without the metabolic syndrome. Nutrition, Metabolism and Cardiovascular Diseases 20(3): 195-201

Krebs, J.D., Elley, C.R., Parry-Strong, A. et al. (2012) The Diabetes Excess Weight Loss (DEWL) Trial: A randomised controlled trial of high-protein versus high-carbohydrate diets over 2 years in type 2 diabetes. Diabetologia 55(4): 905-914

Larsen, R.N., Mann, N.J., Maclean, E. et al. (2011) The effect of high-protein, low-carbohydrate diets in the treatment of type 2 diabetes: A 12 month randomised controlled trial. Diabetologia 54(4): 731-740

Layman, Donald K, Evans, Ellen M, Erickson, Donna et al. (2009) A moderate-protein diet produces sustained weight loss and long-term changes in body composition and blood lipids in obese adults. The Journal of nutrition 139(3): 514-21

Lean, M.E., Leslie, W.S., Barnes, A.C. et al. (2018) Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial. The Lancet 391(10120): 541-551

Lean, M.E.J., Leslie, W.S., Barnes, A.C. et al. (2019) Durability of a primary care-led weight-management intervention for remission of type 2 diabetes: 2-year results of the DiRECT open-label, cluster-randomised trial. The Lancet Diabetes and Endocrinology 7(5): 344-355

Lim, S.S., Noakes, M., Keogh, J.B. et al. (2010) Long-term effects of a low carbohydrate, low fat or high unsaturated fat diet compared to a no-intervention control. Nutrition, Metabolism and Cardiovascular Diseases 20(8): 599-607

McDiarmid, S., Harvie, M., Johnson, R. et al. (2022) Manchester Intermittent versus Daily Diet App Study (MIDDAS): A pilot randomized controlled trial in patients with type 2 diabetes. Diabetes, Obesity and Metabolism 24(3): 432-441

Mellberg, C., Sandberg, S., Ryberg, M. et al. (2014) Long-term effects of a Palaeolithic-type diet in obese postmenopausal women: A 2-year randomized trial. European Journal of Clinical Nutrition 68(3): 350-357

Moreno, B., Bellido, D., Sajoux, I. et al. (2014) Comparison of a very low-calorie-ketogenic diet with a standard low-calorie diet in the treatment of obesity. Endocrine 47(3): 793-805

Moreno, B., Crujeiras, A.B., Bellido, D. et al. (2016) Obesity treatment by very low-calorie-ketogenic diet at two years: reduction in visceral fat and on the burden of disease. Endocrine 54(3): 681-690

Oustric, P., Beaulieu, K., Casanova, N. et al. (2021) Food liking but not wanting decreases after controlled intermittent or continuous energy restriction to >=5% weight loss in women with overweight/obesity. Nutrients 13(1): 1-14

Pannen, S.T., Maldonado, S.G., Nonnenmacher, T. et al. (2021) Adherence and dietary composition during intermittent vs. Continuous calorie restriction: Follow-up data from a randomized controlled trial in adults with overweight or obesity. Nutrients 13(4): 1195

Pedersen, E.; Jesudason, D.R.; Clifton, P.M. (2014) High protein weight loss diets in obese subjects with type 2 diabetes mellitus. Nutrition, Metabolism and Cardiovascular Diseases 24(5): 554-562

Purcell, K, Sumithran, P, Prendergast, LA et al. (2014) The effect of rate of weight loss on long-term weight management: a randomised controlled trial. The lancet. Diabetes & endocrinology 2(12): 954-962

Sacks, Frank M, Bray, George A, Carey, Vincent J et al. (2009) Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. The New England journal of medicine 360(9): 859-73

Saslow, L.R., Daubenmier, J.J., Moskowitz, J.T. et al. (2017) Twelve-month outcomes of a randomized trial of a moderate-carbohydrate versus very low-carbohydrate diet in overweight adults with type 2 diabetes mellitus or prediabetes. Nutrition and Diabetes 7(12): 304

Schubel, R., Nattenmuller, J., Sookthai, D. et al. (2018) Effects of intermittent and continuous calorie restriction on body weight and metabolism over 50 wk: A randomized controlled trial. American Journal of Clinical Nutrition 108(5): 933-945

Seimon, R.V., Wild-Taylor, A.L., Keating, S.E. et al. (2019) Effect of weight loss via severe vs moderate energy restriction on lean mass and body composition among postmenopausal women with obesity: The tempo diet randomized clinical trial. JAMA Network Open 2(10): e1913733

Seimon, Radhika V, Wild-Taylor, Anthony L, McClintock, Sally et al. (2020) 3-Year effect of weight loss via severe versus moderate energy restriction on body composition among postmenopausal women with obesity - the TEMPO Diet Trial. Heliyon 6(6): e04007

Shikany, J.M., Thomas, A.S., Beasley, T.M. et al. (2013) Randomized controlled trial of the Medifast 5 & 1 plan for weight loss. International Journal of Obesity 37(12): 1571-1578

Sundfor, T.M.; Svendsen, M.; Tonstad, S. (2018) Effect of intermittent versus continuous energy restriction on weight loss, maintenance and cardiometabolic risk: A randomized 1-year trial. Nutrition, Metabolism and Cardiovascular Diseases 28(7): 698-706

Taheri, S, Zaghloul, H, Chagoury, O et al. (2020) Effect of intensive lifestyle intervention on bodyweight and glycaemia in early type 2 diabetes (DIADEM-I): an open-label, parallel-group, randomised controlled trial. The lancet. Diabetes & endocrinology 8(6): 477-489

Tay, J., Luscombe-Marsh, N.D., Thompson, C.H. et al. (2015) Comparison of low- and high-carbohydrate diets for type 2 diabetes management: A randomized trial. American Journal of Clinical Nutrition 102(4): 780-790

Tay, J., Thompson, C.H., Luscombe-Marsh, N.D. et al. (2018) Effects of an energy-restricted low-carbohydrate, high unsaturated fat/low saturated fat diet versus a high-carbohydrate, low-fat diet in type 2 diabetes: A 2-year randomized clinical trial. Diabetes, Obesity and Metabolism 20(4): 858-871

Teong, Xiao Tong, Liu, Kai, Vincent, Andrew D et al. (2023) Intermittent fasting plus early time-restricted eating versus calorie restriction and standard care in adults at risk of type 2 diabetes: a randomized controlled trial. Nature medicine

Trepanowski, J.F., Kroeger, C.M., Barnosky, A. et al. (2017) Effect of alternate-day fasting on weight loss, weight maintenance, and cardioprotection among metabolically healthy obese adults: A randomized clinical trial. JAMA Internal Medicine 177(7): 930-938

Tuomilehto, H.P.I., Seppa, J.M., Partinen, M.M. et al. (2009) Lifestyle intervention with weight reduction: First-line treatment in mild obstructive sleep apnea. American Journal of Respiratory and Critical Care Medicine 179(4): 320-327

Tuomilehto, Henri, Gylling, Helena, Peltonen, Markku et al. (2010) Sustained improvement in mild obstructive sleep apnea after a diet- and physical activity-based lifestyle intervention: postinterventional follow-up. The American journal of clinical nutrition 92(4): 688-96

Wei, Xueyun, Lin, Bingquan, Huang, Yan et al. (2023) Effects of Time-Restricted Eating on Nonalcoholic Fatty Liver Disease: The TREATY-FLD Randomized Clinical Trial. JAMA network open 6(3): e233513

Wycherley, T.P., Brinkworth, G.D., Clifton, P.M. et al. (2012) Comparison of the effects of 52 weeks weight loss with either a high-protein or high-carbohydrate diet on body composition and cardiometabolic risk factors in overweight and obese males. Nutrition and Diabetes 2(august): e40

1.1.12.3 Economic

Kent, S., Aveyard, P., Astbury, N., Mihaylova, B. and Jebb, S.A. (2019), Is Doctor Referral to a Low-Energy Total Diet Replacement Program Cost-Effective for the Routine Treatment of Obesity?. Obesity, 27: 391-398. https://doi.org/10.1002/oby.22407

Xin Y, Davies A, Briggs A, McCombie L, Messow CM, Grieve E, Leslie WS, Taylor R, Lean MEJ. Type 2 diabetes remission: 2 year within-trial and lifetime-horizon cost-effectiveness of the Diabetes Remission Clinical Trial (DiRECT)/Counterweight-Plus weight management programme. Diabetologia. 2020 Oct;63(10):2112-2122. doi: 10.1007/s00125-020-05224-2. Epub 2020 Aug 10. PMID: 32776237; PMCID: PMC7476973.

Appendices

Appendix A – Review protocols

Review protocol for diets in achieving and maintaining weight loss

ID	Field	Content
0.	PROSPERO registration number	CRD42022321713
1.	Review title	Effectiveness of different types of diet in achieving and maintaining weight loss in adults living with overweight or obesity.
2.	Review question	What is the effectiveness and cost effectiveness of total or partial diet replacements, intermittent fasting, plant-based and low carbohydrate, in achieving and maintaining weight loss in adults living with overweight or obesity?
3.	Objective	To determine the effectiveness and cost effectiveness of diet types for weight loss and whether any weight loss is maintained after the diet has finished.
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • Epistemonikos • MEDLINE • MEDLINE ePub ahead MEDLINE in process Searches will be restricted by: • Studies published from 2006 onwards • Studies published in OECD countries • English language • Conference abstracts will be excluded from the search

		Other searches: • None The searches will be re-run 6 weeks before final submission of the review and further studies retrieved for inclusion. The full search strategies for all databases will be published in the final review.
5.	Condition or domain being studied	Weight management
6.	Population	**Inclusion:** People aged 18 years and over who are: • Overweight (BMI 25 kg/m^2 to 29.9 kg/m^2) or • living with obesity (BMI ≥ 30 kg/m^2) **Note:** Boundary values for overweight and obesity are lower in adults from ethnic backgrounds. **Population based exclusion criteria:** • Pregnant women • People of healthy weight
7.	Interventions	**Energy restricted diets:** • Low energy (total or partial replacement) diets including low energy liquid diets (defined as diet containing 800-1200 calories per day) • Very low (total or partial replacement) energy diets (defined as diets containing less than 800 calories per day) **Macronutrient diets:** • Low carbohydrate diet (defined as under 130g of carbohydrates) ○ Very low carbohydrate (defined as under 50g of carbohydrates)

		Plant based diets with a calorie deficit. (Plant based diets defined as diets excluding meat and fish e.g., vegetarian, and vegan diets). **Intermittent energy restriction (patient led fasting)** • Time restricted eating: ○ Intermittent fasting (e.g., 16/8 intermittent fasting) • Alternate day fasting • Fasting for two days (e.g. 5:2 diet) Note: Studies providing support to participants, for example behavioural therapy (behavioural weight management advice, psychological support) and exercise alongside the diets will be included.

8.	Comparator	Primary comparators:
		○ Compared to each other
		○ Usual care defined use of conventional/ balanced diet with calorie deficit (restriction in total energy intake)
		○ No intervention
		
		If studies including primary comparators are not identified, studies including secondary comparators will be included:
		
		Secondary comparators:
		• Usual care as defined as:
		    ○ behavioural weight management advice
		    ○ General health promotion advice

9.	Types of study to be included	This review will use a 4-step pragmatic approach: 1. Recent Systematic reviews (2015- current) of parallel and cluster RCTs exploring diets specified in Section 7 will be prioritised. Included systematic reviews, will be evaluated on a case-by-case basis to check whether they match the review protocol specified. If systematic reviews include data is not deemed to be relevant (e.g., not covering diets of interest, not including population of interest or including the wrong study design), this data will be excluded. If partially applicable systematic reviews are included, these will be quality assessed accordingly (See section 15). If several systematic reviews are found covering the same interventions, the most recent systematic review will be included as evidence.

		2. If recent systematic reviews (2015-current) are not identified for the different diets, systematic reviews of parallel and cluster RCTs conducted between 2006-2014 will be utilised. These will also be assessed on a case-by case basis as defined above. 3. Individual parallel and cluster RCTs published between 2015-current will be utilised if gaps are identified in the evidence base. Additionally, studies may be added to the existing systematic reviews that were published after the search date. This will be assessed on a case-by-case basis and will be dependent on when the searches for the systematic reviews were conducted. 4. If additional gaps are identified in the evidence base, individual parallel and cluster RCTs published between 2006-2014 will be included. Studies should have a minimum follow up of 12 months.
10.	Other exclusion criteria	• Non- English language studies • Abstracts • Conference articles • Studies published in non-OECD countries • Studies published before 2006 • Studies comparing different diets to surgery or pharmacological interventions Studies that do not focus on weight loss or improvement of health outcomes
11.	Context	This review is part of an update of the NICE guideline preventing, assessing and managing overweight and obesity (update). This update covers different diets that can help adults who are living with overweight or obesity in achieving and maintaining weight loss.

12.	Primary outcomes (critical outcomes)	• Change in weight (kg) or change in BMI from baseline (including % change)
		• Health related quality of life measured by validated tools
		• Adverse events:
		  ○ Serious adverse events
		  ○ Development of eating disorders or disordered eating
		  ○ Hypoglycaemia
		  ○ Constipation
		  ○ Gallbladder problems
		  ○ Hair loss (transient alopecia)
		  ○ Hypotension

13.	Secondary outcomes (important outcomes)	• Change in waist circumference • Behavioural change measured using validated tools

		• Adherence to intervention offered • Change in HbA1c Secondary outcomes will only be extracted from studies that also report the critical outcomes.
14.	Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. This review will make use of the priority screening functionality within the EPPI-reviewer software. We will split the search up according to study design. SRs published between 2015 to current will be prioritised, followed by primary studies published between 2015 to current. SRs and primary studies published between 2014 – 2006 will only be used to fill in gaps in the evidence base. A stopping criteria will also be used. We will sift at least 60% of the database. After that we will stop screening if a further 5% (of the total records) of the records are sifted and not included. Recent systematic reviews will be prioritised for this review and primary studies will only be included to fill in gaps or update systematic reviews included in the review. As detailed in Section, applicability of included SRs will be assessed on a case-by-case basis. Decisions made on the applicability and usability of SRs will be documented in the evidence review. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). Study investigators may be contacted for missing data where time and resources allow. This review will make use of the priority screening functionality within the EPPI-reviewer software. We will also aim to tabulate macronutrient composition and calorie deficit in each diet, if this information is present in included SRs and primary studies. If SRs, do not cover all outcomes listed in the protocol (Section 12 and 13) or do not present evidence in an extractable form (to allow GRADE), then primary studies included in SRs will be used to extract outcome data.
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. Systematic reviews will be appraised using the ROBIS checklist and will be judged on their applicability. Randomised control trials (individuals or cluster) will be assessed using the Cochrane risk of bias tool 2.0. If included SRs have sufficiently conducted a risk of bias assessment (preferably using Cochrane risk of bias tool 2.0), this will be used as the basis of our quality assessment. If an SR has used a risk of bias tool that is not deemed

		appropriate, the SR will be downgraded using ROBIS checklist. Any decisions made on the applicability of SRs will be captured in the evidence review. If SRs have not conducted quality assessment of included studies, the SR will be downgraded for risk of bias using the ROBIS checklist. Depending on the applicability of the SRs, reviewers may conduct quality assessment of individual studies.
16.	Strategy for data synthesis	For details please see section 6 of Developing NICE guidelines: the manual Meta-analysis will be conducted where appropriate.
17.	Analysis of sub-groups	• People with type 2 diabetes or prediabetes • Ethnicity • Sex • Severity of obesity • People with learning and physical disabilities • People with serious mental illness • Socioeconomic group
18.	Type and method of review	☒ Intervention ☐ Diagnostic ☐ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☒ Other (please specify)
19.	Language	English
20.	Country	England

21.	Anticipated or actual start date	
22.	Anticipated completion date	[Give the date by which the guideline is expected to be published. This field may be edited at any time. All edits will appear in the record audit trail. A brief explanation of the reason for changes should be given in the Revision Notes facility.]
23.	Stage of review at time of this submission	**Review stage** / **Started** / **Completed** Preliminary searches ☐ ☐ Piloting of the study selection process ☐ ☐ Formal screening of search results against eligibility criteria ☐ ☐ Data extraction ☐ ☐ Risk of bias (quality) assessment ☐ ☐ Data analysis ☐ ☐
24.	Named contact	**5a. Named contact** Guideline Updates Team **5b Named contact e-mail** weightmgt@nice.org.uk **5c Organisational affiliation of the review** National Institute for Health and Care Excellence (NICE) and NICE Guideline Updates Team.
25.	Review team members	From the Guideline Updates Team: • Shreya Shukla

		• Alexander Allen • Lindsay Claxton • Kusal Lokuge • Miaoqing Yang • Amy Finnegan
26.	Funding sources/sponsor	This systematic review is being completed by the Centre for Guidelines which receives funding from NICE.
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: [NICE guideline webpage].
29.	Other registration details	-
30.	Reference/URL for published protocol	-
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
32.	Keywords	Weight management, overweight, obesity. Diet, total diet replacement, partial diet replacement, low energy diets, low carbohydrate diets, low fat diets, intermittent fasting.

33.	Details of existing review of same topic by same authors	-
34.	Current review status	☒ Ongoing ☐ Completed but not published ☐ Completed and published ☐ Completed, published and being updated ☐ Discontinued
35..	Additional information	None
36.	Details of final publication	www.nice.org.uk

Appendix B – Literature search strategies

Search design and peer review

A NICE information specialist conducted the literature searches for the evidence review question: What is the effectiveness and cost effectiveness of total or partial meal replacements, intermittent fasting, plant-based and low carbohydrate diets, in achieving and maintaining weight loss in adults living with overweight or obesity?

The searches were run on 21st March 2022 and then re-run on 14th April 2023. The cost-effective searches were run on 4th March 2022. This search report is compliant with the requirements of PRISMA-S.

The MEDLINE strategy below was quality assured (QA) by a trained NICE information specialist. All translated search strategies were peer reviewed to ensure their accuracy. Both procedures were adapted from the 2016 PRESS Checklist.

The principal search strategy was developed in MEDLINE (Ovid interface) and adapted, as appropriate, for use in the other sources listed in the protocol, taking into account their size, search functionality and subject coverage.

Review management

The search results were managed in EPPI-Reviewer v5. Duplicates were removed in EPPI-R5 using a two-step process. First, automated deduplication is performed using a high-value algorithm. Second, manual deduplication is used to assess 'low-probability' matches. All decisions made for the review can be accessed via the deduplication history.

Prior work

In total 8 test papers were identified; 4 test papers were identified by the committee. An additional 4 papers were identified, as they had cited the initial paper identified by the committee.

Limits and restrictions

English language limits were applied in adherence to standard NICE practice and the review protocol.

Limits to exclude letters, editorials, news, conferences were applied in adherence to standard NICE practice and the review protocol.

The search was limited from 2006 to 2022 as defined in the review protocol.

The limit to remove animal studies in the searches was the standard NICE practice, which has been adapted from: Dickersin, K., Scherer, R., & Lefebvre, C. (1994). Systematic Reviews: Identifying relevant studies for systematic reviews. *BMJ*, 309(6964), 1286.

Search filters

Clinical/public health searches

- RCT filters:
    - McMaster Therapy – Medline - "best balance of sensitivity and specificity" version.

Haynes RB et al. (2005) Optimal search strategies for retrieving scientifically strong studies of treatment from Medline: analytical survey. *BMJ*, 330, 1179-1183.

- McMaster Therapy – Embase “best balance of sensitivity and specificity” version.

  Wong SSL et al. (2006) Developing optimal search strategies for detecting clinically sound treatment studies in EMBASE. Journal of the Medical Library Association, 94(1), 41-47.

- Systematic reviews filters:
  - Lee, E. et al. (2012) An optimal search filter for retrieving systematic reviews and meta-analyses. *BMC Medical Research Methodology,* 12(1), 51.

    In MEDLINE, the standard NICE modifications were used: pubmed.tw added; systematic review.pt added from MeSH update 2019.

    In Embase, the standard NICE modifications were used: pubmed.tw added to line medline.tw.

- OECD filter:
  - The OECD countries filters were used without modification:
  - Ayiku, L., Hudson, T., Williams, C., Levay, P., & Jacobs, C. (submitted for publication) The NICE OECD countries geographic search filters: Part 2 - Validation of the MEDLINE and Embase (Ovid) filters. *Journal of the Medical Library Association* (in peer review)

Cost effectiveness searches
The NICE cost utility (sensitive) filter was applied to the Medline and Embase searches to identify cost utility studies.

- Cost Utility filter is available via the ISSG search filters resource

OECD filter:
  - The OECD countries filters were used without modification:
  - Ayiku, L., Hudson, T., Williams, C., Levay, P., & Jacobs, C. (submitted for publication) The NICE OECD countries geographic search filters: Part 2 - Validation of the MEDLINE and Embase (Ovid) filters. *Journal of the Medical Library Association* (in peer review)

Key decisions

The search strategy limited the search to SRs and RCTs from 2006-2015, with non-OECD countries excluded from the results. The search results were exported into four separate files based on study type and two date limit pools (2006-2014 and 2015- 2022). This was to aid a pragmatic approach during the sift.

11 papers were identified by the analysts and added after the main search. The analysts had identified the papers through citation searching.

The numbers reported in this appendix B document reflect the total number of records retrieved for this search. Due to the sifting methods for multiple study types, some records were considered twice for this review question. Records that were double sifted were counted twice, this is reflected in the PRISMA diagram.

Clinical/public health searches

Main search – Databases

Database	Date searched	Database Platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	21/03/2022	Wiley	Issue 3 of 12, March 2022	57
Cochrane Database of Systematic Reviews (CDSR)	21/03/2022	Wiley	Issue 3 of 12, March 2022	5401
Embase	21/03/2022	Ovid	1974 to 2022 March 16	6484
Epistemonikos	21/03/2022	Epistemonikos	n/a	4060
MEDLINE All	21/03/2022	Ovid	1946 to March 18, 2022	6807

Re-run search – Databases

Database	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	14/04/2023	Wiley	Issue 4 of 12, April 2023	463
Cochrane Database of Systematic Reviews (CDSR)	14/04/2023	Wiley	Issue 4 of 12, April 2023	1
Embase	14/04/2023	Ovid	1974 to 2023 April 13	833
Epistemonikos	14/04/2023	Epistemonikos	n/a	1785
MEDLINE All	14/04/2023	Ovid	1946 to April 13, 2023	624

Search strategy history

Database name: Cochrane Database of Systematic Reviews (CDSR) and CENTRAL

#1 MeSH descriptor: [Obesity] explode all trees 15455
#2 MeSH descriptor: [Obesity Management] this term only 21
#3 MeSH descriptor: [Overweight] this term only 5724
#4 MeSH descriptor: [Adiposity] this term only 832
#5 (obes* or preobese* or overweight* or over-weight* or adiposity*):ti,ab 47537
#6 (weight* NEAR/1 (loss* or management* or reduc* or status*)):ti,ab 24072
#7 (("body mass index" or "body mass index" or "body mass indices" or "body fat index" or "body fat indexes" or "body fat indices" or BMI or BFI) NEAR/1 (loss* or management* or reduc* or status*)):ti,ab 1114
#8 {or #1-#7} 59778
#9 MeSH descriptor: [Diet Therapy] this term only 412
#10 MeSH descriptor: [Caloric Restriction] this term only 924
#11 MeSH descriptor: [Diet, Carbohydrate-Restricted] this term only 437
#12 MeSH descriptor: [Diet, Ketogenic] this term only 103
#13 MeSH descriptor: [Diet, Fat-Restricted] this term only 1009
#14 MeSH descriptor: [Diet, Mediterranean] this term only 591
#15 MeSH descriptor: [Diet, Paleolithic] this term only 20
#16 MeSH descriptor: [Diet, Reducing] this term only 2150
#17 MeSH descriptor: [Diet, Vegetarian] this term only 215
#18 MeSH descriptor: [Diet, Vegan] this term only 26
#19 MeSH descriptor: [Fasting] this term only 3446
#20 MeSH descriptor: [Dietary Carbohydrates] this term only 3239
#21 MeSH descriptor: [Foods, Specialized] this term only 29
#22 MeSH descriptor: [Food, Formulated] this term only 796
#23 MeSH descriptor: [Energy Intake] this term only 5025
#24 ((calorie* or kilocalorie* or kilojoule* or energ* or ketogenic*) NEAR/2 (restrict* or reduc* or decreas* or low* or deficit*) NEAR/2 (diet* or intak* or consum* or ingest* or eat* or meal* or program* or plan* or feed*)):ti,ab 4155
#25 ((macrobiotic* or macronutrien* or hypocalori* or total* or partial* or replace* or substitut* or liquid*) NEAR/2 (diet* or meal* or food* or program* or plan*)):ti,ab 6085
#26 (((total* or partial* or prescrib* or substitut* or liquid*) NEAR/2 replace* NEAR/2 (diet* or meal* or food* or program* or plan*)) or TDR):ti,ab 421
#27 ((low or reduc*) NEAR/2 (carb or carbs or carbohydrate* or fat) NEAR/2 (diet* or meal* or food* or program* or plan*)):ti,ab 3377
#28 ((plant-base* or vegan* or vegetarian* or veggie*) NEAR/2 (diet* or lifestyle* or meal* or food* or program* or plan*)):ti,ab 968
#29 (((whole-food* or wholefood*) NEAR/2 diet*) or WFPB):ti,ab 46
#30 ((Intermit* or alternat* or two-day* or "2 day" or "2 days") NEAR/2 (fasting* or fast*)):ti,ab 381
#31 (time-restrict* NEAR/2 (fasting* or fast* or eat*)):ti,ab 88
#32 ((Mediterranean* or paleo* or palaeo*) NEAR/2 diet*):ti,ab 1868
#33 ("5:2 diet" or "5:2 diets"):ti,ab 24
#34 ((point-base* or point-track* or score-base* or score-track*) NEAR/2 (diet* or meal* or food* or program* or plan* or eat*)):ti,ab 21
#35 {or #9-#34} 26260
#36 #8 and #35 9669
#37 "conference":pt or (clinicaltrials or trialsearch):so 586873
#38 #36 not #37 with Cochrane Library publication date Between Jan 2015 and Feb 2022, in Cochrane Reviews 41
#39 #36 not #37 with Cochrane Library publication date Between Jan 2006 and Dec 2014, in Cochrane Reviews 16
#40 #36 not #37 with Publication Year from 2015 to 2022, in Trials 2820
#41 #36 not #37 with Publication Year from 2006 to 2014, in Trials 2581

Database name: Embase

1 exp *obesity/ or obesity management/ (267060)
2 (obes* or preobese* or overweight* or over-weight* or adiposity*).ti,ab. (543673)
3 (weight* adj1 (loss* or management* or reduc* or status*)).ti,ab. (189172)
4 (("body mass ind*" or "body fat ind*" or BMI or BFI) adj1 (loss* or management* or reduc* or status*)).ti,ab. (8663)
5 or/1-4 (709267)
6 *diet therapy/ or *diet restriction/ or *caloric restriction/ or *fasting/ or *diet supplementation/ or *liquid diet/ or *low calorie diet/ or *low carbohydrate diet/ or *carbohydrate intake/ or *ketogenic diet/ or *mediterranean diet/ or *paleolithic diet/ or *vegetarian diet/ or *vegan diet/ or *elemental diet/ or *caloric intake/ (91028)
7 ((calorie* or kilocalorie* or kilojoule* or energ* or ketogenic*) adj2 (restrict* or reduc* or decreas* or low* or deficit*) adj2 (diet* or intak* or consum* or ingest* or eat*3 or meal*1 or program* or plan* or feed*)).ti,ab. (17075)
8 ((macrobiotic* or macronutrien* or hypocalori* or total* or partial* or replace* or substitut* or liquid*) adj2 (diet* or meal*1 or food* or program* or plan*)).ti,ab. (42039)
9 (((total* or partial* or prescrib* or substitut* or liquid*) adj2 replace* adj2 (diet* or meal*1 or food* or program* or plan*)) or TDR).ti,ab. (6278)
10 ((low or reduc*) adj2 (carb or carbs or carbohydrate* or fat) adj2 (diet* or meal*1 or food* or program* or plan*)).ti,ab. (14156)
11 ((plant-base* or vegan* or vegetarian* or veggie*) adj2 (diet* or lifestyle* or meal*1 or food* or program* or plan*)).ti,ab. (11487)
12 ((whole*-food* adj2 diet*) or WFPB).ti,ab. (166)
13 ((Intermit* or alternat* or two-day* or 2-day*) adj2 (fasting*1 or fast*1)).ti,ab. (2290)
14 (time-restrict* adj2 (fasting*1 or fast*1 or eat*3)).ti,ab. (152)
15 ((Mediterranean* or pal?o*) adj2 diet*).ti,ab. (9460)
16 ("5?2 diet" or "5?1 diets").ti,ab. (42)
17 ((point-base* or point-track* or score-base* or score-track*) adj2 (diet* or meal*1 or food* or program* or plan* or eat*3)).ti,ab. (125)
18 or/6-17 (173852)
19 5 and 18 (33298)
20 limit 19 to english language (31533)
21 nonhuman/ not (human/ and nonhuman/) (4949390)
22 20 not 21 (26972)
23 (conference abstract or conference paper or conference proceeding or "conference review").pt. (5121219)
24 22 not 23 (18908)
25 afghanistan/ or africa/ or "africa south of the sahara"/ or albania/ or algeria/ or andorra/ or angola/ or argentina/ or "antigua and barbuda"/ or armenia/ or exp azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belarus/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or exp "bosnia and herzegovina"/ or botswana/ or exp brazil/ or brunei darussalam/ or bulgaria/ or burkina faso/ or burundi/ or cambodia/ or cameroon/ or cape verde/ or central africa/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cook islands/ or cote d'ivoire/ or croatia/ or cuba/ or cyprus/ or democratic republic congo/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or el salvador/ or egypt/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or exp "federated states of micronesia"/ or fiji/ or gabon/ or gambia/ or exp "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or exp india/ or exp indonesia/ or iran/ or exp iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kiribati/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libyan arab jamahiriya/ or madagascar/ or malawi/ or exp malaysia/ or maldives/ or mali/ or malta/ or mauritania/ or mauritius/ or melanesia/ or moldova/ or monaco/ or mongolia/ or "montenegro (republic)"/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nauru/ or nepal/ or nicaragua/ or niger/ or nigeria/ or niue/ or north africa/ or oman/ or exp pakistan/ or

palau/ or palestine/ or panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or polynesia/ or qatar/ or "republic of north macedonia"/ or romania/ or exp russian federation/ or rwanda/ or sahel/ or "saint kitts and nevis"/ or "saint lucia"/ or "saint vincent and the grenadines"/ or saudi arabia/ or senegal/ or exp serbia/ or seychelles/ or sierra leone/ or singapore/ or "sao tome and principe"/ or solomon islands/ or exp somalia/ or south africa/ or south asia/ or south sudan/ or exp southeast asia/ or sri lanka/ or sudan/ or suriname/ or syrian arab republic/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or tuvalu/ or uganda/ or exp ukraine/ or exp united arab emirates/ or uruguay/ or exp uzbekistan/ or vanuatu/ or venezuela/ or viet nam/ or western sahara/ or yemen/ or zambia/ or zimbabwe/ (1518528)
26 exp "organisation for economic co-operation and development"/ (1951)
27 exp australia/ or "australia and new zealand"/ or austria/ or baltic states/ or exp belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or denmark/ or estonia/ or europe/ or exp finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or "Turkey (republic)"/ or exp united kingdom/ or exp united states/ or western europe/ (3553968)
28 european union/ (29215)
29 developed country/ (34450)
30 or/26-29 (3584871)
31 25 not 30 (1379434)
32 24 not 31 (18257)
33 (MEDLINE or pubmed).tw. (336174)
34 exp systematic review/ or systematic review.tw. (405129)
35 meta-analysis/ (240706)
36 intervention$.ti. (233628)
37 or/33-36 (815532)
38 32 and 37 (2038)
39 limit 38 to dc=20150101-20221231 (1315)
40 limit 38 to dc=20060101-20141231 (580)
41 random:.tw. (1766584)
42 placebo:.mp. (491115)
43 double-blind:.tw. (228480)
44 or/41-43 (2033046)
45 32 and 44 (5428)
46 limit 45 to dc=20150101-20221231 (2761)
47 limit 45 to dc=20060101-20141231 (1828)

Database name: Epistemonikos
title:(title:(title:(title:(obes* OR preobese* OR overweight* OR over-weight* OR adiposity*)) OR title:(title:(weight*) AND title:(loss* OR management* OR reduc* OR status*)) OR title:(title:("body mass index" OR "body mass index" OR "body mass indices" OR "body fat index" OR "body fat indexes" OR "body fat indices" OR BMI OR BFI) AND title:(loss* OR management* OR reduc* OR status*))) AND title:(title:(title:(calorie* OR kilocalorie* OR kilojoule* OR energ* OR ketogenic*) AND title:(restrict* OR reduc* OR decreas* OR low* OR deficit*) AND title:(diet* OR intak* OR consum* OR ingest* OR eat* OR meal* OR program* OR plan* OR feed*)) OR title:(title:(macrobiotic* OR macronutrien* OR hypocalori* OR total* OR partial* OR replace* OR substitut* OR liquid*) AND title:(diet* OR meal* OR food* OR program* OR plan*)) OR title:(title:(total* OR partial* OR prescrib* OR substitut* OR liquid*) AND title:(replace*) AND title:(diet* OR meal* OR food* OR program* OR plan*)) OR title:(title:(low OR reduc*) AND title:(carb OR carbs OR carbohydrate* OR fat) AND title:(diet* OR meal* OR food* OR program* OR plan*)) OR title:(title:(plant-base* OR vegan* OR vegetarian* OR veggie*) AND title:(diet* OR lifestyle* OR meal* OR food* OR program* OR plan*)) OR title:(title:(whole-food* OR wholefood*) AND title:(diet*)) OR title:(title:(WFPB)) OR

title:(title:(Intermit* OR alternat* OR two-day* OR "2 day" OR "2 days") AND title:(fasting* OR fast*)) OR title:(title:(time-restrict*) AND title:(fasting* OR fast* OR eat*)) OR title:(title:(Mediterranean* OR paleo* OR palaeo*) AND title:(diet*)) OR title:(title:("5:2 diet" OR "5:2 diets")) OR title:(title:(point-base* OR point-track* OR score-base* OR score-track*) AND title:(diet* OR meal* OR food* OR program* OR plan* OR eat*)))) OR abstract:(abstract:(abstract:(abstract:(abstract:(obes* OR preobese* OR overweight* OR over-weight* OR adiposity*)) OR abstract:(abstract:(weight*) AND abstract:(loss* OR management* OR reduc* OR status*)) OR abstract:(abstract:("body mass index" OR "body mass index" OR "body mass indices" OR "body fat index" OR "body fat indexes" OR "body fat indices" OR BMI OR BFI) AND abstract:(loss* OR management* OR reduc* OR status*))) AND abstract:(abstract:(abstract:(calorie* OR kilocalorie* OR kilojoule* OR energ* OR ketogenic*) AND abstract:(restrict* OR reduc* OR decreas* OR low* OR deficit*) AND abstract:(diet* OR intak* OR consum* OR ingest* OR eat* OR meal* OR program* OR plan* OR feed*)) OR abstract:(abstract:(macrobiotic* OR macronutrien* OR hypocalori* OR total* OR partial* OR replace* OR substitut* OR liquid*) AND abstract:(diet* OR meal* OR food* OR program* OR plan*)) OR abstract:(abstract:(total* OR partial* OR prescrib* OR substitut* OR liquid*) AND abstract:(replace*) AND abstract:(diet* OR meal* OR food* OR program* OR plan*)) OR abstract:(abstract:(low OR reduc*) AND abstract:(carb OR carbs OR carbohydrate* OR fat) AND abstract:(diet* OR meal* OR food* OR program* OR plan*)) OR abstract:(abstract:(plant-base* OR vegan* OR vegetarian* OR veggie*) AND abstract:(diet* OR lifestyle* OR meal* OR food* OR program* OR plan*)) OR abstract:(abstract:(whole-food* OR wholefood*) AND abstract:(diet*)) OR abstract:(abstract:(WFPB)) OR abstract:(abstract:(Intermit* OR alternat* OR two-day* OR "2 day" OR "2 days") AND abstract:(fasting* OR fast*)) OR abstract:(abstract:(time-restrict*) AND abstract:(fasting* OR fast* OR eat*)) OR abstract:(abstract:(Mediterranean* OR paleo* OR palaeo*) AND abstract:(diet*)) OR abstract:(abstract:("5:2 diet" OR "5:2 diets")) OR abstract:(abstract:(point-base* OR point-track* OR score-base* OR score-track*) AND abstract:(diet* OR meal* OR food* OR program* OR plan* OR eat*)))))

Database name: Medline All

1. exp *obesity/ or Obesity Management/ or overweight/ or *adiposity/
2. (obes* or preobese* or overweight* or over-weight* or adiposity*).ti,ab.
3. (weight* adj1 (loss* or management* or reduc* or status*)).ti,ab.
4. (("body mass ind*" or "body fat ind*" or BMI or BFI) adj1 (loss* or management* or reduc* or status*)).ti,ab.
5. or/1-4
6. *diet therapy/ or *caloric restriction/ or *diet, carbohydrate-restricted/ or *diet, ketogenic/ or *diet, fat-restricted/ or *diet, mediterranean/ or *diet, paleolithic/ or *diet, reducing/ or *diet, vegetarian/ or *diet, vegan/ or *Fasting/ or *dietary carbohydrates/ or *foods, specialized/ or *Food, Formulated/ or *Energy Intake/
7. ((calorie* or kilocalorie* or kilojoule* or energ* or ketogenic*) adj2 (restrict* or reduc* or decreas* or low* or deficit*) adj2 (diet* or intak* or consum* or ingest* or eat*3 or meal*1 or program* or plan* or feed*)).ti,ab.
8. ((macrobiotic* or macronutrien* or hypocalori* or total* or partial* or replace* or substitut* or liquid*) adj2 (diet* or meal*1 or food* or program* or plan*)).ti,ab.
9. (((total* or partial* or prescrib* or substitut* or liquid*) adj2 replace* adj2 (diet* or meal*1 or food* or program* or plan*)) or TDR).ti,ab.
10. ((low or reduc*) adj2 (carb or carbs or carbohydrate* or fat)).ti,ab.
11. ((plant-base* or vegan* or vegetarian* or veggie*) adj2 (diet* or lifestyle* or meal*1 or food* or program* or plan*)).ti,ab.
12. (((whole*-food* or wholefood*) adj2 diet*) or WFPB).ti,ab.
13. ((Intermit* or alternat* or two-day* or 2-day*) adj2 (fasting*1 or fast*1)).ti,ab.

14. (time-restrict* adj2 (fasting*1 or fast*1 or eat*3)).ti,ab.
15. ((Mediterranean* or pal?eo*) adj2 diet*).ti,ab.
16. ("5?2 diet" or "5?2 diets").ti,ab.
17. ((point-base* or point-track* or score-base* or score-track*) adj2 (diet* or meal*1 or food* or program* or plan* or eat*3)).ti,ab.
18. or/6-17
19. 5 and 18
20. limit 19 to english language
21. animals/ not humans/
22. 20 not 21
23. limit 22 to (letter or historical article or comment or editorial or news or case reports)
24. 22 not 23
25. afghanistan/ or africa/ or africa, northern/ or africa, central/ or africa, eastern/ or "africa south of the sahara"/ or africa, southern/ or africa, western/ or albania/ or algeria/ or andorra/ or angola/ or "antigua and barbuda"/ or argentina/ or armenia/ or azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or "bosnia and herzegovina"/ or botswana/ or brazil/ or brunei/ or bulgaria/ or burkina faso/ or burundi/ or cabo verde/ or cambodia/ or cameroon/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cote d'ivoire/ or croatia/ or cuba/ or "democratic republic of the congo"/ or cyprus/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or egypt/ or el salvador/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or fiji/ or gabon/ or gambia/ or "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or independent state of samoa/ or exp india/ or indian ocean islands/ or indochina/ or indonesia/ or iran/ or iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libya/ or madagascar/ or malaysia/ or malawi/ or mali/ or malta/ or mauritania/ or mauritius/ or mekong valley/ or melanesia/ or micronesia/ or monaco/ or mongolia/ or montenegro/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nepal/ or nicaragua/ or niger/ or nigeria/ or oman/ or pakistan/ or palau/ or exp panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or qatar/ or "republic of belarus"/ or "republic of north macedonia"/ or romania/ or exp russia/ or rwanda/ or "saint kitts and nevis"/ or saint lucia/ or "saint vincent and the grenadines"/ or "sao tome and principe"/ or saudi arabia/ or serbia/ or sierra leone/ or senegal/ or seychelles/ or singapore/ or somalia/ or south africa/ or south sudan/ or sri lanka/ or sudan/ or suriname/ or syria/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or uganda/ or ukraine/ or united arab emirates/ or uruguay/ or uzbekistan/ or vanuatu/ or venezuela/ or vietnam/ or west indies/ or yemen/ or zambia/ or zimbabwe/
26. "organisation for economic co-operation and development"/
27. australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or exp japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or portugal/ or exp "republic of korea"/ or "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or sweden/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/
28. european union/
29. developed countries/
30. or/26-29
31. 25 not 30
32. 24 not 31
33. (MEDLINE or pubmed).tw.
34. systematic review.tw.
35. systematic review.pt.
36. meta-analysis.pt.
37. intervention$.ti.

38. or/33-37
39. 32 and 38
40. 39 and (2015* or 2016* or 2017* or 2018* or 2019* or 2020* or 2021* or 2022*).ed,dt.
41. 39 and (2006* or 2007* or 2008* or 2009* or 2010* or 2011* or 2012* or 2013* or 2014*).ed,dt.
42. randomized controlled trial.pt.
43. randomi?ed.mp.
44. placebo.mp.
45. or/42-44
46. 32 and 45
47. 46 and (2015* or 2016* or 2017* or 2018* or 2019* or 2020* or 2021* or 2022*).ed,dt.
48. 46 and (2006* or 2007* or 2008* or 2009* or 2010* or 2011* or 2012* or 2013* or 2014*).ed,dt.

Cost-effectiveness searches

Main search – Databases

Database	Date searched	Database Platform	Database segment or version	No. of results downloaded
EconLit	04/03/2022	OVID	Econlit <1886 to February 24, 2022>	36
EED	04/03/2022	CRD	N/A	15
Embase	04/03/2022	Ovid	1974 to 2022 March 03	308
HTA	04/03/2022	CRD	N/A	6
INAHTA	04/03/2022	INAHTA	N/A	585
MEDLINE All	04/03/2022	Ovid	1946 to March 03, 2022	330

Re-run search – Databases

Re-runs were not carried out for this review question, due to the approach taken by the guideline to publish some questions before others.

Search strategy history

Database name: Econlit

1 (obes* or preobese* or overweight* or over-weight* or adiposity*).ti,ab. (2498)
2 (weight* adj1 (loss* or management* or reduc* or status*)).ti,ab. (342)
3 (("body mass ind*" or "body fat ind*" or BMI or BFI) adj1 (loss* or management* or reduc* or status*)).ti,ab. (30)
4 or/1-3 (2712)
5 ((calorie* or kilocalorie* or kilojoule* or energ* or ketogenic*) adj2 (restrict* or reduc* or decreas* or low* or deficit*) adj2 (diet* or intak* or consum* or ingest* or eat*3 or meal*1 or program* or plan* or feed*)).ti,ab. (579)
6 ((macrobiotic* or macronutrien* or hypocalori* or total* or partial* or replace* or substitut* or liquid*) adj2 (diet* or meal*1 or food* or program* or plan*)).ti,ab. (806)
7 (((total* or partial* or prescrib* or substitut* or liquid*) adj2 replace* adj2 (diet* or meal*1 or food* or program* or plan*)) or TDR).ti,ab. (36)
8 ((low or reduc*) adj2 (carb or carbs or carbohydrate* or fat)).ti,ab. (77)
9 ((plant-base* or vegan* or vegetarian* or veggie*) adj2 (diet* or lifestyle* or meal*1 or food* or program* or plan*)).ti,ab. (74)
10 (((whole*-food* or wholefood*) adj2 diet*) or WFPB).ti,ab. (0)
11 ((Intermit* or alternat* or two-day* or 2-day*) adj2 (fasting*1 or fast*1)).ti,ab. (16)
12 (time-restrict* adj2 (fasting*1 or fast*1 or eat*3)).ti,ab. (0)
13 ((Mediterranean* or pal?eo*) adj2 diet*).ti,ab. (29)
14 ("5?2 diet" or "5?2 diets").ti,ab. (0)
15 ((point-base* or point-track* or score-base* or score-track*) adj2 (diet* or meal*1 or food* or program* or plan* or eat*3)).ti,ab. (2)
16 or/5-15 (1604)
17 4 and 16 (38)
18 limit 17 to english (38)
19 (2006* or 2007* or 2008* or 2009* or 2010* or 2011* or 2012* or 2013* or 2014* or 2015* or 2016* or 2017* or 2018* or 2019* or 2020* or 2021* or 2022*).up. (1122744)
20 18 and 19 (36)

Database name: EED

1	MeSH DESCRIPTOR obesity EXPLODE ALL TREES	1025
2	MeSH DESCRIPTOR obesity management	0
3	MeSH DESCRIPTOR overweight	172
4	MeSH DESCRIPTOR adiposity	20
5	(obes* or preobese* or overweight* or over-weight* or adiposity*)	1630
6	(weight* NEAR1 (loss* or management* or reduc* or status*))	1074
7	(("body mass index" or "body mass index" or "body mass indices" or "body fat index" or "body fat indexes" or "body fat indices" or BMI or BFI) NEAR1 (loss* or management* or reduc* or status*))	39
8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	2051
9	MeSH DESCRIPTOR diet therapy	38
10	MeSH DESCRIPTOR Caloric Restriction	19
11	MeSH DESCRIPTOR Diet, Carbohydrate-Restricted	20
12	MeSH DESCRIPTOR Diet, Ketogenic	0
13	MeSH DESCRIPTOR Diet, Fat-Restricted	39
14	MeSH DESCRIPTOR Diet, Mediterranean	12
15	MeSH DESCRIPTOR Diet, Paleolithic	1
16	MeSH DESCRIPTOR Diet, Reducing	106
17	MeSH DESCRIPTOR Diet, Vegetarian	5
18	MeSH DESCRIPTOR Diet, Vegan	0
19	MeSH DESCRIPTOR Fasting	55
20	MeSH DESCRIPTOR Dietary Carbohydrates	33
21	MeSH DESCRIPTOR Foods, Specialized	1
22	MeSH DESCRIPTOR Food, Formulated	42
23	MeSH DESCRIPTOR Energy Intake	98
24	((calorie* or kilocalorie* or kilojoule* or energ* or ketogenic*) NEAR2 (restrict* or reduc* or decreas* or low* or deficit*) NEAR2 (diet* or intak* or consum* or ingest* or eat* or meal* or program* or plan* or feed*))	25
25	((macrobiotic* or macronutrien* or hypocalori* or total* or partial* or replace* or substitut* or liquid*) NEAR2 (diet* or meal* or food* or program* or plan*))	136
26	(((total* or partial* or prescrib* or substitut* or liquid*) NEAR2 replace* NEAR2 (diet* or meal* or food* or program* or plan*)) or TDR)	11
27	((low or reduc*) NEAR2 (carb or carbs or carbohydrate* or fat) NEAR2 (diet* or meal* or food* or program* or plan*))	89
28	((plant-base* or vegan* or vegetarian* or veggie*) NEAR2 (diet* or lifestyle* or meal* or food* or program* or plan*))	10
29	(((whole-food* or wholefood*) NEAR2 diet*) or WFPB)	0
30	((Intermit* or alternat* or two-day* or "2 day" or "2 days") NEAR2 (fasting* or fast*))	0
31	(time-restrict* NEAR2 (fasting* or fast* or eat*))	0
32	((Mediterranean* or paleo* or palaeo*) NEAR2 diet*)	23
33	("5?2 diet" or "5?2 diets")	0
34	((point-base* or point-track* or score-base* or score-track*) NEAR2 (diet* or meal* or food* or program* or plan* or eat*))	0
35	#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34	580
36	(#8 AND #35) IN NHSEED FROM 2006 TO 2022	15

Database name: Embase

1 exp *obesity/ or obesity management/ (266636)
2 (obes* or preobese* or overweight* or over-weight* or adiposity*).ti,ab. (542501)
3 (weight* adj1 (loss* or management* or reduc* or status*)).ti,ab. (188806)
4 (("body mass ind*" or "body fat ind*" or BMI or BFI) adj1 (loss* or management* or reduc* or status*)).ti,ab. (8644)
5 or/1-4 (707778)
6 *diet therapy/ or *diet restriction/ or *caloric restriction/ or *fasting/ or *diet supplementation/ or *liquid diet/ or *low calorie diet/ or *low carbohydrate diet/ or *carbohydrate intake/ or *ketogenic diet/ or *mediterranean diet/ or *paleolithic diet/ or *vegetarian diet/ or *vegan diet/ or *elemental diet/ or *caloric intake/ (90820)
7 ((calorie* or kilocalorie* or kilojoule* or energ* or ketogenic*) adj2 (restrict* or reduc* or decreas* or low* or deficit*) adj2 (diet* or intak* or consum* or ingest* or eat*3 or meal*1 or program* or plan* or feed*)).ti,ab. (17028)
8 ((macrobiotic* or macronutrien* or hypocalori* or total* or partial* or replace* or substitut* or liquid*) adj2 (diet* or meal*1 or food* or program* or plan*)).ti,ab. (41966)
9 (((total* or partial* or prescrib* or substitut* or liquid*) adj2 replace* adj2 (diet* or meal*1 or food* or program* or plan*)) or TDR).ti,ab. (6275)
10 ((low or reduc*) adj2 (carb or carbs or carbohydrate* or fat) adj2 (diet* or meal*1 or food* or program* or plan*)).ti,ab. (14137)
11 ((plant-base* or vegan* or vegetarian* or veggie*) adj2 (diet* or lifestyle* or meal*1 or food* or program* or plan*)).ti,ab. (11411)
12 ((whole*-food* adj2 diet*) or WFPB).ti,ab. (165)
13 ((Intermit* or alternat* or two-day* or 2-day*) adj2 (fasting*1 or fast*1)).ti,ab. (2274)
14 (time-restrict* adj2 (fasting*1 or fast*1 or eat*3)).ti,ab. (151)
15 ((Mediterranean* or pal?o*) adj2 diet*).ti,ab. (9424)
16 ("5?2 diet" or "5?1 diets").ti,ab. (41)
17 ((point-base* or point-track* or score-base* or score-track*) adj2 (diet* or meal*1 or food* or program* or plan* or eat*3)).ti,ab. (125)
18 or/6-17 (173462)
19 5 and 18 (33239)
20 limit 19 to english language (31477)
21 nonhuman/ not (human/ and nonhuman/) (4942125)
22 20 not 21 (26921)
23 (conference abstract or conference paper or conference proceeding or "conference review").pt. (5109010)
24 22 not 23 (18871)
25 afghanistan/ or africa/ or "africa south of the sahara"/ or albania/ or algeria/ or andorra/ or angola/ or argentina/ or "antigua and barbuda"/ or armenia/ or exp azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belarus/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or exp "bosnia and herzegovina"/ or botswana/ or exp brazil/ or brunei darussalam/ or bulgaria/ or burkina faso/ or burundi/ or cambodia/ or cameroon/ or cape verde/ or central africa/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cook islands/ or cote d'ivoire/ or croatia/ or cuba/ or cyprus/ or democratic republic congo/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or el salvador/ or egypt/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or exp "federated states of micronesia"/ or fiji/ or gabon/ or gambia/ or exp "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or exp india/ or exp indonesia/ or iran/ or exp iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kiribati/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libyan arab jamahiriya/ or madagascar/ or malawi/ or exp malaysia/ or maldives/ or mali/ or malta/ or mauritania/ or mauritius/ or melanesia/ or moldova/ or monaco/ or mongolia/ or "montenegro (republic)"/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nauru/ or nepal/ or nicaragua/ or niger/ or nigeria/ or niue/ or north africa/ or oman/ or exp pakistan/ or palau/ or palestine/ or panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or polynesia/ or qatar/ or "republic of north macedonia"/ or romania/ or exp russian federation/

or rwanda/ or sahel/ or "saint kitts and nevis"/ or "saint lucia"/ or "saint vincent and the grenadines"/ or saudi arabia/ or senegal/ or exp serbia/ or seychelles/ or sierra leone/ or singapore/ or "sao tome and principe"/ or solomon islands/ or exp somalia/ or south africa/ or south asia/ or south sudan/ or exp southeast asia/ or sri lanka/ or sudan/ or suriname/ or syrian arab republic/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or tuvalu/ or uganda/ or exp ukraine/ or exp united arab emirates/ or uruguay/ or exp uzbekistan/ or vanuatu/ or venezuela/ or viet nam/ or western sahara/ or yemen/ or zambia/ or zimbabwe/ (1514283)
26 exp "organisation for economic co-operation and development"/ (1942)
27 exp australia/ or "australia and new zealand"/ or austria/ or baltic states/ or exp belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or denmark/ or estonia/ or europe/ or exp finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or "Turkey (republic)"/ or exp united kingdom/ or exp united states/ or western europe/ (3548198)
28 european union/ (29174)
29 developed country/ (34429)
30 or/26-29 (3579058)
31 25 not 30 (1375517)
32 24 not 31 (18223)
33 cost utility analysis/ (10946)
34 quality adjusted life year/ (30961)
35 cost*.ti. (177288)
36 (cost* adj2 utilit*).tw. (11131)
37 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw. (340300)
38 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. (57880)
39 (qualit* adj2 adjust* adj2 life*).tw. (23709)
40 QALY*.tw. (23241)
41 (incremental* adj2 cost*).tw. (24940)
42 ICER.tw. (10993)
43 utilities.tw. (13313)
44 markov*.tw. (35078)
45 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. (64272)
46 ((utility or effective*) adj2 analys*).tw. (32944)
47 (willing* adj2 pay*).tw. (12303)
48 (EQ5D* or EQ-5D*).tw. (21512)
49 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. (4130)
50 (european* adj2 quality adj3 ("5" or five)).tw. (775)
51 or/33-50 (561332)
52 32 and 51 (369)
53 limit 52 to dc=20060101-20221231 (308)

Database name: HTA

1	MeSH DESCRIPTOR obesity EXPLODE ALL TREES	1025
2	MeSH DESCRIPTOR obesity management	0
3	MeSH DESCRIPTOR overweight	172
4	MeSH DESCRIPTOR adiposity	20
5	(obes* or preobese* or overweight* or over-weight* or adiposity*)	1630
6	(weight* NEAR1 (loss* or management* or reduc* or status*))	1074
7	(("body mass index" or "body mass index" or "body mass indices" or "body fat index" or "body fat indexes" or "body fat indices" or BMI or BFI) NEAR1 (loss* or management* or reduc* or status*))	39
8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	2051
9	MeSH DESCRIPTOR diet therapy	38
10	MeSH DESCRIPTOR Caloric Restriction	19
11	MeSH DESCRIPTOR Diet, Carbohydrate-Restricted	20
12	MeSH DESCRIPTOR Diet, Ketogenic	0
13	MeSH DESCRIPTOR Diet, Fat-Restricted	39
14	MeSH DESCRIPTOR Diet, Mediterranean	12
15	MeSH DESCRIPTOR Diet, Paleolithic	1
16	MeSH DESCRIPTOR Diet, Reducing	106
17	MeSH DESCRIPTOR Diet, Vegetarian	5
18	MeSH DESCRIPTOR Diet, Vegan	0
19	MeSH DESCRIPTOR Fasting	55
20	MeSH DESCRIPTOR Dietary Carbohydrates	33
21	MeSH DESCRIPTOR Foods, Specialized	1
22	MeSH DESCRIPTOR Food, Formulated	42
23	MeSH DESCRIPTOR Energy Intake	98
24	((calorie* or kilocalorie* or kilojoule* or energ* or ketogenic*) NEAR2 (restrict* or reduc* or decreas* or low* or deficit*) NEAR2 (diet* or intak* or consum* or ingest* or eat* or meal* or program* or plan* or feed*))	25
25	((macrobiotic* or macronutrien* or hypocalori* or total* or partial* or replace* or substitut* or liquid*) NEAR2 (diet* or meal* or food* or program* or plan*))	136
26	(((total* or partial* or prescrib* or substitut* or liquid*) NEAR2 replace* NEAR2 (diet* or meal* or food* or program* or plan*)) or TDR)	11
27	((low or reduc*) NEAR2 (carb or carbs or carbohydrate* or fat) NEAR2 (diet* or meal* or food* or program* or plan*))	89
28	((plant-base* or vegan* or vegetarian* or veggie*) NEAR2 (diet* or lifestyle* or meal* or food* or program* or plan*))	10
29	(((whole-food* or wholefood*) NEAR2 diet*) or WFPB)	0
30	((Intermit* or alternat* or two-day* or "2 day" or "2 days") NEAR2 (fasting* or fast*))	0
31	(time-restrict* NEAR2 (fasting* or fast* or eat*))	0
32	((Mediterranean* or paleo* or palaeo*) NEAR2 diet*)	23
33	("5?2 diet" or "5?2 diets")	0
34	((point-base* or point-track* or score-base* or score-track*) NEAR2 (diet* or meal* or food* or program* or plan* or eat*))	0
35	#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34	580
36	(#8 AND #35) IN HTA WHERE LPD FROM 01/01/2006 TO 04/03/2022	6

Database name: INAHTA

"Obesity"[mhe]	233
"Obesity Management"[mh]	8
"Overweight"[mh]	15
"Adiposity"[mh]	1
(obes* or preobese* or overweight* or over-weight* or adiposity*)	1958
(weight*) AND (loss* or management* or reduc* or status*)	329
("body mass index" or "body mass index" or "body mass indices" or "body fat index" or "body fat indexes" or "body fat indices" or BMI or BFI) AND (loss* or management* or reduc* or status*)	63
#7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1	1991
"Diet Therapy"[mh]	5
"Caloric Restriction"[mh]	3
"Diet Carbohydrate-Restricted"[mh]	0
"Diet Ketogenic"[mh]	6
"Diet Fat-Restricted"[mh]	1
"Diet Mediterranean"[mh]	0
"Diet Paleolithic"[mh]	0
"Diet Reducing"[mh]	4
"Diet Vegetarian"[mh]	0
"Diet Vegan"[mh]	0
"Fasting"[mh]	1
"Dietary Carbohydrates"[mh]	0
"Foods Specialized"[mh]	0
"Food Formulated"[mh]	3
"Energy Intake"[mh]	2
(calorie* or kilocalorie* or kilojoule* or energ* or ketogenic*) AND (restrict* or reduc* or decreas* or low* or deficit*) AND (diet* or intak* or consum* or ingest* or eat* or meal* or program* or plan* or feed*)	54
(macrobiotic* or macronutrien* or hypocalori* or total* or partial* or replace* or substitut* or liquid*) AND (diet* or meal* or food* or program* or plan*)	534
(total* or partial* or prescrib* or substitut* or liquid*) AND (replace*) AND (diet* or meal* or food* or program* or plan*)	56
(TDR)	3
(low or reduc*) AND (carb or carbs or carbohydrate* or fat) AND (diet* or meal* or food* or program* or plan*)	30
(plant-base* or vegan* or vegetarian* or veggie*) AND (diet* or lifestyle* or meal* or food* or program* or plan*)	1427
(whole-food* or wholefood*) AND (diet*)	37
(WFPB)	0
(Intermit* or alternat* or two-day* or "2 day" or "2 days") AND (fasting* or fast*)	59
(time-restrict*) AND (fasting* or fast* or eat*)	58

(Mediterranean* or paleo* or palaeo*) AND (diet*)	3
("5:2 diet" or "5:2 diets")	174
(point-base* or point-track* or score-base* or score-track*) AND (diet* or meal* or food* or program* or plan* or eat*)	1528
#36 OR #35 OR #34 OR #33 OR #32 OR #31 OR #30 OR #29 OR #28 OR #27 OR #26 OR #25 OR #24 OR #23 OR #22 OR #21 OR #20 OR #19 OR #18 OR #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9	1949
#37 AND #8	585
Limit to English	470
Year 2006 -2022	287

Database name: Medline All

1 exp *obesity/ or Obesity Management/ or overweight/ or *adiposity/ (192128)
2 (obes* or preobese* or overweight* or over-weight* or adiposity*).ti,ab. (369464)
3 (weight* adj1 (loss* or management* or reduc* or status*)).ti,ab. (119572)
4 (("body mass ind*" or "body fat ind*" or BMI or BFI) adj1 (loss* or management* or reduc* or status*)).ti,ab. (4947)
5 or/1-4 (468824)
6 *diet therapy/ or *caloric restriction/ or *diet, carbohydrate-restricted/ or *diet, ketogenic/ or *diet, fat-restricted/ or *diet, mediterranean/ or *diet, paleolithic/ or *diet, reducing/ or *diet, vegetarian/ or *diet, vegan/ or *Fasting/ or *dietary carbohydrates/ or *foods, specialized/ or *Food, Formulated/ or *Energy Intake/ (64923)
7 ((calorie* or kilocalorie* or kilojoule* or energ* or ketogenic*) adj2 (restrict* or reduc* or decreas* or low* or deficit*) adj2 (diet* or intak* or consum* or ingest* or eat*3 or meal*1 or program* or plan* or feed*)).ti,ab. (13374)
8 ((macrobiotic* or macronutrien* or hypocalori* or total* or partial* or replace* or substitut* or liquid*) adj2 (diet* or meal*1 or food* or program* or plan*)).ti,ab. (32436)
9 (((total* or partial* or prescrib* or substitut* or liquid*) adj2 replace* adj2 (diet* or meal*1 or food* or program* or plan*)) or TDR).ti,ab. (5153)
10 ((low or reduc*) adj2 (carb or carbs or carbohydrate* or fat)).ti,ab. (26839)
11 ((plant-base* or vegan* or vegetarian* or veggie*) adj2 (diet* or lifestyle* or meal*1 or food* or program* or plan*)).ti,ab. (9280)
12 (((whole*-food* or wholefood*) adj2 diet*) or WFPB).ti,ab. (125)
13 ((Intermit* or alternat* or two-day* or 2-day*) adj2 (fasting*1 or fast*1)).ti,ab. (1795)
14 (time-restrict* adj2 (fasting*1 or fast*1 or eat*3)).ti,ab. (117)
15 ((Mediterranean* or pal?eo*) adj2 diet*).ti,ab. (6730)
16 ("5?2 diet" or "5?2 diets").ti,ab. (27)
17 ((point-base* or point-track* or score-base* or score-track*) adj2 (diet* or meal*1 or food* or program* or plan* or eat*3)).ti,ab. (78)
18 or/6-17 (140239)
19 5 and 18 (29473)
20 limit 19 to english language (27435)
21 animals/ not humans/ (4933180)
22 20 not 21 (22575)
23 limit 22 to (letter or historical article or comment or editorial or news or case reports) (967)
24 22 not 23 (21608)
25 afghanistan/ or africa/ or africa, northern/ or africa, central/ or africa, eastern/ or "africa south of the sahara"/ or africa, southern/ or africa, western/ or albania/ or algeria/ or andorra/ or angola/ or "antigua and barbuda"/ or argentina/ or armenia/ or azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or "bosnia and herzegovina"/ or botswana/ or brazil/ or brunei/ or bulgaria/ or burkina faso/ or burundi/ or cabo verde/ or cambodia/ or cameroon/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cote d'ivoire/ or croatia/ or cuba/ or "democratic republic of the congo"/ or cyprus/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or egypt/ or el salvador/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or fiji/ or gabon/ or gambia/ or "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or independent state of samoa/ or exp india/ or indian ocean islands/ or indochina/ or indonesia/ or iran/ or iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libya/ or madagascar/ or malaysia/ or malawi/ or mali/ or malta/ or mauritania/ or mauritius/ or mekong valley/ or melanesia/ or micronesia/ or monaco/ or mongolia/ or montenegro/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nepal/ or nicaragua/ or niger/ or nigeria/ or oman/ or pakistan/ or palau/ or exp panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or qatar/ or "republic of belarus"/ or "republic of north macedonia"/ or romania/ or exp russia/ or rwanda/ or "saint kitts and nevis"/

or saint lucia/ or "saint vincent and the grenadines"/ or "sao tome and principe"/ or saudi arabia/ or serbia/ or sierra leone/ or senegal/ or seychelles/ or singapore/ or somalia/ or south africa/ or south sudan/ or sri lanka/ or sudan/ or suriname/ or syria/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or uganda/ or ukraine/ or united arab emirates/ or uruguay/ or uzbekistan/ or vanuatu/ or venezuela/ or vietnam/ or west indies/ or yemen/ or zambia/ or zimbabwe/ (1203534)
26 "organisation for economic co-operation and development"/ (417)
27 australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or exp japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or portugal/ or exp "republic of korea"/ or "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or sweden/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/ (3387634)
28 european union/ (17121)
29 developed countries/ (21087)
30 or/26-29 (3402916)
31 25 not 30 (1116651)
32 24 not 31 (20830)
33 Cost-Benefit Analysis/ (88590)
34 Quality-Adjusted Life Years/ (14433)
35 Markov Chains/ (15615)
36 exp Models, Economic/ (16072)
37 cost*.ti. (133171)
38 (cost* adj2 utilit*).tw. (6763)
39 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw. (244233)
40 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. (40710)
41 (qualit* adj2 adjust* adj2 life*).tw. (15547)
42 QALY*.tw. (12491)
43 (incremental* adj2 cost*).tw. (15116)
44 ICER.tw. (4989)
45 utilities.tw. (8254)
46 markov*.tw. (28136)
47 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. (49312)
48 ((utility or effective*) adj2 analys*).tw. (21941)
49 (willing* adj2 pay*).tw. (8159)
50 (EQ5D* or EQ-5D*).tw. (10981)
51 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. (3028)
52 (european* adj2 quality adj3 ("5" or five)).tw. (553)
53 or/33-52 (448596)
54 32 and 53 (419)
55 54 and (2006* or 2007* or 2008* or 2009* or 2010* or 2011* or 2012* or 2013* or 2014* or 2015* or 2016* or 2017* or 2018* or 2019* or 2020* or 2021* or 2022*).ed,dt. (330)

Appendix C – Effectiveness evidence study selection

40,030 records identified

Records removed as duplicated (n=17,538)

Additional records identified (n=11)

Records screened at title and abstract (n=22,503)

Records identified through database searching (n=20,414)
Records identified through updated database searching (n=2,078)
Additional records identified (n=11)

Records excluded (n=21,986)

Full text articles assessed for eligibility (n=517)
Systematic reviews published 2006-2014 (n=0)
Systematic reviews published 2015- 2022 (n=149)

RCTs published 2006- 2014 (n=96)
RCTs published 2015-2022 (n=213)

Systematic reviews identified through updated searching (n=25)
RCTs identified through updated searching (n=34)

Systematic reviews excluded (n=168)
7 = Not relevant study design/ incorrect study design
46= Study does not contain a relevant intervention
1 = Data not reported in an extractable form
16= Incorrect analysis
38= More recent systematic review included that covers the same topic
4= Review article but not a systematic review
3= More appropriate systematic review included for this diet
2= Incorrect outcomes
1= Incorrect comparisons
21= Incorrect population
4= Systematic review used as source of primary studies
25= Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.

RCTs excluded (n=283)
2= Protocol of an included study
1= Secondary publication of an excluded study
8= Incorrect comparison/ Comparator in study does not match that specified in protocol
1= Errata for paper not included
1= Editorial comment
10= Incorrect study design
7= Incorrect population
7= Secondary publication of an included study that does not provide any additional relevant information
1= Study conducted in a non OEDCED country
11= Incorrect outcomes
3= Data not reported in an extractable form
1= Duplicate reference
2= Conference abstract
2= Unable to acquire paper
42= Study does not contain a relevant intervention
188= Insufficient follow up

Studies included in review (n=66)

Systematic reviews (n=6)

RCTs (n=60)
- RCTs identified from included systematic review (n=36)
- New RCTs identified (n=24)

Appendix D – Effectiveness evidence

Evidence from Systematic Reviews

For individual study characteristics for primary studies included from SRs, please see the relevant systematic review.

Astbury 2019

Bibliographic Reference	Astbury, N.M.; Piernas, C.; Hartmann-Boyce, J.; Lapworth, S.; Aveyard, P.; Jebb, S.A.; A systematic review and meta-analysis of the effectiveness of meal replacements for weight loss; Obesity Reviews; 2019; vol. 20 (no. 4); 569-587

Study characteristics

Study design	Systematic review
Study details	Dates searched Inception to the end of August 2018 Databases searched MEDLINE, Embase, PsycINFO, CINAHL, Web of Science, and the Cochrane Controlled Register of Trials (CENTRAL) Sources of funding This review was funded by National Institute of Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care Oxford at Oxford Health NHS Foundation Trust. 4 of the authors are supported by the National Institute for Health Research (NIHR) Oxford Biomedical Research Centre (BRC).

Inclusion criteria	Population: Adults (≥18 years) with a body mass index (BMI) ≥25 kg/m^2. Intervention: RCTs of interventions incorporating the use of one or more low energy meal replacements (MR) daily, as part of a hypoenergetic diet intended for weight loss Comparator: Either a weight loss intervention that did not include low energy MR or offered no or minimal intervention. Studies were required to report participants' weight at least 1 year after enrolment.
Exclusion criteria	Population: Studies in pregnant women, people with eating disorders, those who had undergone bariatric surgery, or in those that included concomitant use of pharmacotherapies for the purposes of weight loss. Intervention: Diets providing <3347 kJ/(800 kcal)/day (very low calorie diets) and those which used formula total diet replacement (TDR) Comparator: Studies which compared different types of MR but did not include a control arm were excluded.
Intervention(s)	Low energy meal replacement diets (total or partial meal replacement)
Outcome(s)	Change in weight (kg) Change in HbA1c
Number of studies included in the systematic review	23 RCTs across 5 comparisons • Low energy MR diet versus diet only (6 RCTs) • Low energy MR diet + support versus diet + support (10 RCTs) • Low energy MR diet + support versus diet only (2 RCTs) • Low energy MR diet + enhanced support versus diet + support (2 RCTs)

	• Low energy MR diet + support versus minimal intervention (3 RCTs)
Studies from the systematic review that are relevant for use in the current review	**Low energy MR diet vs diet only** Khoo 2011 **Low energy MR diet + support vs diet + support** Ashley 2007 **Low energy MR diet + support vs diet only** Shikany 2013
Studies from the systematic review that are not relevant for use in the current review	**Low energy MR diet vs diet only** Ahrens 2003: published prior to 2006 Cheskin 2008: diet is not low energy as defined in the protocol Ditschuneit 2001: published prior to 2006 Khoo 2014: not a low energy diet and insufficient follow-up Rothacker 2001: published prior to 2006 **Low energy MR diet + support vs diet + support** Ashley 2001: published prior to 2006 Chaiyasoot 2018: insufficient follow-up for relevant outcomes

	Chee 2017: diet is not low energy as defined in the protocol Davis 2010: insufficient follow-up Flechtner-Mors 2010: diet was not low energy as defined in the protocol and both groups received meal replacement Li 2005: published prior to 2006 Lowe 2018: Unclear if the replacement diet is low energy as defined in the protocol Ptomey 2017: diet is not low energy as defined in the protocol Rolls 2017: diet is not low energy as defined in the protocol **Low energy MR diet + support vs diet only** Rock 2007: diet is not low energy as defined in the protocol **Low energy MR diet + enhanced support vs diet + support** Rock 2010: diet is not low energy as defined in the protocol Rock 2014: diet is not low energy as defined in the protocol **Low energy MR + support vs minimal intervention** Kempf 2017: comparator group observational rather than randomised. Look Ahead Research Group 2007: diet is not low energy as defined in the protocol Xu 2013: diet is not low energy as defined in the protocol

Critical appraisal – RoB in SRs – ROBIS checklist

Overall study ratings	Overall risk of bias	Moderate *(Due to not assessing the quality of the results and through doing so engage with the risk of bias of the included studies.)*
Overall study ratings	Applicability as a source of data	Fully applicable

Naude 2022

Bibliographic Reference	Naude, Celeste E; Brand, Amanda; Schoonees, Anel; Nguyen, Kim A; Chaplin, Marty; Volmink, Jimmy; Low-carbohydrate versus balanced-carbohydrate diets for reducing weight and cardiovascular risk.; The Cochrane database of systematic reviews; 2022; vol. 1; cd013334

Study Characteristics

Study design	Systematic review
Study details	Dates searched Inception until 25th June 2021 Databases searched MEDLINE (PubMed), Embase (Ovid), the Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science Core Collection (Clarivate Analytics), ClinicalTrials.gov and WHO International Clinical Trials Registry Platform (ICTRP) Sources of funding No external funding for the review stated. 3 authors are partly supported by the Research, Evidence and Development Initiative (READ-It). READ-It (project number 300342-104) is funded by UK aid from the UK government.
Inclusion criteria	Population: Adults who were living with overweight or obesity as defined by the trial. This included people with, or without, type 2 diabetes, cardiovascular conditions, or risk factors such as hypertension or dyslipidaemia.

	Intervention: Low-carbohydrate weight-reducing diets for at least 12 weeks. Carbohydrate content <45% of total energy or <150g per day. Comparator(s): Balanced -carbohydrate diets (carbohydrate content within the range of 45% to 65% of total energy) that were explicitly implemented for the primary purpose of reducing weight. Study design: Parallel arm individual and cluster randomised controlled trials
Exclusion criteria	Studies where pregnant and lactating women were included, as well as studies in people with specific medical conditions such as bipolar disorder, polycystic ovary syndrome, or chronic renal disease.
Intervention(s)	Low carbohydrate diet (carbohydrate intake of >50g to 150g per day or <45% of total energy intake) Very low carbohydrate diet (carbohydrate intake of ≤50g per day or less than 10% of total daily energy intake)
Outcome(s)	Change in weight (kg) Adverse events Change in HbA1c
Number of studies included in the systematic review	61 studies were included with 58 contained in the meta-analysis
Studies from the systematic review that are relevant for use in the current review	**Very low carbohydrate diet + support versus control diet + support** Bazzano 2014 Foster 2010 Layman 2009 Lim 2010

	Low carbohydrate + support versus control diet + support Calleja-Fernández 2012 Ebbeling 2007 Foraker 2014 Frisch 2009 Griffin 2013 Klemsdal 2010 Mellberg 2014 Sacks 2009 Wycherley 2012 **Low carbohydrate diet + support versus control diet plus support in people with T2D** Elhayany 2010 Guldbrand 2012 Krebs 2012 Larsen 2011 **Low carbohydrate diet versus control diet**

	Pedersen 2014 **Very low carbohydrate diet + support versus control diet + support in people with T2D** Saslow 2017a
Studies from the systematic review that are not relevant for use in the current review	Aude 2004: excluded due to date limit Bales 2017: insufficient follow-up Benassi-Evans 2009: no relevant outcomes for this review Brehm 2003: excluded due to date limit Brehm 2005: excluded due to date limit Cornier 2005: excluded due to date limit Dyson 2007: insufficient follow-up Evangelista 2021: insufficient follow-up Farnsworth 2003: excluded due to date limit Foster 2003: excluded due to date limit Gardner 2007: insufficient follow-up Goni 2018: insufficient follow-up Haufe 2013: no relevant outcomes

	Hockaday 1978: excluded due to date limit Jesudason 2013: not a relevant diet Josse 2011: not a relevant diet Juanola-Falgarona 2014: insufficient follow-up Keogh 2007: insufficient follow-up Kitabchi 2013: insufficient follow-up Landers 2002: excluded due to date limit Lasker 2008 insufficient follow-up Layman 2005: excluded due to date limit Lean 1997: excluded due to date limit Liu 2013: insufficient follow-up Marco-Benedi 2019: insufficient follow-up Mateo-Gallego 2017: insufficient follow-up Ooi 2021: insufficient follow-up Parr 2016: insufficient follow-up Pittas 2005: excluded due to date limit Racette 1995: excluded due to date limit

	Ruth 2013: insufficient follow-up Samaha 2003: excluded due to date limit Sato 2017: insufficient follow-up Stentz 2016: insufficient follow-up Tay 2008: insufficient follow-up Tay 2014: insufficient follow-up Veum 2017: insufficient follow-up Volek 2009: insufficient follow-up Watson 2016: insufficient follow-up Westman 2008: insufficient follow-up Wycherley 2010: insufficient follow-up Yamada 2014: insufficient follow-up

Critical appraisal - RoB in SRs - ROBIS checklist

Overall study ratings	Overall risk of bias	Low
Overall study ratings	Applicability as a source of data	Fully applicable

Nicholas 2021

Bibliographic Reference	Nicholas, A.P.; Soto-Mota, A.; Lambert, H.; Collins, A.L.; Restricting carbohydrates and calories in the treatment of type 2 diabetes: A systematic review of the effectiveness of 'low-carbohydrate' interventions with differing energy levels; Journal of Nutritional Science; 2021; vol. 10; e76

Study Characteristics

Study design	Systematic review
Study details	Dates searched Inception to 7 July 2020 Databases searched Medline, EMBASE, CINAHL, Scopus and Cochrane Central Register of Controlled Trials (CENTRAL). Sources of funding No source of funding stated
Inclusion criteria	Population: adults (≥18 years) with T2D Intervention: low carbohydrate diets or very low-energy diets with <130 g/d or <26% total energy from carbohydrate Comparator: any other type of dietary intervention or usual care Outcomes: studies reporting change in weight and markers of glucose control All countries and languages were eligible.
Exclusion criteria	Studies that included people with other chronic diseases (except hypertension or CVD) or taking systemic corticosteroids, or had any progressive disease requiring hospital care Studies involving intermittent fasting protocols

Intervention(s)	Low energy (total or partial meal replacement) diets Very low energy (total or partial meal replacement) diets Low carbohydrate diet (<26% of total energy from carbohydrates or 130g/day)
Outcome(s)	Change in weight (kg) Change in HbA1c
Number of studies included in the systematic review	15
Studies from the systematic review that are relevant for use in the current review	**Low energy total MR diet + support vs control diet** Brown 2020 Lean 2019 Taheri 2020
Studies from the systematic review that are not relevant for use in the current review	Athinarayanan 2019: incorrect study design Daly 2006: incorrect diet Davis 2009: incorrect diet Iqbal 2010: incorrect diet Sato 2017: incorrect diet Westman 2008: incorrect diet

	Yamada 2014: incorrect diet Guldbrand 2012: incorrect diet Tay 2018: incorrect diet Goday 2016: incorrect diet Morris 2020: incorrect diet Gulsin 2020: follow-up limited to 12 weeks

Critical appraisal - RoB in SRs - ROBIS checklist

Overall study ratings	Overall risk of bias	High *(Due to the unclear inclusion criteria linked to the diets being studied, and the use of narrative synthesis rather than meta-analysis (due to heterogeneity of included studies))*
Overall study ratings	Applicability as a source of data	Fully applicable

Parretti 2016

Bibliographic Reference	Parretti, H.M.; Jebb, S.A.; Johns, D.J.; Lewis, A.L.; Christian-Brown, A.M.; Aveyard, P.; Clinical effectiveness of very-low-energy diets in the management of weight loss: A systematic review and meta-analysis of randomized controlled trials; Obesity Reviews; 2016; vol. 17 (no. 3); 225-234

Study Characteristics

Study design	Systematic review
Study details	Dates searched Inception to November 2014 Databases searched Medline, Embase and the Cochrane Central Register of Controlled Trials. Grey literature such as the ISCRTN database, ANZCTR database and websites including Clinicaltrials.gov, Opengrey and Oaister were also searched Sources of funding This study received no specific funding
Inclusion criteria	Population: Adults (≥18 years) living with a BMI ≥ 25 with or without co-morbidities related to excess adiposity Intervention: a very low energy diet (VLED; defined as 800kcal/day or less) for initial weight loss. Comparator: no intervention or an intervention that could be given in a general medical context, including primary care. Outcomes: a measure of weight change at 12 months or greater from baseline. Study type: RCTs only
Exclusion criteria	Studies in pregnant women or people with eating disorders. Interventions that used VLEDs on a few days each week and studies where a VLED was used only for weight-loss maintenance were excluded. Studies comparing VLED to VLED
Intervention(s)	Very low energy diet (total meal replacement)

Outcome(s)	Change in weight (kg) Adverse events Change in HbA1c
Number of studies included in the systematic review	12 RCTs
Studies from the systematic review that are relevant for use in the current review	**Very low energy meal replacement diet + support versus usual care** Tuomilehto 2009 & 2010 **Very low energy meal replacement diet + support versus usual care + support** Purcell 2014
Studies from the systematic review that are not relevant for use in the current review	Pekkarinen 1997: excluded due to date limit Rolland 2009 & 2010: insufficient follow-up Rossner 1997: excluded due to date limit Ryttig 1997: excluded due to date limit Stenius 2000: excluded due to date limit Torgerson 1997 & Lantz 2003: excluded due to date limit Madden 1986 & 1988: excluded due to date limit Wadden 1994: excluded due to date limit

	Wing 1991: excluded due to date limit Wing 1994-1996: excluded due to date limit

Critical appraisal - RoB in SRs - ROBIS checklist

Overall study ratings	Overall risk of bias	Moderate *(There was variation in included studies criteria)*
Overall study ratings	Applicability as a source of data	Fully applicable

Rafiullah 2022

Bibliographic Reference	Rafiullah, M.; Musambil, M.; David, S.K.; Effect of a very low-carbohydrate ketogenic diet vs recommended diets in patients with type 2 diabetes: A meta-analysis; Nutrition Reviews; 2022; vol. 80 (no. 3); 488-502

Study Characteristics

Study design	Systematic review
Study details	Dates searched January 1st 1980 to September 30th 2019 Databases searched Ovid MEDLINE, Ovid Embase, CENTRAL (Cochrane Central Register of Controlled Trials), and CINAHL (Cumulative Index to Nursing and Allied Health) Sources of funding

	No external funds supported this review PROSPERO registration number CRD42020154700
Inclusion criteria	Population: Adults living with type 2 diabetes Intervention: Very low-carbohydrate ketogenic diet, defined as carbohydrate intake of <50 g/d or < 10% of energy Comparator(s): Any diet recommended for patients with type 2 diabetes Study design: RCTs
Exclusion criteria	None reported
Intervention(s)	Very low-carbohydrate ketogenic diet
Outcome(s)	Change in weight (kg) Change in HbA1c
Number of studies included in the systematic review	8 RCTs
Studies from the systematic review that are relevant for use in the current review	**Very low carbohydrate diet + support versus control diet + support** Goldstein (2011) Iqbal (2010) Saslow (2017) Tay et al (2015)

Studies from the systematic review that are not relevant for use in the current review	Davis (2009): insufficient follow-up Goday (2016): insufficient follow-up Saslow (2014): insufficient follow-up Tay et al (2014): insufficient follow-up Westman et al (2008): insufficient follow-up

Critical appraisal - RoB in SRs - ROBIS checklist

Overall study ratings	Overall risk of bias	Low
Overall study ratings	Applicability as a source of data	Fully applicable

Schwingshackl 2021

Bibliographic Reference	Schwingshackl, L.; Zahringer, J.; Nitschke, K.; Torbahn, G.; Lohner, S.; Kuhn, T.; Fontana, L.; Veronese, N.; Schmucker, C.; Meerpohl, J.J.; Impact of intermittent energy restriction on anthropometric outcomes and intermediate disease markers in patients with overweight and obesity: systematic review and meta-analyses; Critical reviews in food science and nutrition; 2021; vol. 61 (no. 8); 1293-1304

Study Characteristics

Study design	Systematic review
Study details	Dates searched

	Inception to 25th March 2019 Databases searched Medline, Web of Science and the Cochrane Central Register of Controlled Trials (CENTRAL) Sources of funding No funding for this review PROSPERO registration number CRD42019138577
Inclusion criteria	Population: Adult participants with a mean age ≥18 years Intervention: Intermittent energy restriction (IER), including alternate day fasting (ADF) characterised by at least one feast day (24 h) where participants are permitted to eat ad libitum, and at least one fast day (24 h) per week, where energy intake is rigorously reduced (to about 25%) or withheld completely. For instance, in an (5:2)-ADF regimen there are 5 feast and 2 fast days. Comparator(s): a) CER: continuous energy restriction defined as daily energy restriction by at least 15% b) Usual diet (or minimal intervention: e.g. distribution of a brochure with nutritional recommendation at baseline) Study design: Randomized controlled trials (RCTs; with a parallel or cross-over design). Minimum duration of the intervention: >/=12 weeks.
Exclusion criteria	Population: patients with eating disorders; critically ill and hospitalized patients; patients undergoing bariatric surgery Interventions: Liquid/formula diets, meal replacement interventions or dietary supplements. Co-interventions (e.g. drug, diet, or physical activity) not applied in all intervention arms.
Intervention(s)	Intermittent energy restriction

Outcome(s)	Change in weight (kg) Change in BMI Adverse events Change in waist circumference
Number of studies included in the systematic review	17
Studies from the systematic review that are relevant for use in the current review	**Intermittent energy restriction + support versus continuous energy restriction + support** Carter 2018 Schubel 2018 Sundfor 2018 Trepanowski 2017 **Intermittent energy restriction + support versus no/minimal intervention** Trepanowski 2017
Studies from the systematic review that are not relevant for use in the current review	Bhutani 2013: excluded due to insufficient follow-up Carter 2016: excluded due to insufficient follow-up Conley 2018: excluded due to insufficient follow-up Harvie 2013: excluded due to insufficient follow-up

	Harvie 2011: excluded due to insufficient follow-up Hill 1989: excluded due to date limit Mraovic 2018: excluded due to insufficient follow-up Panizza 2019: excluded due to insufficient follow-up Teng 2011: excluded due to insufficient follow-up Teng 2013: excluded due to insufficient follow-up Todd 2015: excluded due to insufficient follow-up Varady 2013: excluded due to insufficient follow-up Viegener 1990: excluded due to date limit

Critical appraisal - RoB in SRs - ROBIS checklist

Overall study ratings	Overall risk of bias	Low
Overall study ratings	Applicability as a source of data	Fully applicable

Evidence from primary RCTs identified from search

Low energy diet - TOTAL meal replacement

Mixed population

Ard 2019

Bibliographic Reference	Ard, J.D.; Lewis, K.H.; Rothberg, A.; Auriemma, A.; Coburn, S.L.; Cohen, S.S.; Loper, J.; Matarese, L.; Pories, W.J.; Periman, S.; Effectiveness of a Total Meal Replacement Program (OPTIFAST Program) on Weight Loss: Results from the OPTIWIN Study; Obesity; 2019; vol. 27 (no. 1); 22-29

Study details

Trial registration number and/or trial name	OPTIWIN Study: ClinicalTrials.gov identifier NCT02635698
Study type	Randomised controlled trial (RCT) Open-label and multicentre
Study location	USA
Study setting	5 private clinics and 4 academic medical centres
Inclusion criteria	Weight: BMI of 30 to 55kg/m² Age: 18 to 70 years old and non-smokers
Exclusion criteria	People who had received or were scheduled for bariatric surgery Recent weight loss or use of weight-loss medications

	Comorbidities: organ failure, type 1 diabetes or hemoglobin A1c > 10%, cardiovascular disease event or mental health hospitalization in the past 6 months, alcohol or drug dependence, positive screening for potential eating disorder, or poorly controlled depression
Intervention(s)	**Low energy total meal replacement** OPTIFAST protocol: • Participants with BMI < 45 were instructed to use five MRs per day (800 kcal total) with 40% of calories as protein, 40% as carbohydrate, and 20% as fat • Participants with BMI of 45 to 49.9 received six MRs per day (960 kcal) • Participants with BMI ≥ 50 received six MRs plus one meal daily of lean protein (3-4 ounces) and one nonstarchy vegetable serving (1,100-1,200 kcal). • All participants followed their prescription for 12 to 16 weeks based on provider discretion and patient preference, after which there was gradual reintroduction of food through week 26. • After week 26, participants' calories were gradually increased to achieve weight stability. During this time, participants were advised to use one to two MRs daily to facilitate weight-loss maintenance. Participants saw a clinician regularly to address health concerns and adjust medications for a total of 11 medical monitoring visits during the first 26 weeks and 4 medical monitoring visits in weeks 27 to 52. Labs for medical monitoring, including either a basic or comprehensive metabolic panel, were obtained at weeks 2, 4, 6, 8, 10, 12, and 16. Participants had individual counselling with trained interventionists for a total of 16 individual counselling visits through the first 26 weeks and 11 individual counselling visits from week 27 through week 52. Both treatment groups had weekly 45- to 60-minute group behavioural sessions for the duration of the intervention.
Comparator	The control program was a modified version of the Diabetes Prevention Program (DPP) intervention. During active weight loss (0-26 weeks), participants were prescribed a calorie-restricted diet emphasizing lower fat intake (25%-30% of total calories). They were advised to reduce calories by 500 to 750 kcal below estimated total energy expenditure, calculated based on resting metabolic rate measured by indirect calorimetry plus an activity factor based on self-reported physical activity.

	To balance the incentive of free MR in the OP arm, control participants received gift cards totalling $800 to offset the cost of groceries during the active weight-loss phase. They also had two medical monitoring visits and seven individual counselling visits through week 26. During the maintenance phase (27-52 weeks), they had two medical monitoring visits and five individual counselling visits. Both treatment groups had weekly 45- to 60-minute group behavioural sessions for the duration of the intervention.
Outcome measures	Change in weight (kg) Serious adverse events Change in waist circumference (cm)
Number of participants	330
Duration of follow-up	1 year
Loss to follow-up	57 (17%)

Characteristics

Study-level characteristics

Characteristic	Study (N = 330)
% Female Sample size	n = 225 ; % = 82
Mean age (SD) Mean (SD)	47 (11)
BMI	38.8 (5.9)

Characteristic	Study (N = 330)
Mean (SD)	
Type 2 diabetes Sample size	n = 33 ; % = 12.1

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0)

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Due to no detailing of the randomisation procedure, allocation concealment, number of people dropping out and the potential effect of not blinding the assessment of subjective outcomes.)*
Overall bias and Directness	Overall Directness	Directly applicable

Astbury 2018 and Astbury 2021 (DROPLET Trial)

Bibliographic Reference	Astbury, N.M.; Aveyard, P.; Nickless, A.; Hood, K.; Corfield, K.; Lowe, R.; Jebb, S.A.; Doctor Referral of Overweight People to Low Energy total diet replacement Treatment (DROPLET): Pragmatic randomised controlled trial; BMJ (Online); 2018; vol. 362; k3760

Study details

Other publications associated with this study included in review	Astbury 2021: Extended follow-up of a short total diet replacement programme: results of the Doctor Referral of Overweight People to Low Energy total diet replacement Treatment (DROPLET) randomised controlled trial at 3 years

Trial registration number and/or trial name	International Standard Randomised Controlled Trials No ISRCTN75092026
Study type	Randomised controlled trial (RCT)
Study location	Oxfordshire, UK
Study setting	Primary care practices
Study dates	Participants were recruited between 12 January 2016 and 28 July 2016. Follow-up was completed on 4 August 2017.
Sources of funding	Research grant from Cambridge Weight Plan UK to the University of Oxford and also supported by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care Oxford at Oxford Health NHS Foundation Trust.
Inclusion criteria	Overweight / obesity: People living with a BMI of at least 30 whose health would benefit from weight loss
Exclusion criteria	People who had received or were scheduled for bariatric surgery Those participating in a weight management programme Contraindications to an intervention diet
Intervention(s)	**Low energy total diet replacement (TDR) program.** People replaced all food with four formula food products daily (soups, shakes, and bars), 750 mL of skimmed milk, 2.25 L of water or other low or no energy drinks, and a fibre supplement; energy intake comprised 810 kcal/day. After eight weeks, there was a four week stepwise reduction in use of the formula food products and reintroduction of conventional food based meals. Participants were asked to contact a local counsellor who was aware of the research study and the protocol for the provision of formula food products but who had not received any additional training to deliver the behavioural support programme. For the first 12 weeks, participants met with the counsellor weekly for support, which comprised goal setting, feedback, encouragement, reassurance, and problem solving.

	During the weight maintenance phase from week 13 to 24, counsellors encouraged participants to attend monthly appointments and to consume one formula food product a day, with the remainder of the diet provided by food. If weight was regained, the protocol allowed for participants to return to the TDR stage for up to four weeks.
Comparator	People followed each practice's usual weight management protocol. People were not prevented from attending other weight management groups, but no National Health Service referrals to these schemes were offered during the intervention period.
Outcome measures	Change in weight (kg) at 12 months Serious adverse events
Number of participants	N=278: 138 in the intervention group and 140 in the comparator group
Duration of follow-up	1 year
Loss to follow-up	34 in the intervention group 45 in the comparator group

Characteristics

Arm-level characteristics

Characteristic	Low energy meal replacement group (N = 138)	Usual care group (N = 140)
% Female Sample size	n = 84 ; % = 60	n = 81 ; % = 60.5
Mean age (SD) Mean (SD)	47.4 (12.8)	48.2 (11.5)
BMI	36.8 (5.1)	37.6 (5.7)

Characteristic	Low energy meal replacement group (N = 138)	Usual care group (N = 140)
Mean (SD)		
Type 2 diabetes No of events	n = 20 ; % = 14	n = 21 ; % = 16

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0)

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Moderate *(Due to missing data and the potential effects of not blinding participants or outcome assessors)*
Overall bias and Directness	Overall Directness	Directly applicable

In people with type 2 diabetes

Lean 2019

Bibliographic Reference	Lean, M.E.J.; Leslie, W.S.; Barnes, A.C.; Brosnahan, N.; Thom, G.; McCombie, L.; Peters, C.; Zhyzhneuskaya, S.; Al-Mrabeh, A.; Hollingsworth, K.G.; Rodrigues, A.M.; Rehackova, L.; Adamson, A.J.; Sniehotta, F.F.; Mathers, J.C.; Ross, H.M.; McIlvenna, Y.; Welsh, P.; Kean, S.; Ford, I.; McConnachie, A.; Messow, C.-M.; Sattar, N.; Taylor, R.; Durability of a primary care-led weight-management intervention for remission of type 2 diabetes: 2-year results of the DiRECT open-label, cluster-randomised trial; The Lancet Diabetes and Endocrinology; 2019; vol. 7 (no. 5); 344-355

Study details

Secondary publication of another included study- see primary study for details	Lean ME, Leslie WS, Barnes AC, Brosnahan N, Thom G, McCombie L, Peters C, Zhyzhneuskaya S, Al-Mrabeh A, Hollingsworth KG, Rodrigues AM, Rehackova L, Adamson AJ, Sniehotta FF, Mathers JC, Ross HM, McIlvenna Y, Stefanetti R, Trenell M, Welsh P, Kean S, Ford I, McConnachie A, Sattar N, Taylor R. Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial. Lancet. 2018 Feb 10;391(10120):541-551. doi: 10.1016/S0140-6736(17)33102-1. This paper contains 2 year outcomes linked to the included trial detailed above As Lean 2018 was picked up from a systematic review (Nicholas 2021) additional evidence tables were not created.

McDiarmid 2022

Bibliographic Reference	McDiarmid, S.; Harvie, M.; Johnson, R.; Vyas, A.; Aglan, A.; Moran, J.; Ruane, H.; Hulme, A.; Sellers, K.; Issa, B.G.; Manchester Intermittent versus Daily Diet App Study (MIDDAS): A pilot randomized controlled trial in patients with type 2 diabetes; Diabetes, Obesity and Metabolism; 2022; vol. 24 (no. 3); 432-441

Study details

Trial registration number and/or trial name	The trial protocol (V5.0 08.04.19) was granted ethical approval by the North West Greater Manchester South Research Ethics Committee (ref. 17/NW/0389).
Study type	Randomised controlled trial (RCT)
Study location	Manchester, UK
Study setting	Participants were recruited from 3 general practices, 2 NHS hospital trusts and a volunteer research register

Study dates	
Sources of funding	Supported by Néstle Health Science and Oviva UK Limited
Inclusion criteria	Overweight / obesity: BMI>27 kg/m² and <50 kg/m² or >25 kg/m² and <50 kg/m² in people with a South Asian, Black African, or African Caribbean family background. Age: 18-75 years old Type 2 diabetes: Diagnosed with type 2 diabetes <8 years
Exclusion criteria	Comorbidities: Currently diagnosed eating disorder, previous bariatric surgery, or severe anxiety or depression HbA1c: ≥108 mmol/mol
Intervention(s)	Intermittent energy restriction. Active Weight Loss Phase (28 weeks): the ILED group was asked to include 2 consecutive days per week of the Optifast LED plus 5 days of a Mediterranean diet for 28 weeks. An energy deficit was applied to the Mediterranean diet (up to a value of 265 kcal [1109 kJ] per day) to ensure that the ILED and CLED diets were isocaloric during the active weight loss phase. Weight Maintenance or Continued Weight Loss Phase (24 weeks): Participants were asked to follow a food-based ILED. Participants who had achieved 15% weight loss, and/or their target weight if greater, were asked to follow the food-based LED described above for one day per week and a euenergetic Mediterranean diet aimed at weight maintenance. Participants who had not achieved 15% weight loss or wished to lose more weight were asked to follow the food-based LED for 2 consecutive days per week and an energy-restricted Mediterranean diet per day for 5 days.
Comparator	Continuous energy restriction. Active Weight Loss Phase (12 weeks): Weeks 1 to 8 involved the Optifast LED. This provided approximately 820 kcal (3430 kJ) per day and consisted of 3 sachets per day. Participants who were unable to tolerate Optifast were offered a food-based LED with a similar macronutrient profile. Diet reintroduction in weeks 9-12 allowed a food-based, energy-restricted Mediterranean diet providing1000 kcal (4184 kJ) daily in week 1, 1200 kcal (5021 kJ) daily in week 2, 1400 kcal (5858 kJ) daily inweek 3, and 1500 kcal (6276 kJ) daily in week 4. Weight Maintenance or Continued Weight Loss Phase (40 Weeks): Participants who achieved a trial weightloss goal of 15%, and/or their target weight if greater, were advised to follow a euenergetic Mediterranean diet for weight maintenance. Those who had not achieved 15% weight loss or wished to lose more weight were asked to follow a 25% energy-restricted Mediterranean diet.

Outcome measures	Change in weight (kg) Serious adverse events Change in HbA1c Adherence to intervention offered Retention rate
Number of participants	79
Duration of follow-up	12 months
Loss to follow-up	22 (28%)

Characteristics

Study-level characteristics

Characteristic	Study (N = 79)
% Female Sample size	n = 30 ; % = 53
Mean age (SD) Mean (SD)	57 (11)
BMI Mean (SD)	36.4 (5.8)
White British family background Sample size	n = 65 ; % = 82

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0)

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Moderate *(Due to the number of drop-outs by final analysis)*
Overall bias and Directness	Overall Directness	Directly applicable

Very low energy diet – TOTAL meal replacement

Mixed population

Seimon 2019, Seimon 2020 and Jin 2022 (TEMPO Trial)

Bibliographic Reference	Seimon, R.V.; Wild-Taylor, A.L.; Keating, S.E.; McClintock, S.; Harper, C.; Gibson, A.A.; Johnson, N.A.; Fernando, H.A.; Markovic, T.P.; Center, J.R.; Franklin, J.; Liu, P.Y.; Grieve, S.M.; Lagopoulos, J.; Caterson, I.D.; Byrne, N.M.; Sainsbury, A.; Effect of weight loss via severe vs moderate energy restriction on lean mass and body composition among postmenopausal women with obesity: The tempo diet randomized clinical trial; JAMA Network Open; 2019; vol. 2 (no. 10); e1913733

Study details

Other publications associated with this study included in review	Seimon 2020 and Jin 2022
Trial registration number and/or trial name	TEMPO study: Registered at www.anzctr.org.au as ACTRN12612000651886.
Study type	Randomised controlled trial (RCT)
Study location	Australia

Study setting	Charles Perkins Centre Royal Prince Alfred Clinic on the University of Sydney campus in Sydney, New South Wales, Australia
Study dates	Recruitment from March 2013 to July 2016
Sources of funding	Supported by a National Health and Medical Research Council (NHMRC) of Australia project grant 1026005
Inclusion criteria	Weight: Stable weight of BMI 30-40 kg/m² Sex: Women who were postmenopausal for at least 5 years Age: 40-65 years old
Exclusion criteria	Comorbidities: Osteoporosis, cardiovascular disease, gastrointestinal disease, hepatic or renal impairments, hyperthyroidism or hypothyroidism Ambulatory or physical restrictions
Intervention(s)	Very low energy total meal replacement diet via FAST intervention involved KicStart meal replacement products (soups and shakes supplemented with a whey protein isolate) involving severe energy restriction (target range for energy restriction was 65–75% relative to estimated energy expenditure) for 16 weeks, or until a BMI of no lower than 20 kg/m². This was followed by moderate energy restriction of 25-35% (i.e. the MODERATE intervention) for the remaining time up until 52 weeks. Participants were required to attend individual dietary appointments with the trial dietitian every 2 weeks for the first 26 weeks then approximately monthly until 52 weeks.
Comparator	Energy-restricted diet via the moderate intervention. Food-based, moderately energy-restricted diet (target range for energy restriction was 25–35% relative to estimated energy expenditure) for a total of 52 weeks. The control intervention was based on the Australian Guide to Healthy Eating (AGHE) and provides recommendations on the average number of standard servings of the 5 core food groups (i.e. vegetables, fruit, grains and cereals, meat and meat alternatives, and reduced fat dairy). Participants were required to attend individual dietary appointments with the trial dietitian every 2 weeks for the first 26 weeks then approximately monthly until 52 weeks.
Outcome measures	Change in weight (kg) Change in BMI Serious adverse events

	Change in waist circumference (cm)
Number of participants	101
Duration of follow-up	36 months
Loss to follow-up	8% loss in the intervention group and 22% in the comparator group at 1 year 18% loss in the intervention group and 38% in the comparator group at 3 years

Characteristics

Study-level characteristics

Characteristic	Study (N = 101)
Mean age (SD) Mean (SD)	58 (4.2)
Smoking status Sample size	n = 0 ; % = 0
BMI Mean (SD)	34.4 (2.5)
White ethnicity Sample size	n = 95 ; % = 95

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0)

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Moderate *(Due to missing data at both 12 months and 3 years)*
Overall bias and Directness	Overall Directness	Directly applicable

Low carbohydrate diet

Mixed population

Brinkworth 2009 and Brinkworth 2016a

Bibliographic Reference	Brinkworth, G.D.; Wycherley, T.P.; Noakes, M.; Buckley, J.D.; Clifton, P.M.; Long-term effects of a very-low-carbohydrate weight-loss diet and an isocaloric low-fat diet on bone health in obese adults; Nutrition; 2016; vol. 32 (no. 9); 1033-1036

Study details

Other publications associated with this study included in review	Brinkworth 2016a
Trial registration number and/or trial name	
Study type	Randomised controlled trial (RCT)
Study location	Adelaide, South Australia, Australia
Study setting	Conducted in CSIRO Clinical Research Unit (Adelaide, Australia)
Study dates	May 2012 - September 2013.

Sources of funding	Supported by project grants from the National Heart Foundation of Australia and the National Health and Medical Research Council of Australia (APP ID 401818).
Inclusion criteria	Overweight / obesity Living with abdominal obesity Adults
Exclusion criteria	Comorbidities Cancer Pregnancy Medical history Liver, respiratory, gastrointestinal, cardiovascular, or peripheral vascular disease Diabetes
Intervention(s)	Very low carbohydrate diet: moderate energy restriction 1450 kcal/d for females and 1650 kcal/d for males and initially (4% of total energy as carbohydrate [<20 g]. After 8 weeks, participants could raise carbohydrate intake up to 40 g per day. Participants also met individually with a qualified dietitian who provided detailed dietary advice, meal plans, and recipe information pertaining to each diet every 2 weeks.
Comparator	Low fat diet: moderate energy restriction 1450 kcal/d for females and 1650 kcal/d for males and initially (46% of total energy as carbohydrate. Participants also met individually with a qualified dietitian who provided detailed dietary advice, meal plans, and recipe information pertaining to each diet every 2 weeks.
Outcome measures	Change in weight (kg)
Number of participants	118
Duration of follow-up	12 months

Loss to follow-up	53 (45%)

Characteristics

Study-level characteristics

Characteristic	Very low carb group (N = 32)	Low fat group (N = 33)
BMI Mean (SD)	33.7 (4)	33.2 (4)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0)

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Due to unclear randomisation procedure and allocation concealment combined with high number of drop outs)*
Overall bias and Directness	Overall Directness	Directly applicable

Very low carbohydrate diet

Mixed population

Hu 2015

Bibliographic Reference	Hu, T.; Yao, L.; Reynolds, K.; Whelton, P.K.; Niu, T.; Li, S.; He, J.; Bazzano, L.A.; The effects of a low-carbohydrate diet vs. a low-fat diet on novel cardiovascular risk factors: A randomized controlled trial; Nutrients; 2015; vol. 7 (no. 9); 7978-7994

Study details

Trial registration number and/or trial name	Clinicaltrials.gov; Identifier: NCT00609271)
Study type	Randomised controlled trial (RCT)
Study location	USA
Study setting	Tulane University Health Sciences Center in New Orleans, Louisiana.
Sources of funding	National Center for Research Resources of the National Institutes of Health (NIH/NCRR P20-RR017659) and the Tulane University Hypertension and Renal Center of Excellence
Inclusion criteria	Overweight / obesity: BMI of 30-45 kg/m² Age: Adults 22-75 years old
Exclusion criteria	People who had received or were scheduled for bariatric surgery Weight change: Stable weight for 6 months Comorbidities: CVD or chronic renal disease; Diabetes
Intervention(s)	Net carbohydrate intake (total carbohydrate minus total fibre) was restricted to <40 grams/day. Participants met with a dietitian in weekly individual counselling sessions for the first month, followed by small group counselling sessions every other week for the subsequent five months, and then monthly for the last six months. Individual sessions lasted 1 h and included supportive counselling and dietary instructions in the form of recipes. Group sessions

	were held separately for participants in the low-fat and low-carbohydrate groups but participants received the same dietary behavioural curriculum, which included identical information on dietary fibre intake and education on the different types of fat with an emphasis on the benefits of monounsaturated fats and recommendations to limit or eliminate trans-fats. Behavioural counselling also emphasized portion control and change in eating patterns. An optional daily low-carbohydrate or low-fat meal replacement (bar or shake) was provided to participants in each group for the duration of the intervention. Participants were counselled to maintain their baseline levels of physical activity.
Comparator	Low-fat diet which restricted total fat to <30% of daily energy, with <7% from saturated fat. Participants met with a dietitian in weekly individual counselling sessions for the first month, followed by small group counselling sessions every other week for the subsequent five months, and then monthly for the last six months. Individual sessions lasted 1 h and included supportive counselling and dietary instructions in the form of recipes. Group sessions were held separately for participants in the low-fat and low-carbohydrate groups but participants received the same dietary behavioural curriculum, which included identical information on dietary fibre intake and education on the different types of fat with an emphasis on the benefits of monounsaturated fats and recommendations to limit or eliminate trans-fats. Behavioural counselling also emphasized portion control and change in eating patterns. An optional daily low-carbohydrate or low-fat meal replacement (bar or shake) was provided to participants in each group for the duration of the intervention. Participants were counselled to maintain their baseline levels of physical activity.
Outcome measures	Change in weight (kg)
Number of participants	148
Duration of follow-up	12 months from baseline
Loss to follow-up	30% of participants dropped out before the 12 month assessment

Characteristics

Study-level characteristics

Characteristic	**Study (N = 148)**
% Female Sample size	n = 131 ; % = 89

Characteristic	Study (N = 148)
African American family background Sample size	n = 76
White family background Sample size	n = 67 ; % = 45
Weight (kg) Low carbohydrate group Mean (SD)	96.3 (12.7)
Weight (kg) Low fat group Mean (SD)	97.9 (13.5)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0)

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Due to unclear randomisation, allocation concealment, and high numbers of drop outs prior to 12 months)*
Overall bias and Directness	Overall Directness	Partially applicable *(Partially applicable due to no calorie deficit for comparator)*

Moreno 2014 and Moreno 2016

Bibliographic Reference	Moreno, B.; Bellido, D.; Sajoux, I.; Goday, A.; Saavedra, D.; Crujeiras, A.B.; Casanueva, F.F.; Comparison of a very low-calorie-ketogenic diet with a standard low-calorie diet in the treatment of obesity; Endocrine; 2014; vol. 47 (no. 3); 793-805

Study details

Other publications associated with this study included in review	Moreno 2016 (2 year follow-up)
Trial registration number and/or trial name	
Study type	Randomised controlled trial (RCT)
Study location	Madrid, Spain
Study setting	Obesity unit at a hospital in Madrid
Study dates	
Sources of funding	The funding for the study as well as the high-biological value protein preparations was provided by Protein Supplies, S.L., (Barcelona, Spain) free of charge to the patients. The funding source had no involvement in the study design, recruitment of patients, study interventions, data collection, or interpretation of the results.
Inclusion criteria	Weight: BMI ≥ 30. Stable body weight in the previous 3 months Desire to lose weight History of failed dietary efforts Age: 18-65 years
Exclusion criteria	Those participating in a weight management programme Use of any weight loss diet or pills in the previous 6 months Comorbidities: Severe depression or any other psychiatric disease; abuse of narcotics or alcohol; severe hepatic insufficiency; any type of renal insufficiency or gout episodes; neoplasia (except basal cell skin cancer), previous events of cardiovascular or cerebrovascular disease, kidney Itiasis, uncontrolled hypertension, and hydroelectrolytic alterations.

	Pregnancy: Females with child-bearing potential, who were pregnant, breast-feeding, intending to become pregnant, or not using adequate contraceptive methods were excluded Medical history: None of the participants had a serious medical condition Diabetes: Participants with type 1 diabetes or insulin therapy were excluded
Intervention(s)	The very low calorie ketogenic (VLCK) diet group followed a very low-calorie-ketogenic diet according to a commercial weight loss program (PronoKal method) based on a high-biological-value protein preparations diet and natural foods, alongside lifestyle and behavioural modification support. Each protein preparation contained 15 g protein, 4g carbohydrates, and 3 g fat, and provided 90–100 kcal. The diet plan begins with 600–800 kcal/day through 5 preparations that are low in carbohydrates (<50 g) and lasted 45–60 days in total. Then followed a low-calorie diet initiated for the remainder of the trial, involving progressive incorporation of different food groups and an eating plan balanced in carbohydrates, protein and fat (calories consumed ranged from 800-1500 kcal/day for a continued weight loss phase then 1500-2000 kcal/day for a maintenance phase, depending on the individual). Participants attended 9 group meetings and 3 individual support meetings, with regular reinforcement phone calls.
Comparator	The standard low calorie diet of the Obesity unit; this was an equilibrated diet that had a caloric value 10% below the total metabolic expenditure of each individual. The calories provided to this group ranged between 1400 and 1800 kcal/day. The ration of macronutrients provided was 45–55 % carbohydrates, 15–25 % proteins, and 25–35 % fat. Participants attended 9 group meetings and 3 individual support meetings, with regular reinforcement phone calls.
Outcome measures	Change in weight (kg) Serious adverse events: Constipation; hair loss Change in HbA1c
Number of participants	N = 79
Duration of follow-up	12 months 2 years (data from Moreno 2016)

Loss to follow-up	VLCK diet group = 12 lost to follow-up Low calorie diet group = 14 lost to follow-up

Characteristics

Arm-level characteristics

Characteristic	VLCK diet (N = 27)	Low calorie diet (N = 26)
% Female Sample size	% = 81.4	% = 96.1
Mean age (SD) Mean (SD)	44.4 (8.6)	46.3 (9.3)
BMI Mean (SD)	35.1 (4.5)	35.1 (5.3)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0)

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Limited information on randomisation or allocation procedures; no information on blinding of participants or outcome assessors; relatively high drop-out rate; trial not registered)*
Overall bias and Directness	Overall Directness	Directly applicable

In people with type 2 diabetes

Brinkworth 2016b, Tay 2018 and Kakoschke 2021

Bibliographic Reference	Brinkworth, G.D.; Luscombe-Marsh, N.D.; Thompson, C.H.; Noakes, M.; Buckley, J.D.; Wittert, G.; Wilson, C.J.; Long-term effects of very low-carbohydrate and high-carbohydrate weight-loss diets on psychological health in obese adults with type 2 diabetes: randomized controlled trial; Journal of Internal Medicine; 2016; vol. 280 (no. 4); 388-397

Study details

Secondary publication of another included study- see primary study for details	The following publications are linked: Tay 2015 - Tay J, Luscombe-Marsh ND, Thompson CH, et al. Comparison of low- and highcarbohydrate diets for type 2 diabetes management: a randomized trial. Am J Clin Nutr. 2015;102:780–790. Brinkworth 2016 (current paper)- Brinkworth, G.D.; Luscombe-Marsh, N.D.; Thompson, C.H.; Noakes, M.; Buckley, J.D.; Wittert, G.; Wilson, C.J.; Long-term effects of very low-carbohydrate and high-carbohydrate weight-loss diets on psychological health in obese adults with type 2 diabetes: randomized controlled trial; Journal of Internal Medicine; 2016; vol. 280 (no. 4); 388-397 Tay 2018 - Tay, J.; Thompson, C.H.; Luscombe-Marsh, N.D.; Wycherley, T.P.; Noakes, M.; Buckley, J.D.; Wittert, G.A.; Yancy, W.S.; Brinkworth, G.D.; Effects of an energy-restricted low-carbohydrate, high unsaturated fat/low saturated fat diet versus a high-carbohydrate, low-fat diet in type 2 diabetes: A 2-year randomized clinical trial; Diabetes, Obesity and Metabolism; 2018; vol. 20 (no. 4); 858-871 Kakoschke 2021 - Kakoschke, N.; Zajac, I.T.; Tay, J.; Luscombe-Marsh, N.D.; Thompson, C.H.; Noakes, M.; Buckley, J.D.; Wittert, G.; Brinkworth, G.D.; Effects of very low-carbohydrate vs. high-carbohydrate weight loss diets on psychological health in adults with obesity and type 2 diabetes: a 2-year randomized controlled trial; European Journal of Nutrition; 2021; vol. 60 (no. 8); 4251-4262 As Tay 2015 was included as part of a systematic review (Rafiullah 2022) and additional evidence tables were not developed for these papers.

Intermittent energy restriction – 5:2 diet

Mixed population

Hajek 2021

Bibliographic Reference	Hajek, P.; Przulj, D.; Pesola, F.; McRobbie, H.; Peerbux, S.; Phillips-Waller, A.; Bisal, N.; Smith, K.M.; A randomised controlled trial of the 5:2 diet; PLoS ONE; 2021; vol. 16 (no. 11november); e0258853

Study details

Trial registration number and/or trial name	ISRCTN registry: ISRCTN79408248
Study type	Randomised controlled trial (RCT)
Study location	Tower Hamlets in London, UK
Study setting	Weight Management Clinic run by the Health and Lifestyle Research Unit, Queen Mary University of London
Study dates	
Sources of funding	The study was funded by the UK Medical Research Council.
Inclusion criteria	Overweight / obesity: BMI >30 kg/m² or >28 kg/m², with co-morbidities Age: At least 18 years old
Exclusion criteria	Weight change: Stable weight for 6 months Pregnancy: People who are pregnant or breastfeeding Medical history: History of eating disorders Diabetes: Using insulin

Intervention(s)	**5:2 diet: self-help format (5:2SH)**. Participants received a leaflet on restricting their caloric intake to 500 kcal for women and 600 kcal for men, and on doing this on two non-consecutive days a week. An advisor explained the programme and answered questions. Participants were also provided with the same leaflet about local resources for exercise that was given out with SBA. **5:2 diet: group support format (5:2G)**. Participants received the 5:2SH intervention and in addition were invited to attend six group support sessions (in weeks 1–6), each lasting one hour. Sessions were moderated by advisors. Participants were weighed and reported on their experience over the past week, whether they managed to adhere to the plan, whether they cook or use pre-prepared food on the fasting days, how they cope with hunger, etc. The focus of the sessions was on participants' sharing their experience and maintaining motivation to carry on with 5:2. Participants were also encouraged to join an internet forum to report on their 5:2 adherence and weight change, and discuss their experience with other participants.
Comparator	**Standard Brief Advice (SBA)**. Participants received a copy of the British Heart Foundation guides 'Facts Not Fads' and 'Get Active, Stay Active' plus the NHS 'Change 4 Life' series of booklets and a leaflet listing local resources for exercise. An advisor explained the programme, went over the key advice and tips in the written materials (e.g. portion control, food diaries, 'eat-well' plate, avoiding unnecessary snacks etc.), and answered questions. The individual session took approximately 20 minutes.
Outcome measures	Change in weight (kg) Adherence to intervention offered Retention rate
Number of participants	300
Duration of follow-up	12 months from baseline
Loss to follow-up	5% of participants dropped out

Characteristics

Study-level characteristics

Characteristic	Study (N = 300)
% Female Sample size	n = 199 ; % = 66
Mean age (SD) Mean (SD)	48 (13)
White family background Sample size	n = 170 ; % = 57
Black family background Sample size	n = 55 ; % = 19
Asian family background Sample size	n = 43 ; % = 14

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0)

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Directly applicable

Mixed population

Carter 2019

Bibliographic Reference	Carter, S.; Clifton, P.M.; Keogh, J.B.; The effect of intermittent compared with continuous energy restriction on glycaemic control in patients with type 2 diabetes: 24-month follow-up of a randomised noninferiority trial; Diabetes Research and Clinical Practice; 2019; vol. 151; 11-19

Study details

Secondary publication of another included study- see primary study for details	Paper linked to Carter 2018 - Carter, S.; Clifton, P.M.; Keogh, J.B.; Effect of Intermittent Compared With Continuous Energy Restricted Diet on Glycemic Control in Patients With Type 2 Diabetes: A Randomized Noninferiority Trial; JAMA network open; 2018; vol. 1 (no. 3); e180756 As Carter 2018 was identified through a systematic review (Schwingshackl 2021) additional evidence tables were not created.

Pannen 2021

Bibliographic Reference	Pannen, S.T.; Maldonado, S.G.; Nonnenmacher, T.; Sowah, S.A.; Gruner, L.F.; Watzinger, C.; Nischwitz, K.; Ulrich, C.M.; Kaaks, R.; Schubel, R.; Grafetstatter, M.; Kuhn, T.; Adherence and dietary composition during intermittent vs. Continuous calorie restriction: Follow-up data from a randomized controlled trial in adults with overweight or obesity; Nutrients; 2021; vol. 13 (no. 4); 1195

Study details

Secondary publication of another included	Linked to Schubel 2018 (HELENA Trial) - Schubel, R.; Nattenmuller, J.; Sookthai, D.; Nonnenmacher, T.; Graf, M.E.; Riedl, L.; Schlett, C.L.; Von Stackelberg, O.; Johnson, T.; Nabers, D.; Kirsten, R.; Kratz, M.; Kauczor, H.-U.; Ulrich, C.M.; Kaaks,

study- see primary study for details	R.; Kuhn, T.; Effects of intermittent and continuous calorie restriction on body weight and metabolism over 50 wk: A randomized controlled trial; American Journal of Clinical Nutrition; 2018; vol. 108 (no. 5); 933-945 As this paper was picked up from Schwingshackl 2021 additional evidence tables weren't created.

Intermittent energy restriction – alternate day fasting

Mixed population

Oustric 2021

Bibliographic Reference	Oustric, P.; Beaulieu, K.; Casanova, N.; O'connor, D.; Gibbons, C.; Hopkins, M.; Blundell, J.; Finlayson, G.; Food liking but not wanting decreases after controlled intermittent or continuous energy restriction to >=5% weight loss in women with overweight/obesity; Nutrients; 2021; vol. 13 (no. 1); 1-14

Study details

Study type	Randomised controlled trial (RCT)
Study location	UK
Study setting	University of Leeds and surrounding area.
Study dates	Recruited in 2018
Sources of funding	Funded by a Research Fellowship awarded to Kristine Beaulieu by the European Society for Clinical Nutrition and Metabolism (ESPEN)
Inclusion criteria	Overweight / obesity: BMI of 25.0–34.9 kg/m² Sex: Women Age: 18-55 years old

Exclusion criteria	Weight change: Lost or gained significant amount of weight in the previous 6 months Comorbidities: Significant health problems which, in the opinion of the investigator, might jeopardize participant's safety or compliance with the protocol; Pregnancy: Pregnant, planning to become pregnant or breastfeeding Medical history: Eating disorders Smoking: Smokers or had recently ceased smoking
Intervention(s)	Intermittent energy restriction: ad libitum day alternating with 75% energy restriction day with LighterLife (UK) total diet replacement products provided. Until ≥5% weight loss or up to 12 weeks. Participants met weekly with a dietitian to monitor weight loss and were provided with pre-portioned food that required minimal preparation.
Comparator	Continuous energy restriction (25% daily energy restriction with all foods provided) to ≥5% weight loss or up to 12 weeks. Participants met weekly with a dietitian to monitor weight loss and were provided with pre-portioned food that required minimal preparation.
Outcome measures	Change in weight (kg) % changed reported Adherence to intervention offered Assessed using a weekly meal plan booklet
Number of participants	46
Duration of follow-up	1 year from baseline
Loss to follow-up	35% lost to follow-up

Characteristics

Study-level characteristics

Characteristic	Study (N = 46)
% Female Sample size	n = 46 ; % = 100

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0)

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Due to not specifying how randomisation was achieved, whether allocation was concealed, limited details of the treatment groups, and number of people who dropped out prior to final follow-up)*
Overall bias and Directness	Overall Directness	Directly applicable

Intermittent energy restriction – time restricted eating

Mixed population

Byrne 2018

Bibliographic Reference	Byrne, N M; Sainsbury, A; King, N A; Hills, A P; Wood, R E; Intermittent energy restriction improves weight loss efficiency in obese men: the MATADOR study.; International journal of obesity (2005); 2018; vol. 42 (no. 2); 129-138

Study details

Trial registration number and/or trial name	The MATADOR (Minimising Adaptive Thermogenesis And Deactivating Obesity Rebound) study
Study type	Randomised controlled trial (RCT)

Study location	Australia
Study setting	Single centre in Queensland
Sources of funding	This trial was funded by an Australian National Health and Medical Research Council (NHMRC) project grant (497223).
Inclusion criteria	Overweight / obesity: BMI of 30-45 kg/m² and stable for previous 6 months Sex: Male Age: 25-54 years old Exercise: Sedentary:<60 min of structured moderate to vigorous intensity physical activity per week
Exclusion criteria	Comorbidities: People with a thyroid condition or taking thyroid medicine. People with significant metabolic, cardiovascular, haematological, neurological, pulmonary, gastrointestinal, renal conditions Ambulatory or physical restrictions: Individuals with medical conditions or disorders that impede mobility Diabetes: Individuals with a fasting blood glucose concentration >6 mmol/L Exercise: Individuals who were planning to begin an exercise program, or who express interest in beginning an exercise program over the duration of the study
Intervention(s)	8 × 2-week blocks of energy restriction (ER) interspersed with 7 × 2-week blocks of energy balance (30 weeks total). 8-week post-weight loss energy balance phase. This was designed to give 67% of individual weight maintenance energy requirements (33% reduction in energy intake). Food was provided for each of the trial phases: participants were provided with all main meals and morning and afternoon snacks for the duration of the study; meals were prepared by a commercial kitchen under the direction of a dietician and delivered to the participants' homes each week
Comparator	16 weeks of continuous energy restriction followed by 8-week postweight loss energy balance phase. This was designed to give 67% of individual weight maintenance energy requirements (33% reduction in energy intake). Food was provided for each of the trial phases: participants were provided with all main meals and morning and afternoon snacks for the duration of the study; meals were prepared by a commercial kitchen under the direction of a dietician and delivered to the participants' homes each week

Outcome measures	Change in weight (kg)
Number of participants	51
Duration of follow-up	6 months after intervention
Loss to follow-up	55% lost to follow-up
Methods of analysis	
Additional comments	

Characteristics

Arm-level characteristics

Characteristic	IER (N = 26)	CER (N = 25)
% Female Sample size	n = 0 ; % = 0	n = 0 ; % = 0
Age Mean (SD)	39.9 (9.2)	39.3 (6.6)
BMI Mean (SD)	34.6 (4.2)	43.4 (3.3)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0)

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Due to unclear blinding and allocation concealment, no blinding, and missing data due to people dropping out of the trial.)*
Overall bias and Directness	Overall Directness	Directly applicable

Keogh 2014

Bibliographic Reference	Keogh, J.B.; Pedersen, E.; Petersen, K.S.; Clifton, P.M.; Effects of intermittent compared to continuous energy restriction on short-term weight loss and long-term weight loss maintenance; Clinical Obesity; 2014; vol. 4 (no. 3); 150-156

Study details

Trial registration number and/or trial name	Study registered with the Australia New Zealand Clinical Trial Registry (ANZCTR) and given the registration number ACTRN12612000197831
Study type	Randomised controlled trial (RCT)
Study location	Not stated; assumed Australia
Study setting	A research centre
Study dates	
Sources of funding	PMC was supported by a Principal Research Fellowship from the National Health and Medical Research Council of Australia. JBK was supported by a Heart Foundation and Government of South Australia Research Fellowship.
Inclusion criteria	Overweight / obesity: BMI above 27 kg/m² Sex: Women only Age: Aged 18 years and older
Exclusion criteria	People who had received or were scheduled for bariatric surgery

Intervention(s)	**Intermittent energy restriction -** participants followed an energy restricted diet based on the 'Total Wellbeing Diet' portion and recipe system from the Commonwealth Scientific and Industrial Research Organisation (CSIRO). Intervention group followed a 5500-kJ energy restriction for 1 week, followed by 1 week of their usual diet. Participants attended the research centre every 2 weeks for 8 weeks and for a follow-up visit at 52 weeks. Participants were instructed to continue their allocated IER strategy from week 8 to week 52 but did not attend the research centre during that time.
Comparator	**Continuous energy restriction -** participants followed an energy restricted diet based on the 'Total Wellbeing Diet' portion and recipe system from the Commonwealth Scientific and Industrial Research Organisation (CSIRO). Control group participants followed a 5500-kJ energy restriction continuously for the duration of the study. Participants attended the research centre every 2 weeks for 8 weeks and for a follow-up visit at 52 weeks. Participants were instructed to continue their allocated CER strategy from week 8 to week 52 but did not attend the research centre during that time.
Outcome measures	Change in weight (kg) Change in waist circumference (cm)
Number of participants	36
Duration of follow-up	12 months from baseline
Loss to follow-up	75 women were recruited for this study; 65 commenced and 44 completed the 8-week intensive weight loss intervention period and 36 completed the unsupported follow-up period and were included in the analysis (19 IER and 17 CER). Intervention loss to follow up = 51% Control loss to follow up = 53%

Characteristics

Study-level characteristics

Characteristic	Study (N = 36)
% Female Sample size	n = 36 ; % = 100

Characteristic	Study (N = 36)
Age (years) IER group Mean (SD)	59.5 (8.7)
Age (years) CER group Mean (SD)	60.8 (12.5)
BMI (kg m^2) IER group Mean (SD)	33.1 (3.8)
BMI (kg m^2) CER group Mean (SD)	33 (7.5)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0)

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(No information on participant blinding or blinding of outcome assessors; poor adherence and high loss to follow up (>50% in both groups).)*
Overall bias and Directness	Overall Directness	Directly applicable

Intermittent energy restriction: intermittent fasting

Mixed population

Wei 2023

Bibliographic Reference	Wei, Xueyun; Lin, Bingquan; Huang, Yan; Yang, Shunyu; Huang, Chensihan; Shi, Linna; Liu, Deying; Zhang, Peizhen; Lin, Jiayang; Xu, Bingyan; Guo, Dan; Li, Changwei; He, Hua; Liu, Shiqun; Xue, Yaoming; Xu, Yikai; Zhang, Huijie; Effects of Time-Restricted Eating on Nonalcoholic Fatty Liver Disease: The TREATY-FLD Randomized Clinical Trial.; JAMA network open; 2023; vol. 6 (no. 3); e233513

Study details

Other publications associated with this study included in review	
Trial registration number and/or trial name	NCT03786523 and NCT04988230
Study type	Randomised controlled trial (RCT)
Study location	China
Study setting	Nanfang Hospital in Guangzhou,
Study dates	April 9, 2019, and August 28, 2021.
Sources of funding	This study was supported by grants from the National Key Research and Development Project (2018YFA0800404), Joint Funds of the National Natural Science Foundation of China (U22A20288), National Natural Science Foundation of China (81970736), and Key-Area Clinical Research Program of Southern Medical University (LC2019ZD010 and 2019CR022).
Inclusion criteria	Overweight / obesity

	[BMI] between 28.0 and 45.0 Age 18-75 NAFLD
Exclusion criteria	exclusion acute or chronic viral hepatitis, drug-induced liver disease, autoimmune hepatitis, diabetes, serious liver dysfunction, chronic kidney disease, excessive alcohol consumption (>20 g/d for women or >30 g/d for men), serious cardiovascular or cerebrovascular disease within 6 months, severe gastrointestinal diseases or gastrointestinal surgery in the past 12 months, active participation in a weight loss program, use of medications that affect weight or energy balance, and current or planned pregnancy.
Intervention(s)	Participants were instructed to follow a diet of 1500 to 1800 kcal/d for men and 1200 to 1500 kcal/d for women. The diets were composed of 40% to 55% carbohydrate, 15% to 20% protein, and 20% to 30% fat. All participants were provided with 1 protein shake (Nutriease; Zhejiang Nutriease Co) per day for the first 6 months and received dietary counseling for the duration of the study. TRE group were instructed to consume the prescribed calories from 8:00 am to 4:00 pm every day, and only noncaloric beverages were permitted outside of the daily eating window.
Comparator	Participants were instructed to follow a diet of 1500 to 1800 kcal/d for men and 1200 to 1500 kcal/d for women. The diets were composed of 40% to 55% carbohydrate, 15% to 20% protein, and 20% to 30% fat. All participants were provided with 1 protein shake (Nutriease; Zhejiang Nutriease Co) per day for the first 6 months and received dietary counseling for the duration of the study.

	Participants in the DCR/habitual meal timings group had no eating time restriction during the 12-month study period.
Outcome measures	Change in weight (kg) Change in waist circumference (cm) Constipation
Number of participants	88
Duration of follow-up	12 months
Loss to follow-up	11 in intervention arm, 3 in comparator arm
Methods of analysis	'We estimated that with a sample size of 68 individuals, the trial would provide greater than 90% statistical power to detect a significant difference of 0.8% (unit value) in the reduction of IHTG content (SD, 1.0%) between the TRE group and the DCR group at a significance level of .05 using a 2-tailed test. The expected group difference and SD of reduction in IHTG content were based on preliminary data for comparison between the TRE regimen with caloric intake restriction and regular caloric intake (no time restriction).23,35 Accounting for an 80% follow-up rate, a total of 88 participants were enrolled in this trial. Data were analysed according to participants' randomization assignment (intention-to-treat). PROC MIXED of SAS statistical software, version 9.4 (SAS Institute Inc) was used to obtain point estimates and SEs of the treatment effects and to test for differences between treatments. Group differences in the study outcomes were evaluated using the general linear model for continuous variables and the χ^2 test for categorical variables. We also used a linear mixed-effects model to compare the effects of the 2 diet programs on the IHTG content and main outcomes. In the linear mixed model, an autoregressive correlation matrix was used to correct within-participant correlation for repeated measurements, participants were treated as a random effect, and intervention group, follow-up time, and their 2-factor interactions were assumed to be estimable fixed effects. Missing data were handled by multiple imputations (n = 20) at random using the Markov chain Monte Carlo method. Data are presented as least-squares means with 95% CIs for continuous variables and risk ratios for categorical outcomes. *P* < .05 was considered statistically significant.'
Additional comments	

Study arms
Time restricted eating (N = 45)

Habitual meal time (N = 43)

Characteristics

Arm-level characteristics

Characteristic	Time restricted eating (N = 45)	Habitual meal time (N = 43)
% Female Custom value	47 %	42%
Mean age (SD) Mean (SD)	32.3 (10.5)	31.7 (8.3)
BMI (kg/m²) Mean (SD)	32.2 (3.4)	32.2 (3.2)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Low *(Intention to treat analysis done, sensitivity analysis of adherence showed no significant differences between groups, outcome assessors blinded.)*

Section	Question	Answer
Overall bias and Directness	Overall Directness	Directly applicable

Teong 2023

Bibliographic Reference	Teong, Xiao Tong; Liu, Kai; Vincent, Andrew D; Bensalem, Julien; Liu, Bo; Hattersley, Kathryn J; Zhao, Lijun; Feinle-Bisset, Christine; Sargeant, Timothy J; Wittert, Gary A; Hutchison, Amy T; Heilbronn, Leonie K; Intermittent fasting plus early time-restricted eating versus calorie restriction and standard care in adults at risk of type 2 diabetes: a randomized controlled trial.; Nature medicine; 2023

Study details

Secondary publication of another included study- see primary study for details	No
Other publications associated with this study included in review	
Trial registration number and/or trial name	NCT03689608
Study type	Randomised controlled trial (RCT)

Study location	Australia
Study setting	University of Adelaide,
Study dates	26 September 2018 and 4 May 2020
Sources of funding	This work was supported by the National Health and Medical Research Council Project Grant (APP1143092). X.T.T. was supported by an Australian Government Research Training Program Scholarship from The University of Adelaide. This work was supported by a Diabetes Australia Research Program Grant (Y21G-SART) awarded to T.J.S., J.B. and L.K.H. The funder had no role in the design of this study and the interpretation of the study results. We thank all the trial participants.
Inclusion criteria	Overweight / obesity Type 2 diabetes 'adults at elevated risk of developing type 2 diabetes.'
Intervention(s)	Intermittent fasting plus early time-restricted eating (iTRE), by allowing 30% energy requirement to be consumed before 1200 hours, followed by a 20-h fasting period on three non-consecutive days per week (NB Calorie restriction was also included as an intervention arm in this study, however the details of this did not match the calorie restriction specified in the protocol for this guideline, therefore this comparison has not been included)
Comparator	Standard care (weight loss booklet)
Outcome measures	Change in weight (kg) Change in HbA1c Constipation Serious Adverse Event Adverse event

Number of participants	209
Duration of follow-up	18 months
Loss to follow-up	iTRE: 30 at 18 months Standard care: 13 at 18 months
Methods of analysis	RCT parallel design - no further details
Additional comments	

Study arms
Intermittent fasting - time restricted eating (N = 85)

Standard care (N = 41)

Characteristics
Arm-level characteristics

Characteristic	Intermittent fasting - time restricted eating (N = 85)	Standard care (N = 41)
% Female (Percentage) Nominal	49	22
Mean age (SD)	57 (10)	59 (11)

Characteristic	Intermittent fasting - time restricted eating (N = 85)	Standard care (N = 41)
Mean (SD)		
BMI (kg/m²) Mean (SD)	34.7 (4.6)	33.8 (4.9)
HbA1c (%) Mean (SD)	5.8 (0.4)	5.9 (0.4)

Critical appraisal - GDT Crit App - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Moderate *(No information on allocation concealment, intention to treat analysis not conducted and no information on whether the outcome assessors were blinded (while recognising the objective nature of outcomes provided)*
Overall bias and Directness	Overall Directness	Directly applicable

Appendix E – Forest plots

Low energy diet - TOTAL meal replacement

Mixed population

Low energy TOTAL MR + support vs Usual care (conventional diet) + support

Figure 2. % Change in weight at 1 year from baseline

Study or Subgroup	Low energy MR Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Ard 2019	-10.5	0.6	135	-5.5	0.6	138	100.0%	-5.00 [-5.14, -4.86]
Total (95% CI)			**135**			**138**	**100.0%**	**-5.00 [-5.14, -4.86]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 68.84 (P < 0.00001)								

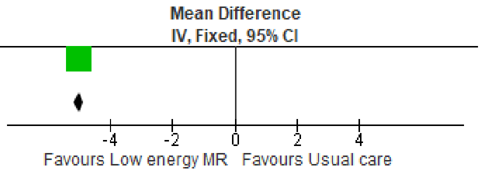


Figure 3. Change in waist circumference (WC; cm) at 1 year from baseline

Study or Subgroup	Low energy MR Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Ard 2019	-11.9	12.1	135	-7.2	9.3	138	100.0%	-4.70 [-7.26, -2.14]
Total (95% CI)			**135**			**138**	**100.0%**	**-4.70 [-7.26, -2.14]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.59 (P = 0.0003)								

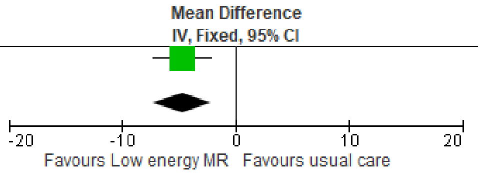


Figure 4. Serious adverse events (AEs) at 1 year from baseline

Study or Subgroup	Low energy MR Events	Total	Usual care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ard 2019	7	155	3	150	100.0%	2.26 [0.59, 8.57]
Total (95% CI)		**155**		**150**	**100.0%**	**2.26 [0.59, 8.57]**
Total events	7		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.20 (P = 0.23)						

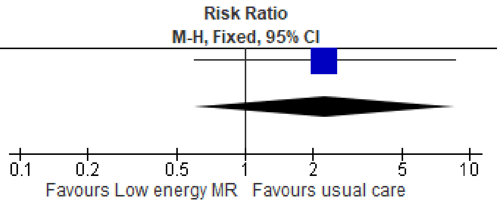
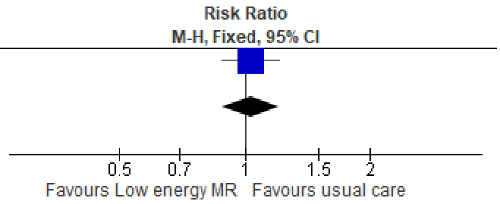


Figure 5. Adherence 1 year from baseline

Study or Subgroup	Low energy MR Events	Total	Usual care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ard 2019 (1)	95	135	94	138	100.0%	1.03 [0.88, 1.21]
Total (95% CI)		**135**		**138**	**100.0%**	**1.03 [0.88, 1.21]**
Total events	95		94			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.40 (P = 0.69)						



Footnotes

(1) Calculated using data on discontinuation rates. Main reasons for discontinuation: participants no longer wanting to participate and lost to follow up.

Low energy TOTAL MR + support vs Usual care (advice)

Figure 6. Change in weight (kg) at 1 year from baseline

Study or Subgroup	Low energy MR Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Astbury 2018 (DROPLET)	-10.7	9.6	104	-3.1	7	95	100.0%	-7.60 [-9.92, -5.28]
Total (95% CI)			**104**			**95**	**100.0%**	**-7.60 [-9.92, -5.28]**

Heterogeneity: Not applicable
Test for overall effect: Z = 6.42 (P < 0.00001)

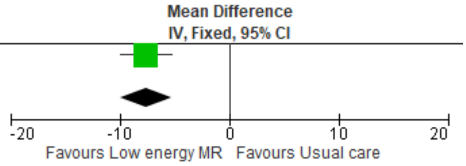


Figure 7. Change in WC (cm) at 1 year from baseline

Study or Subgroup	Low energy MR Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Astbury 2018 (DROPLET)	-10.5	9.1	99	-5.5	6.5	91	100.0%	-5.00 [-7.24, -2.76]
Total (95% CI)			**99**			**91**	**100.0%**	**-5.00 [-7.24, -2.76]**

Heterogeneity: Not applicable
Test for overall effect: Z = 4.38 (P < 0.0001)

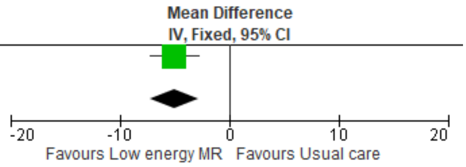


Figure 8. Change in HbA1c (mmol/mol) at 1 year from baseline

Study or Subgroup	Low energy MR Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Astbury 2018 (DROPLET)	-3.2	8.8	91	-1	7.7	75	100.0%	-2.20 [-4.71, 0.31]
Total (95% CI)			**91**			**75**	**100.0%**	**-2.20 [-4.71, 0.31]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.72 (P = 0.09)

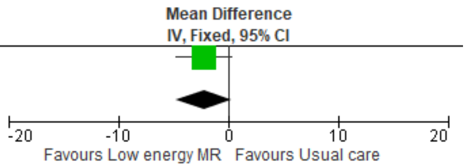


Figure 9. Change in Quality of life (QoL; EQ-5D Index) at 1 year from baseline (Higher value demonstrates improvement)

Study or Subgroup	Low energy MR Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Astbury 2018 (DROPLET)	0.09	0.17	100	0.07	0.14	93	100.0%	0.02 [-0.02, 0.06]
Total (95% CI)			**100**			**93**	**100.0%**	**0.02 [-0.02, 0.06]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.89 (P = 0.37)

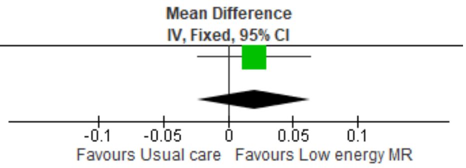


Figure 10. Change in QoL (EQ-5D VAS) at 1 year from baseline (Higher value demonstrates improvement)

Study or Subgroup	Low energy MR Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Astbury 2018 (DROPLET)	13	18.7	101	9.2	17	96	100.0%	3.80 [-1.19, 8.79]
Total (95% CI)			**101**			**96**	**100.0%**	**3.80 [-1.19, 8.79]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.49 (P = 0.14)

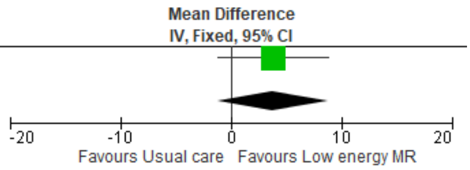


Figure 11. Change in QoL (OWL-QOL) at 1 year from baseline (Higher value demonstrates improvement)

Study or Subgroup	Low energy MR Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Astbury 2018 (DROPLET)	17	20.9	99	14	16.7	94	100.0%	3.00 [-2.32, 8.32]
Total (95% CI)			**99**			**94**	**100.0%**	**3.00 [-2.32, 8.32]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.10 (P = 0.27)

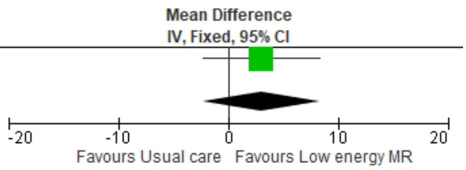


Figure 12. Serious AEs at 1 year from baseline

Study or Subgroup	Low energy MR Events	Low energy MR Total	Usual care Events	Usual care Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Astbury 2018 (DROPLET)	15	138	17	140	100.0%	0.90 [0.47, 1.72]
Total (95% CI)		**138**		**140**	**100.0%**	**0.90 [0.47, 1.72]**
Total events	15		17			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.33 (P = 0.74)

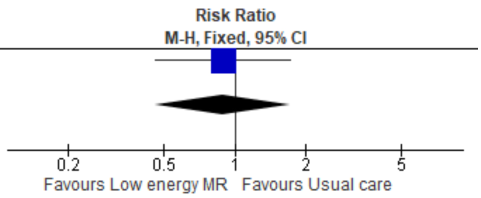


Figure 13. Adverse event: constipation at 1 year from baseline

Study or Subgroup	Low energy MR Events	Low energy MR Total	Usual care Events	Usual care Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Astbury 2018 (DROPLET)	20	138	0	140	100.0%	41.59 [2.54, 680.93]
Total (95% CI)		**138**		**140**	**100.0%**	**41.59 [2.54, 680.93]**
Total events	20		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.61 (P = 0.009)

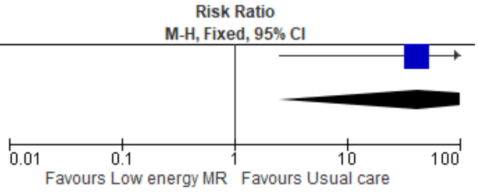


Figure 14. Change in weight (kg) at 3 years from baseline

Study or Subgroup	Low energy MR Mean	Low energy MR SD	Low energy MR Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Astbury 2018 (DROPLET)	-6.3	9.1	96	-2.7	7.7	83	100.0%	-3.60 [-6.06, -1.14]
Total (95% CI)			**96**			**83**	**100.0%**	**-3.60 [-6.06, -1.14]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.87 (P = 0.004)

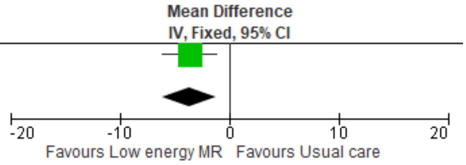


Figure 15. Change in WC (cm) at 3 years from baseline

Study or Subgroup	Low energy MR Mean	Low energy MR SD	Low energy MR Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Astbury 2018 (DROPLET)	-10.5	9.1	77	-5.5	7.3	70	100.0%	-5.00 [-7.66, -2.34]
Total (95% CI)			**77**			**70**	**100.0%**	**-5.00 [-7.66, -2.34]**

Heterogeneity: Not applicable
Test for overall effect: Z = 3.69 (P = 0.0002)

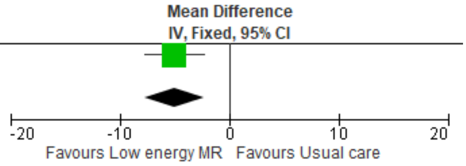


Figure 16. Change in HbA1c (mmol/mol) at 3 years from baseline

Study or Subgroup	Low energy MR Mean	Low energy MR SD	Low energy MR Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Astbury 2018 (DROPLET)	3.1	9.8	71	-0.8	6.4	61	100.0%	3.90 [1.11, 6.69]
Total (95% CI)			**71**			**61**	**100.0%**	**3.90 [1.11, 6.69]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.74 (P = 0.006)

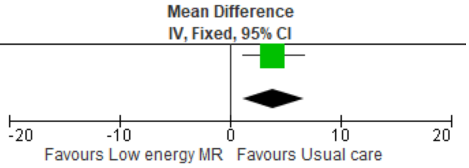


Figure 17. Change in QoL (EQ-5D Index) at 3 years from baseline (Higher value demonstrates improvement)

Study or Subgroup	Low energy MR Mean	Low energy MR SD	Low energy MR Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Astbury 2021 (DROPLET)	0	0.17	67	-0.02	0.016	70	100.0%	0.02 [-0.02, 0.06]
Total (95% CI)			**67**			**70**	**100.0%**	**0.02 [-0.02, 0.06]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.96 (P = 0.34)

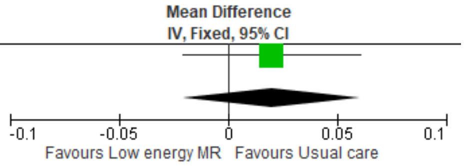


Figure 18. Change in QoL (EQ-5D VAS) at 3 years from baseline (Higher value demonstrates improvement)

Study or Subgroup	Low energy diet Mean	SD	Total	Control diet Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Astbury 2021 (DROPLET) 3	6.6	19.9	79	22.6	115.1	70	100.0%	-16.00 [-43.32, 11.32]
Total (95% CI)			**79**			**70**	**100.0%**	**-16.00 [-43.32, 11.32]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.15 (P = 0.25)

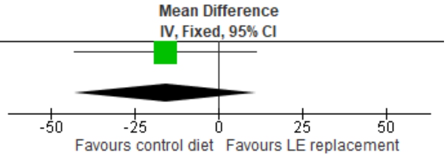
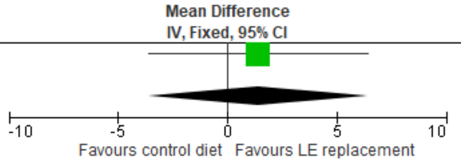


Figure 19. Change in QoL (OWL-QOL) at 3 years from baseline (Higher value demonstrates improvement)

Study or Subgroup	Low energy diet Mean	SD	Total	Control diet Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Astbury 2021 (DROPLET) 2	9.5	16.2	77	8.1	14.7	70	100.0%	1.40 [-3.60, 6.40]
Total (95% CI)			**77**			**70**	**100.0%**	**1.40 [-3.60, 6.40]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.55 (P = 0.58)



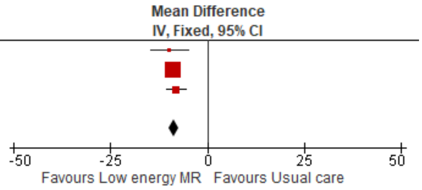
In people with type 2 diabetes

Low energy TOTAL MR + support vs Usual care (advice)

Figure 20. Change in weight (kg) at 1 year from baseline

Study or Subgroup	Mean Difference	SE	Low energy MR Total	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Astbury 2018 (DROPLET)	-9.8	2.5131	18	17	6.4%	-9.80 [-14.73, -4.87]
Lean 2018 (DiRECT) (1)	-8.8	0.7653	137	148	69.0%	-8.80 [-10.30, -7.30]
Taheri 2020	-8	1.2814	70	77	24.6%	-8.00 [-10.51, -5.49]
Total (95% CI)			**225**	**242**	**100.0%**	**-8.67 [-9.91, -7.42]**

Heterogeneity: Chi² = 0.50, df = 2 (P = 0.78); I² = 0%
Test for overall effect: Z = 13.63 (P < 0.00001)



Footnotes

(1) Cluster RCT. Effect estimate based on mixed effects linear regression model, adjusted for randomised group, baseline value, study centre, and practice list size as fixed effects, and GP practice as a random effect.

Figure 21. Change in WC (cm) at 1 year from baseline

Study or Subgroup	Low energy MR Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Astbury 2018 (DROPLET)	-11.8	10.9	17	-5.7	6	17	16.8%	-6.10 [-12.01, -0.19]
Taheri 2020	-11.44	9.9	69	-4.03	5.68	77	83.2%	-7.41 [-10.07, -4.75]
Total (95% CI)			**86**			**94**	**100.0%**	**-7.19 [-9.61, -4.77]**

Heterogeneity: Chi² = 0.16, df = 1 (P = 0.69); I² = 0%
Test for overall effect: Z = 5.81 (P < 0.00001)

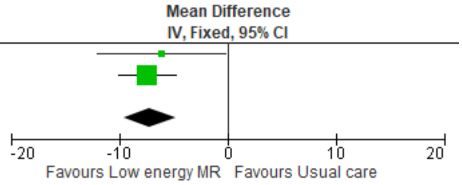
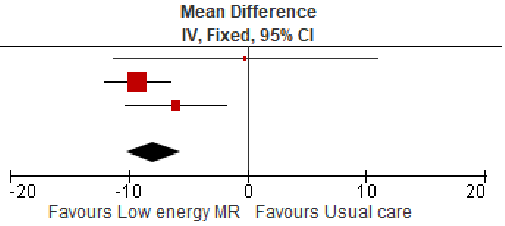


Figure 22. Change in HbA1c (mmol/mol) at 1 year from baseline

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Astbury 2018 (DROPLET)	-0.2	5.7086	4.2%	-0.20 [-11.39, 10.99]
Lean 2018 (DiRECT) (1)	-9.3	1.4286	67.2%	-9.30 [-12.10, -6.50]
Taheri 2020	-6.04	2.1887	28.6%	-6.04 [-10.33, -1.75]
Total (95% CI)			**100.0%**	**-7.98 [-10.28, -5.69]**

Heterogeneity: Chi² = 3.50, df = 2 (P = 0.17); I² = 43%
Test for overall effect: Z = 6.82 (P < 0.00001)



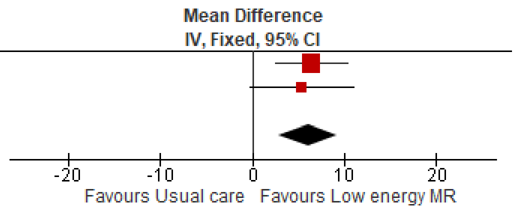
Footnotes

(1) Cluster RCT. Effect estimate based on mixed effects linear regression model, adjusted for randomised group, baseline value, study centre, and practice list size as fixed effects, and GP practice as a random effect.

Figure 23. Change in QoL (EQ-5D VAS) at 1 year from baseline (Higher value demonstrates improvement)

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Lean 2018 (DiRECT) (1)	6.4	1.9898	67.2%	6.40 [2.50, 10.30]
Taheri 2020	5.35	2.851	32.8%	5.35 [-0.24, 10.94]
Total (95% CI)			**100.0%**	**6.06 [2.86, 9.25]**

Heterogeneity: Chi² = 0.09, df = 1 (P = 0.76); I² = 0%
Test for overall effect: Z = 3.71 (P = 0.0002)



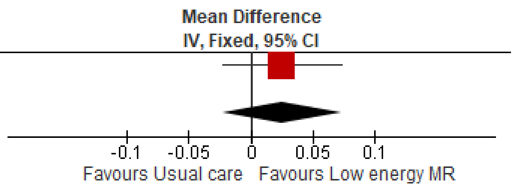
Footnotes

(1) Cluster RCT. Effect estimate based on mixed effects linear regression model, adjusted for randomised group, baseline value, study centre, and practice list size as fixed effects, and GP practice as a random effect.

Figure 24. Change in QoL (EQ-5D Health utility score) at 1 year from baseline (Higher value demonstrates improvement)

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Lean 2018 (DiRECT) (1)	0.025	0.0245	100.0%	0.03 [-0.02, 0.07]
Total (95% CI)			**100.0%**	**0.03 [-0.02, 0.07]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.02 (P = 0.31)



Footnotes

(1) Cluster RCT. Effect estimate based on mixed effects linear regression model, adjusted for randomised group, baseline value, study centre, and practice list size as fixed effects, and GP practice as a random effect.

Figure 25. Serious AEs at 1 year from baseline

Study or Subgroup	Low energy MR Events	Low energy MR Total	Usual care Events	Usual care Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lean 2018 (DiRECT)	7	157	2	149	32.4%	3.32 [0.70, 15.73]
Taheri 2020	0	70	4	77	67.6%	0.12 [0.01, 2.23]
Total (95% CI)		**227**		**226**	**100.0%**	**1.16 [0.40, 3.36]**
Total events	7		6			

Heterogeneity: Chi² = 4.07, df = 1 (P = 0.04); I² = 75%
Test for overall effect: Z = 0.27 (P = 0.79)

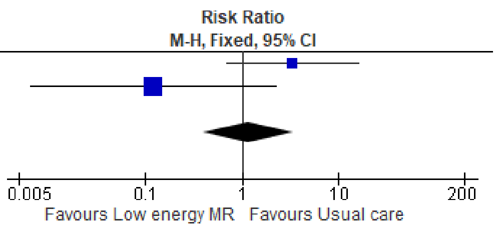
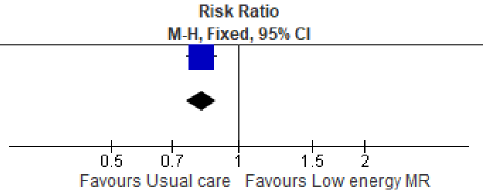


Figure 26. Adherence at 1 year from baseline

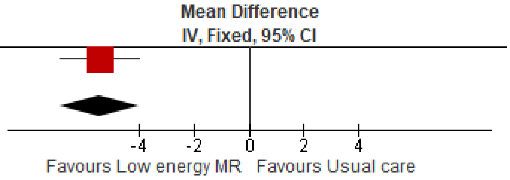
Study or Subgroup	Low energy MR Events	Low energy MR Total	Usual care Events	Usual care Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lean 2018 (DiRECT) (1)	117	143	115	115	100.0%	0.82 [0.76, 0.89]
Total (95% CI)		**143**		**115**	**100.0%**	**0.82 [0.76, 0.89]**
Total events	117		115			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.97 (P < 0.00001)						



Footnotes
(1) Caclulated using data on withdrawals from treatment.

Figure 27. Change in weight (kg) at 2 years from baseline

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Lean 2019 (DiRECT) (1)	-5.43	0.7347	100.0%	-5.43 [-6.87, -3.99]
Total (95% CI)			**100.0%**	**-5.43 [-6.87, -3.99]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 7.39 (P < 0.00001)				

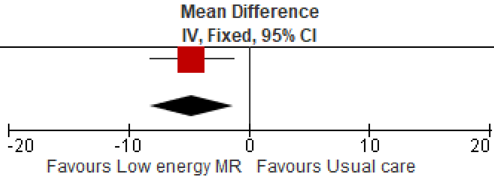


Footnotes

(1) Cluster RCT. Effect estimate based on mixed effects linear regression model, adjusted for randomised group, baseline value, study centre, and practice list size as fixed effects, and GP practice as a random effect.

Figure 28. Change in HbA1c (mmol/mol) at 2 years from baseline

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Lean 2019 (DiRECT) (1)	-4.82	1.7653	100.0%	-4.82 [-8.28, -1.36]
Total (95% CI)			**100.0%**	**-4.82 [-8.28, -1.36]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 2.73 (P = 0.006)				

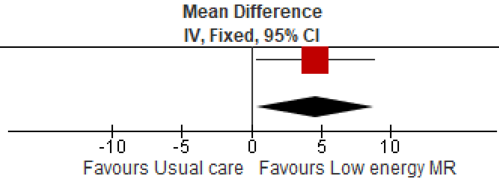


Footnotes

(1) Cluster RCT. Effect estimate based on mixed effects linear regression model, adjusted for randomised group, baseline value, study centre, and practice list size as fixed effects, and GP practice as a random effect.

Figure 29. Change in QoL (EQ-5D VAS) at 2 years from baseline (Higher value demonstrates improvement)

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Lean 2019 (DiRECT) (1)	4.64	2.1684	100.0%	4.64 [0.39, 8.89]
Total (95% CI)			**100.0%**	**4.64 [0.39, 8.89]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 2.14 (P = 0.03)				



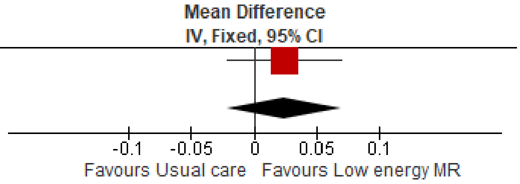
Footnotes

(1) Cluster RCT. Effect estimate based on mixed effects linear regression model, adjusted for randomised group, baseline value, study centre, and practice list size as fixed effects, and GP practice as a random effect.

Figure 30. Change in QoL (EQ-5D Health utility score) at 2 years from baseline (Higher value demonstrates improvement)

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Lean 2019 (DiRECT) (1)	0.024	0.023	100.0%	0.02 [-0.02, 0.07]
Total (95% CI)			**100.0%**	**0.02 [-0.02, 0.07]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.04 (P = 0.30)



Footnotes

(1) Cluster RCT. Effect estimate based on mixed effects linear regression model, adjusted for randomised group, baseline value, study centre, and practice list size as fixed effects, and GP practice as a random effect.

Figure 31. Serious AEs at 2 years from baseline

Study or Subgroup	Low energy MR Events	Low energy MR Total	Usual care Events	Usual care Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lean 2019 (DiRECT)	11	157	19	149	100.0%	0.55 [0.27, 1.12]
Total (95% CI)		**157**		**149**	**100.0%**	**0.55 [0.27, 1.12]**
Total events	11		19			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.66 (P = 0.10)

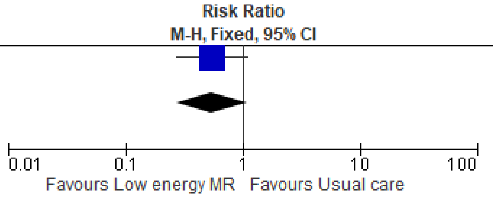


Figure 32. Change in weight (kg) at 3 years from baseline

Study or Subgroup	Low energy MR Mean	Low energy MR SD	Low energy MR Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Astbury 2018 (DROPLET)	-8.5	10.1	19	-5	5.1	17	100.0%	-3.50 [-8.65, 1.65]
Total (95% CI)			**19**			**17**	**100.0%**	**-3.50 [-8.65, 1.65]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.33 (P = 0.18)

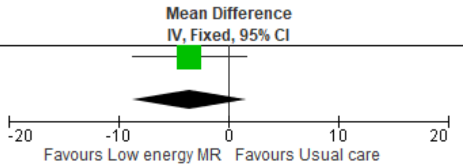


Figure 33. Change in WC (cm) at 3 years from baseline

Study or Subgroup	Low energy MR Mean	Low energy MR SD	Low energy MR Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Astbury 2018 (DROPLET)	-9	11.6	15	-5.2	7.5	14	100.0%	-3.80 [-10.86, 3.26]
Total (95% CI)			**15**			**14**	**100.0%**	**-3.80 [-10.86, 3.26]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.05 (P = 0.29)

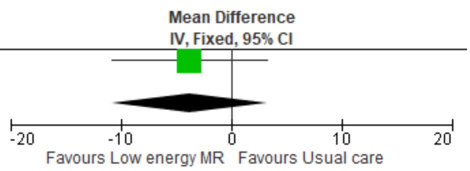
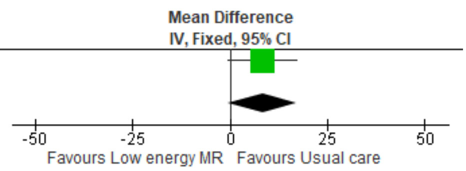


Figure 34. Change in HbA1c (mmol/mol) at 3 years from baseline

Study or Subgroup	Low energy MR Mean	Low energy MR SD	Low energy MR Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Astbury 2018 (DROPLET)	6.2	14	16	-2.1	11.5	17	100.0%	8.30 [-0.47, 17.07]
Total (95% CI)			**16**			**17**	**100.0%**	**8.30 [-0.47, 17.07]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.85 (P = 0.06)



Low energy TOTAL MR + support vs Usual care (conventional diet) + support

Figure 35. Change in weight (kg) at 1 year from baseline

	Low energy MR			Usual care				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Brown 2020	-9.8	4.9	45	-5.6	6.1	45	100.0%	-4.20 [-6.49, -1.91]
Total (95% CI)			**45**			**45**	**100.0%**	**-4.20 [-6.49, -1.91]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.60 (P = 0.0003)								

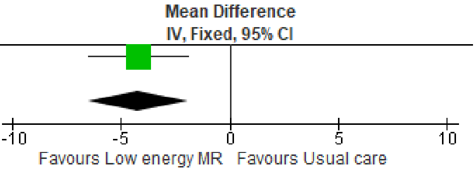


Figure 36. Change in WC (cm) at 1 year from baseline

	Low energy MR			Usual care				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Brown 2020	-12.8	11.27	45	-2.4	14.01	45	100.0%	-10.40 [-15.65, -5.15]
Total (95% CI)			**45**			**45**	**100.0%**	**-10.40 [-15.65, -5.15]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.88 (P = 0.0001)								

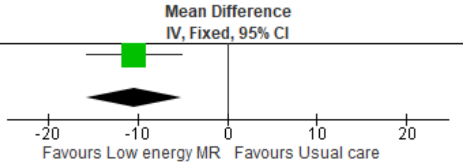


Figure 37. % Change in HbA1c at 1 year from baseline

	Low energy diet			Control diet				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Brown 2020	-0.43	1.01	45	-0.09	1.64	45	100.0%	-0.34 [-0.90, 0.22]
Total (95% CI)			**45**			**45**	**100.0%**	**-0.34 [-0.90, 0.22]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.18 (P = 0.24)								

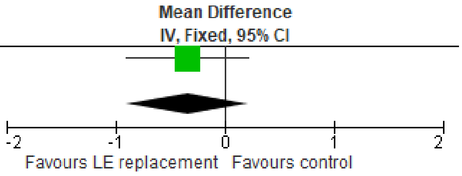


Figure 38. Change in QoL (EQ-5D) at 1 year from baseline (Higher value demonstrates improvement)

	Low energy MR			Usual care				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Brown 2020	11.1	21.8	45	0.71	19.4	45	100.0%	10.39 [1.86, 18.92]
Total (95% CI)			**45**			**45**	**100.0%**	**10.39 [1.86, 18.92]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.39 (P = 0.02)								

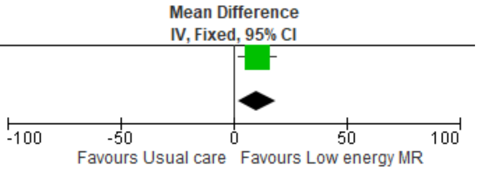
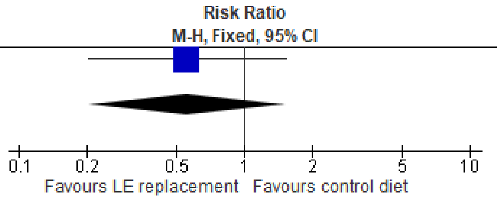


Figure 39. Serious AEs at 1 year from baseline

	Low energy diet		Control diet			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
Brown 2020	5	45	9	45	100.0%	0.56 [0.20, 1.53]
Total (95% CI)		**45**		**45**	**100.0%**	**0.56 [0.20, 1.53]**
Total events	5		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.14 (P = 0.26)						



Low energy TOTAL MR + support vs Intermittent energy restriction (5:2 diet) + support

Figure 40. Change in weight (kg) at 1 year from baseline

Study or Subgroup	Low energy MR Mean	SD	Total	IER Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
McDiarmid 2022	-6.2	5.8613	40	-5.1	6.2536	39	100.0%	-1.10 [-3.77, 1.57]
Total (95% CI)			**40**			**39**	**100.0%**	**-1.10 [-3.77, 1.57]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.81 (P = 0.42)

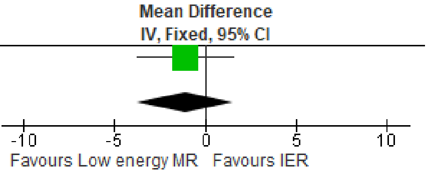


Figure 41. Change in HbA1c (mmol/mol) at 1 year from baseline

Study or Subgroup	Low energy MR Mean	SD	Total	IER Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
McDiarmid 2022	-8.5	10.9438	40	-7.9	11.1055	39	100.0%	-0.60 [-5.46, 4.26]
Total (95% CI)			**40**			**39**	**100.0%**	**-0.60 [-5.46, 4.26]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.24 (P = 0.81)

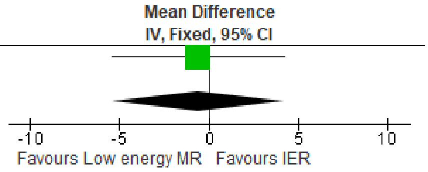


Figure 42. Serious AEs at 1 year from baseline

Study or Subgroup	Low energy MR Events	Total	IER Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
McDiarmid 2022	4	40	4	39	100.0%	0.97 [0.26, 3.63]
Total (95% CI)		**40**		**39**	**100.0%**	**0.97 [0.26, 3.63]**
Total events	4		4			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.04 (P = 0.97)

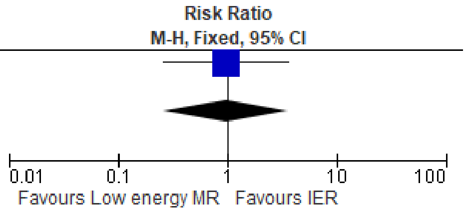
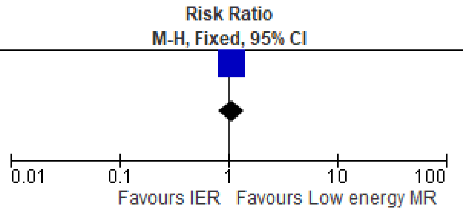


Figure 43. Adherence at 1 year from baseline

Study or Subgroup	Low energy MR Events	Total	IER Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
McDiarmid 2022 (1)	30	40	27	39	100.0%	1.08 [0.82, 1.43]
Total (95% CI)		**40**		**39**	**100.0%**	**1.08 [0.82, 1.43]**
Total events	30		27			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.57 (P = 0.57)



Footnotes
(1) Study reported retention of trial participants.

Low energy diet - PARTIAL meal replacement

Mixed population

Low energy PARTIAL MR + support vs Usual care (conventional diet) + support

Figure 44. Change in weight (kg) at 1 year from baseline

Study or Subgroup	Low energy MR Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Ashley 2007	-5	4.9	35	-6.1	6.7	35	100.0%	1.10 [-1.65, 3.85]
Total (95% CI)			**35**			**35**	**100.0%**	**1.10 [-1.65, 3.85]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.78 (P = 0.43)

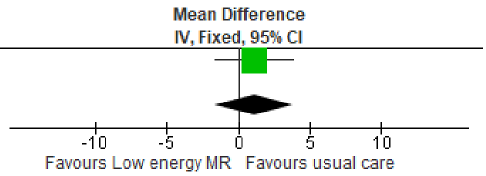
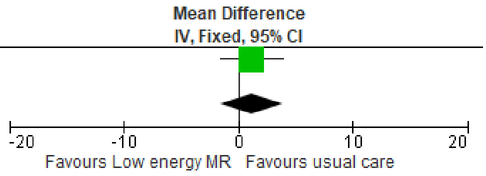


Figure 45. Change in WC (cm) at 1 year from baseline

	Low energy MR			Usual care				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Ashley 2007	-4.9	4.6	35	-6.1	7	35	100.0%	1.20 [-1.57, 3.97]
Total (95% CI)			**35**			**35**	**100.0%**	**1.20 [-1.57, 3.97]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.85 (P = 0.40)

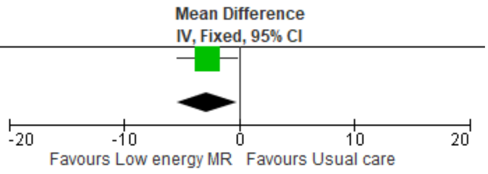


Low energy PARTIAL MR + support vs Usual care (advice + conventional diet)

Figure 46. Change in weight (kg) at 1 year from baseline

	Low energy MR			Usual care				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Shikany 2013 (1)	-4.7	7	57	-1.9	7	56	100.0%	-2.80 [-5.38, -0.22]
Total (95% CI)			**57**			**56**	**100.0%**	**-2.80 [-5.38, -0.22]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.13 (P = 0.03)

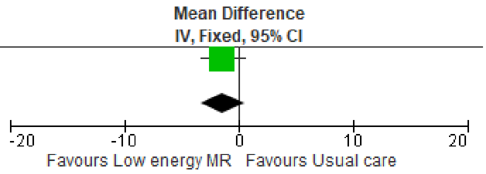


Footnotes
(1) Data reported adjusted for ethnicity.

Figure 47. Change in WC (cm) at 1 year from baseline

	Low energy MR			Usual care				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Shikany 2013 (1)	-5	5.1	57	-3.6	5.2	56	100.0%	-1.40 [-3.30, 0.50]
Total (95% CI)			**57**			**56**	**100.0%**	**-1.40 [-3.30, 0.50]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.44 (P = 0.15)



Footnotes
(1) Data reported adjusted for ethnicity.

In people with type 2 diabetes

Low energy PARTIAL MR vs Usual care (conventional diet)

Figure 48. Change in weight (kg) at 1 year from baseline

	Low energy MR			Usual care				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Khoo 2011	-9.6	4.15	19	-9	5.15	12	100.0%	-0.60 [-4.06, 2.86]
Total (95% CI)			**19**			**12**	**100.0%**	**-0.60 [-4.06, 2.86]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.34 (P = 0.73)

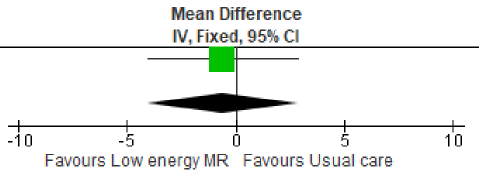
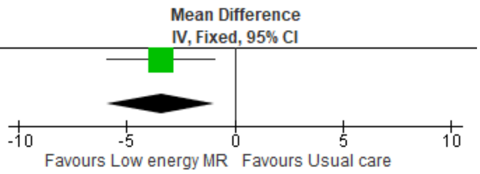


Figure 49. Change in WC (cm) at 1 year from baseline

	Low energy MR			Usual care				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Khoo 2011	-12.5	2.98	19	-9.1	3.68	12	100.0%	-3.40 [-5.88, -0.92]
Total (95% CI)			**19**			**12**	**100.0%**	**-3.40 [-5.88, -0.92]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.69 (P = 0.007)



Very low energy diet - TOTAL meal replacement

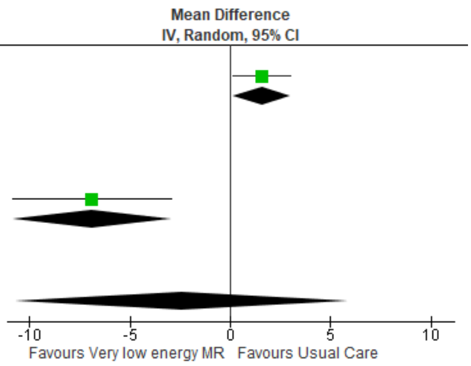
Mixed population

Very low energy total meal replacement + support vs Usual care (conventional diet) + support

Figure 50. Change in weight (kg) at 1 year from baseline

Study or Subgroup	Very low energy MR Mean	SD	Total	Usual Care Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
4.2.1 Mixed population (Males and females)								
Purcell 2014 (1)	-10.72	5.86	97	-12.3	4.3	103	52.5%	1.58 [0.15, 3.01]
Subtotal (95% CI)			**97**			**103**	**52.5%**	**1.58 [0.15, 3.01]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.16 (P = 0.03)								
4.2.2 Only females								
Seimon 2019 TEMPO	-15.3	9.4288	46	-8.4	9.2546	39	47.5%	-6.90 [-10.88, -2.92]
Subtotal (95% CI)			**46**			**39**	**47.5%**	**-6.90 [-10.88, -2.92]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.40 (P = 0.0007)								
Total (95% CI)			**143**			**142**	**100.0%**	**-2.45 [-10.75, 5.85]**

Heterogeneity: Tau² = 33.62; Chi² = 15.42, df = 1 (P < 0.0001); I² = 94%
Test for overall effect: Z = 0.58 (P = 0.56)
Test for subgroup differences: Chi² = 15.42, df = 1 (P < 0.0001), I² = 93.5%



Footnotes
(1) Data taken from systematic review (Paretti 2016)

Figure 51. Change in WC (cm) at 1 year from baseline

Study or Subgroup	Very low energy MR Mean	SD	Total	Usual Care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Seimon 2020 TEMPO	-14.3	10.1023	46	-6.9	9.7356	38	100.0%	-7.40 [-11.65, -3.15]
Total (95% CI)			**46**			**38**	**100.0%**	**-7.40 [-11.65, -3.15]**

Heterogeneity: Not applicable
Test for overall effect: Z = 3.41 (P = 0.0007)

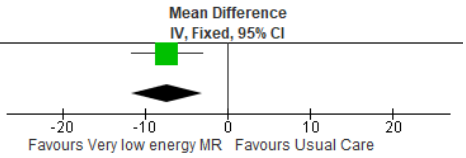
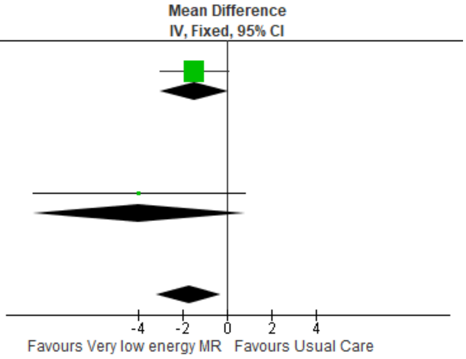


Figure 52. Change in weight (kg) at 2 years from baseline

Study or Subgroup	Very low energy MR Mean	SD	Total	Usual Care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
4.6.1 Mixed population (Males and females)								
Purcell 2014 (1)	-3.3	6.2	97	-1.8	4.7	103	90.7%	-1.50 [-3.03, 0.03]
Subtotal (95% CI)			**97**			**103**	**90.7%**	**-1.50 [-3.03, 0.03]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.92 (P = 0.05)								
4.6.2 Only females								
Seimon 2020 TEMPO	-10	10.9841	45	-6	10.0872	31	9.3%	-4.00 [-8.79, 0.79]
Subtotal (95% CI)			**45**			**31**	**9.3%**	**-4.00 [-8.79, 0.79]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.64 (P = 0.10)								
Total (95% CI)			**142**			**134**	**100.0%**	**-1.73 [-3.19, -0.27]**

Heterogeneity: Chi² = 0.95, df = 1 (P = 0.33); I² = 0%
Test for overall effect: Z = 2.33 (P = 0.02)
Test for subgroup differences: Chi² = 0.95, df = 1 (P = 0.33), I² = 0%



Footnotes
(1) Data taken from systematic review (Paretti 2016) who used baseline-observation-carried-forward (BOCF) method to handle missing data.

Figure 53. Change in WC (cm) at 2 years from baseline

Study or Subgroup	Very low energy MR Mean	SD	Total	Usual Care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Seimon 2020 TEMPO	-9.4	10.9841	45	-5.1	10.0872	31	100.0%	-4.30 [-9.09, 0.49]
Total (95% CI)			**45**			**31**	**100.0%**	**-4.30 [-9.09, 0.49]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.76 (P = 0.08)

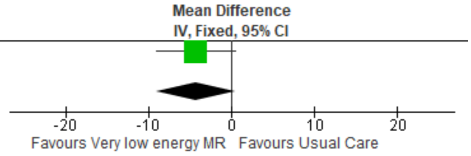


Figure 54. Change in weight (kg) at 3 years from baseline

Study or Subgroup	Very low energy MR Mean	SD	Total	Usual Care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
4.9.1 Mixed population (Males and females)								
Purcell 2014 (1)	-4.1	7.8091	61	-4.3	6.4987	43	78.4%	0.20 [-2.56, 2.96]
Subtotal (95% CI)			**61**			**43**	**78.4%**	**0.20 [-2.56, 2.96]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.14 (P = 0.89)								
4.9.2 Only females								
Seimon 2020 TEMPO	-8	11.7223	41	-4.9	10.905	31	21.6%	-3.10 [-8.35, 2.15]
Subtotal (95% CI)			**41**			**31**	**21.6%**	**-3.10 [-8.35, 2.15]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.16 (P = 0.25)								
Total (95% CI)			**102**			**74**	**100.0%**	**-0.51 [-2.96, 1.93]**

Heterogeneity: Chi² = 1.19, df = 1 (P = 0.28); I² = 16%
Test for overall effect: Z = 0.41 (P = 0.68)
Test for subgroup differences: Chi² = 1.19, df = 1 (P = 0.28), I² = 15.8%
Footnotes
(1) Study reports data for all study completers.

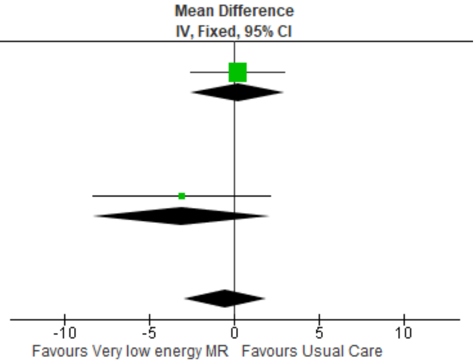
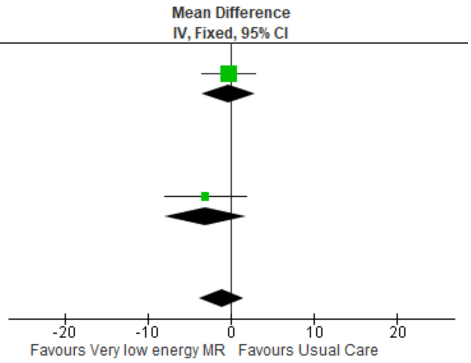


Figure 55. Change in WC (cm) at 3 years from baseline

Study or Subgroup	Very low energy MR Mean	SD	Total	Usual Care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
4.11.1 Mixed population (Males and females)								
Purcell 2014 (1)	-4.4	7.8091	61	-4.1	8.4483	43	70.3%	-0.30 [-3.50, 2.90]
Subtotal (95% CI)			**61**			**43**	**70.3%**	**-0.30 [-3.50, 2.90]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.18 (P = 0.85)								
4.11.2 Only females								
Seimon 2020 TEMPO	-7.4	10.7718	41	-4.3	10.3598	31	29.7%	-3.10 [-8.02, 1.82]
Subtotal (95% CI)			**41**			**31**	**29.7%**	**-3.10 [-8.02, 1.82]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.24 (P = 0.22)								
Total (95% CI)			**102**			**74**	**100.0%**	**-1.13 [-3.81, 1.55]**

Heterogeneity: Chi² = 0.88, df = 1 (P = 0.35); I² = 0%
Test for overall effect: Z = 0.83 (P = 0.41)
Test for subgroup differences: Chi² = 0.88, df = 1 (P = 0.35), I² = 0%
Footnotes
(1) Study reports data for all study completers.



Very low energy total meal replacement + support vs Usual care (advice)

Figure 56. Change in weight (kg) at 1 year from baseline

Study or Subgroup	Very low energy MR Mean	SD	Total	Usual Care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tuomilehto 2009	-10.7	6.5	35	-2.4	5.6	37	100.0%	-8.30 [-11.11, -5.49]
Total (95% CI)			**35**			**37**	**100.0%**	**-8.30 [-11.11, -5.49]**

Heterogeneity: Not applicable
Test for overall effect: Z = 5.79 (P < 0.00001)

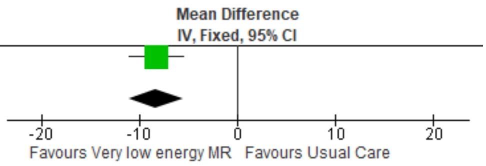


Figure 57. Change in WC (cm) at 1 year from baseline

Study or Subgroup	Very low energy MR Mean	SD	Total	Usual Care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tuomilehto 2009	-11.6	6.6	35	-3	6	37	100.0%	-8.60 [-11.52, -5.68]
Total (95% CI)			**35**			**37**	**100.0%**	**-8.60 [-11.52, -5.68]**

Heterogeneity: Not applicable
Test for overall effect: Z = 5.78 (P < 0.00001)

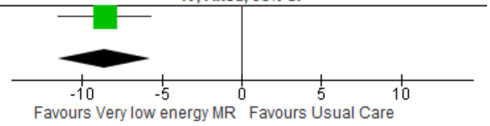


Figure 58. Change in weight (kg) at 2 years from baseline

Study or Subgroup	Very low energy MR Mean	SD	Total	Usual Care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tuomilehto 2010	-7.3	6.5	35	-2.9	7.5	36	100.0%	-4.40 [-7.66, -1.14]
Total (95% CI)			**35**			**36**	**100.0%**	**-4.40 [-7.66, -1.14]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.64 (P = 0.008)

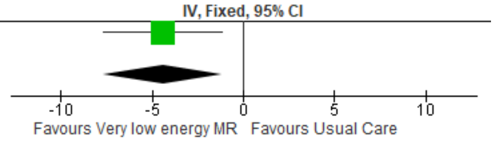
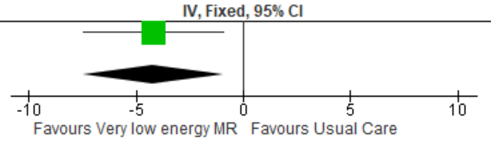


Figure 59. Change in WC (cm) at 2 years from baseline

Study or Subgroup	Very low energy MR Mean	SD	Total	Usual Care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Tuomilehto 2010	-7.7	6.7	35	-3.5	7.3	36	100.0%	-4.20 [-7.46, -0.94]
Total (95% CI)			**35**			**36**	**100.0%**	**-4.20 [-7.46, -0.94]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.53 (P = 0.01)



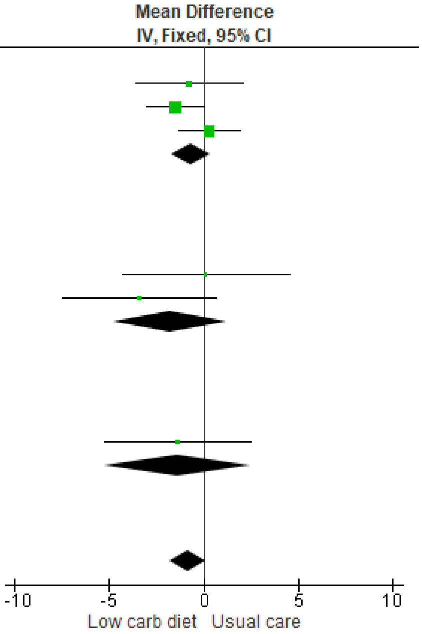
Low carbohydrate diet

Mixed population

Low carbohydrate diet + support vs Usual care (diet) + support

Figure 60. Change in weight (kg) at 1 year from baseline

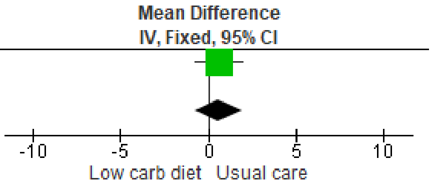
Study or Subgroup	Low carb diet Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.1.1 Mixed population (males and females)								
Ebbeling 2007 (1)	-2.46	6.36	36	-1.7	6.14	37	11.1%	-0.76 [-3.63, 2.11]
Frisch 2009	-5.8	6.1	100	-4.3	5.1	100	37.7%	-1.50 [-3.06, 0.06]
Klemsdal 2010 (2)	-4	5.5	100	-4.3	6.2	102	35.0%	0.30 [-1.32, 1.92]
Subtotal (95% CI)			**236**			**239**	**83.8%**	**-0.65 [-1.69, 0.40]**
Heterogeneity: Chi² = 2.48, df = 2 (P = 0.29); I² = 19%								
Test for overall effect: Z = 1.22 (P = 0.22)								
1.1.2 Only females								
Foraker 2014 (3)	80.7	4.23	7	80.6	5.99	14	4.7%	0.10 [-4.33, 4.53]
Griffin 2013	-6.9	11.33	36	-3.5	5.28	35	5.5%	-3.40 [-7.49, 0.69]
Subtotal (95% CI)			**43**			**49**	**10.1%**	**-1.79 [-4.80, 1.22]**
Heterogeneity: Chi² = 1.29, df = 1 (P = 0.26); I² = 23%								
Test for overall effect: Z = 1.17 (P = 0.24)								
1.1.3 Only males								
Wycherley 2012 (4)	-12.3	10.57	57	-10.9	10.93	61	6.1%	-1.40 [-5.28, 2.48]
Subtotal (95% CI)			**57**			**61**	**6.1%**	**-1.40 [-5.28, 2.48]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.71 (P = 0.48)								
Total (95% CI)			**336**			**349**	**100.0%**	**-0.81 [-1.77, 0.15]**
Heterogeneity: Chi² = 4.36, df = 5 (P = 0.50); I² = 0%								
Test for overall effect: Z = 1.66 (P = 0.10)								
Test for subgroup differences: Chi² = 0.59, df = 2 (P = 0.75), I² = 0%								



Footnotes
(1) Data taken from SR (Naude 2022). Change at 74 weeks.
(2) Data taken from SR (Naude 2022).
(3) Data taken from SR (Naude 2022).
(4) Data taken from SR (Naude 2022).

Figure 61. Change in weight (kg) at 2 years from baseline

Study or Subgroup	Low carb diet Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Sacks 2009 (1)	-2.9	7.3	201	-3.5	6.7	204	100.0%	0.60 [-0.77, 1.97]
Total (95% CI)			**201**			**204**	**100.0%**	**0.60 [-0.77, 1.97]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.86 (P = 0.39)								

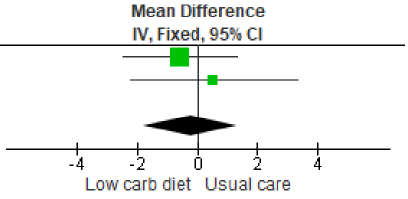


Footnotes
(1) Data taken from SR (Naude 2022).

Figure 62. Change in BMI at 1 year from baseline

Study or Subgroup	Low carb diet Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Calleja Fernández 2012 (1)	29.26	2.63	13	29.84	2.18	12	68.7%	-0.58 [-2.47, 1.31]
Calleja Fernández 2012 (2)	30.52	2.9	8	29.98	2.63	7	31.3%	0.54 [-2.26, 3.34]
Total (95% CI)			**21**			**19**	**100.0%**	**-0.23 [-1.80, 1.34]**

Heterogeneity: Chi² = 0.42, df = 1 (P = 0.52); I² = 0%
Test for overall effect: Z = 0.29 (P = 0.77)

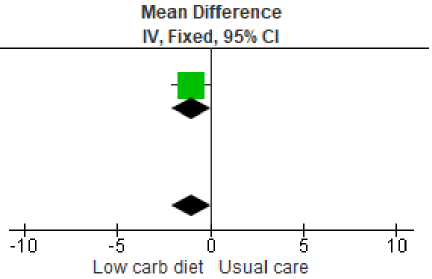


Footnotes
(1) In people with insulin resistance. End values at 12 months
(2) In people without insulin resistance. End values at 12 months

Figure 63. Change in BMI at 2 years from baseline

Study or Subgroup	Low carb diet Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.4.1 Only females								
Mellberg 2014 (1)	-2.4	2.13	27	-1.4	1.59	22	100.0%	-1.00 [-2.04, 0.04]
Subtotal (95% CI)			**27**			**22**	**100.0%**	**-1.00 [-2.04, 0.04]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.88 (P = 0.06)								
Total (95% CI)			**27**			**22**	**100.0%**	**-1.00 [-2.04, 0.04]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.88 (P = 0.06)
Test for subgroup differences: Not applicable



Footnotes
(1) Data taken from SR (Naude 2022).

Figure 64. Change in WC (cm) at 1 year from baseline

Study or Subgroup	Low carb diet Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.5.1 Mixed population (males and females)								
Frisch 2009	-6.9	6.1	100	-4.7	8.9	100	29.3%	-2.20 [-4.31, -0.09]
Klemsdal 2010	-3.9	11	100	-5.8	11.14	102	21.5%	1.90 [-1.15, 4.95]
Subtotal (95% CI)			**200**			**202**	**50.8%**	**-0.30 [-4.31, 3.70]**
Heterogeneity: Tau² = 6.61; Chi² = 4.68, df = 1 (P = 0.03); I² = 79%								
Test for overall effect: Z = 0.15 (P = 0.88)								
1.5.2 Only males								
Wycherley 2012	-12.6	6.4	57	-11.3	7	61	26.5%	-1.30 [-3.72, 1.12]
Subtotal (95% CI)			**57**			**61**	**26.5%**	**-1.30 [-3.72, 1.12]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.05 (P = 0.29)								
1.5.3 Only females								
Griffin 2013	-5.7	7.9799	36	-2.2	3.7844	35	22.7%	-3.50 [-6.39, -0.61]
Subtotal (95% CI)			**36**			**35**	**22.7%**	**-3.50 [-6.39, -0.61]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.37 (P = 0.02)								
Total (95% CI)			**293**			**298**	**100.0%**	**-1.37 [-3.36, 0.61]**

Heterogeneity: Tau² = 2.33; Chi² = 7.05, df = 3 (P = 0.07); I² = 57%
Test for overall effect: Z = 1.36 (P = 0.17)
Test for subgroup differences: Chi² = 2.02, df = 2 (P = 0.36), I² = 1.0%

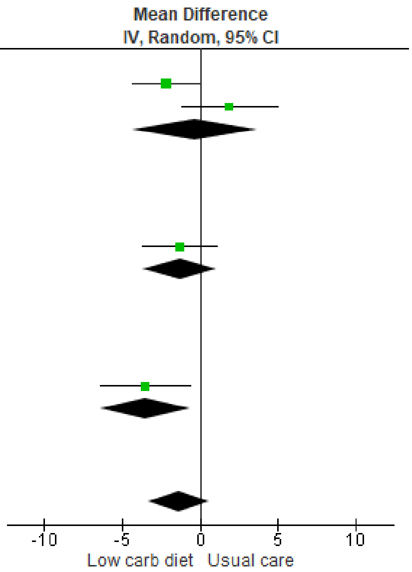
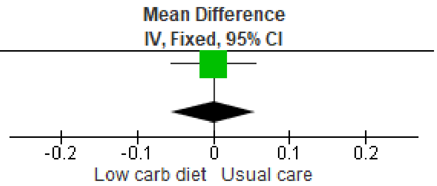


Figure 65. % Change in HbA1c at 1 year from baseline

Study or Subgroup	Low carb diet Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Frisch 2009	-0.2	0.2	100	-0.2	0.2	100	100.0%	0.00 [-0.06, 0.06]
Total (95% CI)			**100**			**100**	**100.0%**	**0.00 [-0.06, 0.06]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)



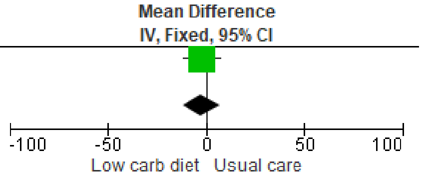
In people with type 2 diabetes

Low carbohydrate diet vs Usual care (diet)

Figure 66. Weight (kg) at 1 year from baseline

Study or Subgroup	Low carb diet Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Pedersen 2014 (1)	96.5	19.49	31	98.8	18.38	33	100.0%	-2.30 [-11.59, 6.99]
Total (95% CI)			**31**			**33**	**100.0%**	**-2.30 [-11.59, 6.99]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.48 (P = 0.63)

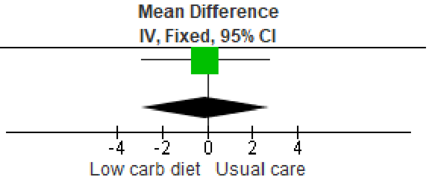


Footnotes
(1) Data taken from SR (Naude 2022). End values at 12 months

Figure 67. % Change in HbA1c at 1 year from baseline

Study or Subgroup	Low carb diet Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Pedersen 2014 (1)	-0.4	5.18	21	-0.3	4.31	24	100.0%	-0.10 [-2.91, 2.71]
Total (95% CI)			**21**			**24**	**100.0%**	**-0.10 [-2.91, 2.71]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.07 (P = 0.94)



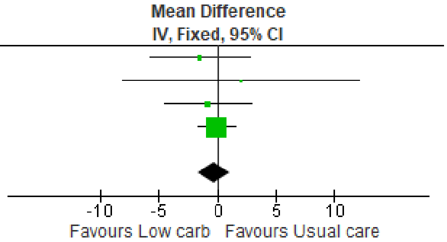
Footnotes
(1) Data taken from SR (Naude 2022).

Low carbohydrate diet + support vs Usual care (diet) + support

Figure 68. Change in weight (kg) at 1 year from baseline

Study or Subgroup	Low carb Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Elhayany 2010	-8.9	13.74	61	-7.4	10.27	63	10.3%	-1.50 [-5.78, 2.78]
Guldbrand 2012	-1.9	19	30	-3.9	21	31	1.9%	2.00 [-8.04, 12.04]
Krebs 2012	-3.2	18.82	207	-2.4	19.62	212	13.9%	-0.80 [-4.48, 2.88]
Larsen 2011 (1)	-2.23	3.78	53	-2.17	4.27	46	73.9%	-0.06 [-1.66, 1.54]
Total (95% CI)			**351**			**352**	**100.0%**	**-0.27 [-1.65, 1.10]**

Heterogeneity: Chi² = 0.66, df = 3 (P = 0.88); I² = 0%
Test for overall effect: Z = 0.39 (P = 0.70)



Footnotes
(1) Data taken from SR (Naude 2022).

Figure 69. Change in weight (kg) at 2 years from baseline

Study or Subgroup	Low carb Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Guldbrand 2012	-2	20.66	30	-2.9	21	31	10.5%	0.90 [-9.55, 11.35]
Krebs 2012	-3.9	18.58	207	-6	18.78	212	89.5%	2.10 [-1.48, 5.68]
Total (95% CI)			**237**			**243**	**100.0%**	**1.97 [-1.41, 5.36]**

Heterogeneity: Chi² = 0.05, df = 1 (P = 0.83); I² = 0%
Test for overall effect: Z = 1.14 (P = 0.25)

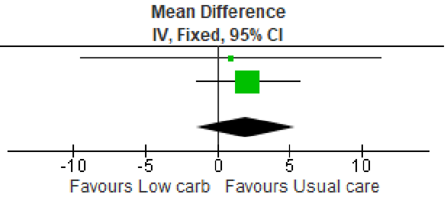


Figure 70. Change in WC (cm) at 1 year from baseline

	Low carb			Usual care				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Elhayany 2010	-10.4	9.96	61	-9.3	8.49	63	17.3%	-1.10 [-4.36, 2.16]
Guldbrand 2012	-2	15	30	-4	13.53	31	3.6%	2.00 [-5.18, 9.18]
Krebs 2012	-3	13.27	207	-3.1	13.7	212	27.6%	0.10 [-2.48, 2.68]
Larsen 2011	-3.54	4.7853	53	-3.35	4.7853	46	51.5%	-0.19 [-2.08, 1.70]
Total (95% CI)			**351**			**352**	**100.0%**	**-0.19 [-1.55, 1.17]**

Heterogeneity: Chi² = 0.71, df = 3 (P = 0.87); I² = 0%
Test for overall effect: Z = 0.27 (P = 0.78)

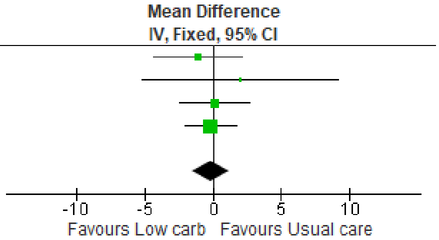


Figure 71. Change in WC (cm) at 2 years from baseline

	Low carb			Usual care				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Guldbrand 2012	-2	15.52	30	-2	14.73	31	10.2%	0.00 [-7.60, 7.60]
Krebs 2012	-4.3	13.9	207	-6.4	12.86	212	89.8%	2.10 [-0.47, 4.67]
Total (95% CI)			**237**			**243**	**100.0%**	**1.89 [-0.55, 4.32]**

Heterogeneity: Chi² = 0.26, df = 1 (P = 0.61); I² = 0%
Test for overall effect: Z = 1.52 (P = 0.13)

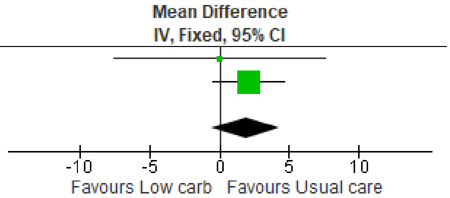


Figure 72. % Change in HbA1c at 1 year from baseline

	Low carb			Usual care				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Elhayany 2010	-2	1.25	61	-1.8	0.92	63	22.0%	-0.20 [-0.59, 0.19]
Guldbrand 2012	-2	15	30	-4	13.53	31	0.1%	2.00 [-5.18, 9.18]
Krebs 2012	-0.1	1.25	207	-0.2	1.25	212	57.7%	0.10 [-0.14, 0.34]
Larsen 2011	-0.23	1.06	53	-0.28	0.99	46	20.2%	0.05 [-0.35, 0.45]
Total (95% CI)			**351**			**352**	**100.0%**	**0.03 [-0.16, 0.21]**

Heterogeneity: Chi² = 1.98, df = 3 (P = 0.58); I² = 0%
Test for overall effect: Z = 0.27 (P = 0.79)

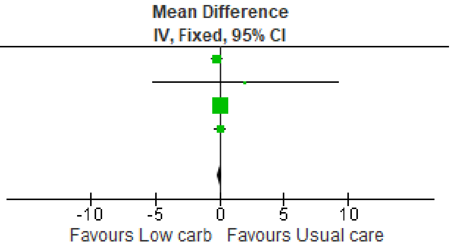


Figure 73. % Change in HbA1c at 2 years from baseline

	Low carb			Usual care				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Guldbrand 2012	-2	15.52	30	-2	14.73	31	0.1%	0.00 [-7.60, 7.60]
Krebs 2012	0.1	1.37	207	0.1	1.31	212	99.9%	0.00 [-0.26, 0.26]
Total (95% CI)			**237**			**243**	**100.0%**	**0.00 [-0.26, 0.26]**

Heterogeneity: Chi² = 0.00, df = 1 (P = 1.00); I² = 0%
Test for overall effect: Z = 0.00 (P = 1.00)

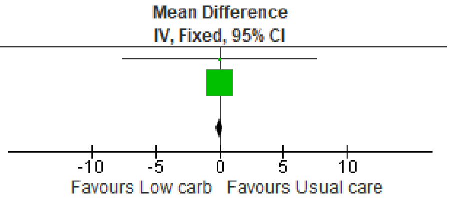


Figure 74. Change in QoL (SF-36 Physical component score (PCS) at 1 year from baseline (Higher value shows improvement)

	Low carb			Usual care				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Guldbrand 2014	2.6	10.26	30	0.6	9.8	31	11.3%	2.00 [-3.04, 7.04]
Krebs 2012	1.7	9.5	207	0.8	9.25	212	88.7%	0.90 [-0.90, 2.70]
Total (95% CI)			**237**			**243**	**100.0%**	**1.02 [-0.67, 2.72]**

Heterogeneity: Chi² = 0.16, df = 1 (P = 0.69); I² = 0%
Test for overall effect: Z = 1.19 (P = 0.24)

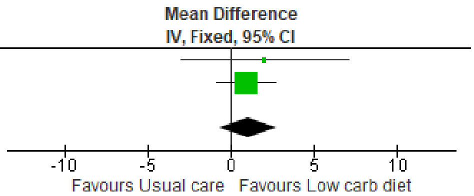


Figure 75. Change in QoL (SF-36 Physical component score (PCS) at 2 years from baseline (Higher value shows improvement)

Study or Subgroup	Low carb Mean	Low carb SD	Low carb Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Guldbrand 2014	-2.7	12.49	30	-1.7	10.5	31	8.9%	-1.00 [-6.80, 4.80]
Krebs 2012	-0.9	9.75	207	1.1	9.2	212	91.1%	-2.00 [-3.82, -0.18]
Total (95% CI)			**237**			**243**	**100.0%**	**-1.91 [-3.64, -0.18]**

Heterogeneity: Chi² = 0.10, df = 1 (P = 0.75); I² = 0%
Test for overall effect: Z = 2.16 (P = 0.03)

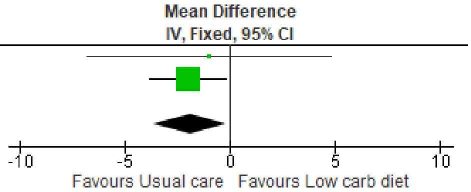


Figure 76. Change in QoL (SF-36 Mental component score (MCS) at 1 year from baseline (Higher value shows improvement)

Study or Subgroup	Low carb Mean	Low carb SD	Low carb Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Guldbrand 2014	0.9	6.46	30	1.1	9.65	31	16.2%	-0.20 [-4.31, 3.91]
Krebs 2012	1.4	9.62	207	-0.1	9.25	212	83.8%	1.50 [-0.31, 3.31]
Total (95% CI)			**237**			**243**	**100.0%**	**1.22 [-0.43, 2.88]**

Heterogeneity: Chi² = 0.55, df = 1 (P = 0.46); I² = 0%
Test for overall effect: Z = 1.45 (P = 0.15)

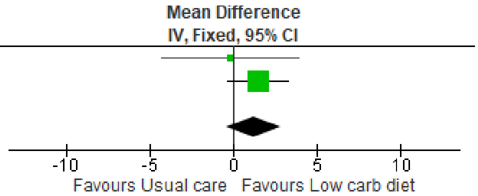
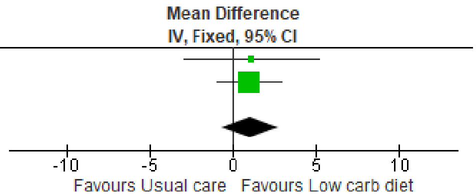


Figure 77. Change in QoL (SF-36 Mental component score (MCS) at 2 years from baseline (Higher value shows improvement)

Study or Subgroup	Low carb Mean	Low carb SD	Low carb Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Guldbrand 2014	1.4	6.27	30	0.3	9.61	31	18.0%	1.10 [-2.96, 5.16]
Krebs 2012	0.7	9.62	207	-0.3	10.26	212	82.0%	1.00 [-0.90, 2.90]
Total (95% CI)			**237**			**243**	**100.0%**	**1.02 [-0.71, 2.74]**

Heterogeneity: Chi² = 0.00, df = 1 (P = 0.97); I² = 0%
Test for overall effect: Z = 1.16 (P = 0.25)



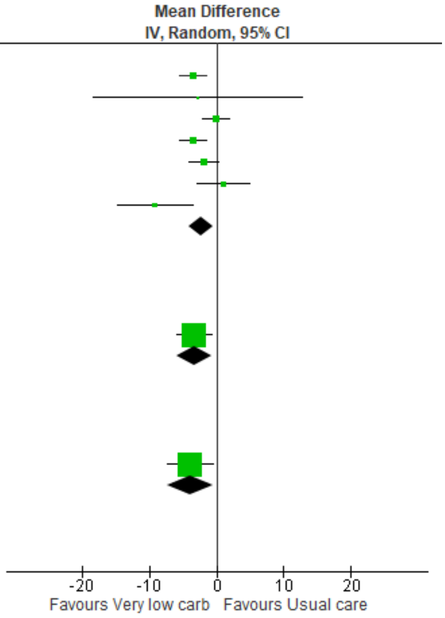
Very low carbohydrate diet

Mixed population

Very low carbohydrate diet + support bs Usual care (diet)+ support

Figure 78. Change in weight (kg) at 1 year from baseline

Study or Subgroup	Very low carb diet Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
4.1.1 Mixed population (Mixed family backgrounds)								
Bazzano 2014	-5.3	6.52	75	-1.8	6.43	73	19.9%	-3.50 [-5.59, -1.41]
Brinkworth 2016a	-14.5	14.8	32	-11.7	13.03	3	1.3%	-2.80 [-18.41, 12.81]
Foster 2010	-10.87	7.7007	153	-10.81	9.9876	154	20.4%	-0.06 [-2.05, 1.93]
Hu 2015	-5.3	6.5195	75	-1.8	6.429	73	19.9%	-3.50 [-5.59, -1.41]
Layman 2009 (1)	-9.3	7.21	52	-7.4	4.28	51	18.9%	-1.90 [-4.18, 0.38]
Lim 2010 (2)	-2.9	4.9	17	-3.9	6.3	15	12.0%	1.00 [-2.95, 4.95]
Moreno 2014	-13.7	13.8	27	-4.5	5.6	26	7.6%	-9.20 [-14.83, -3.57]
Subtotal (95% CI)			**431**			**395**	**100.0%**	**-2.38 [-4.22, -0.55]**
Heterogeneity: Tau² = 3.26; Chi² = 15.93, df = 6 (P = 0.01); I² = 62%								
Test for overall effect: Z = 2.55 (P = 0.01)								
4.1.2 Black family background								
Bazzano 2014	-4.4	5.9409	40	-1.1	5.911	36	100.0%	-3.30 [-5.97, -0.63]
Subtotal (95% CI)			**40**			**36**	**100.0%**	**-3.30 [-5.97, -0.63]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.42 (P = 0.02)								
4.1.3 White family background								
Bazzano 2014	-6.5	7.165	34	-2.6	7.0505	33	100.0%	-3.90 [-7.30, -0.50]
Subtotal (95% CI)			**34**			**33**	**100.0%**	**-3.90 [-7.30, -0.50]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.25 (P = 0.02)								

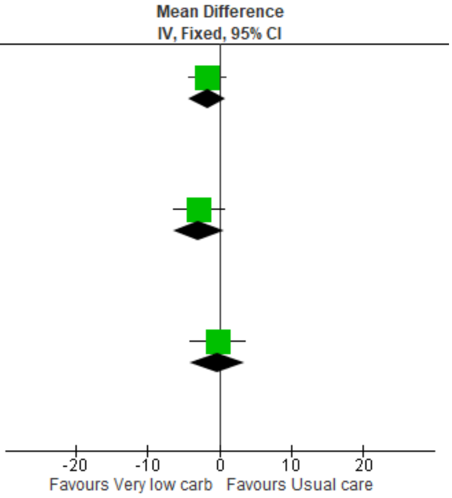


Test for subgroup differences: Chi² = 0.72, df = 2 (P = 0.70), I² = 0%

Footnotes
(1) Data taken from SR (Naude 2022).
(2) Change at 15 months

Figure 79. Change in WC (cm) at 1 year from baseline

Study or Subgroup	Very low carb diet Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
4.2.1 Mixed population (Mixed family backgrounds)								
Bazzano 2014	-6.7	7.8234	75	-5	7.7148	73	100.0%	-1.70 [-4.20, 0.80]
Subtotal (95% CI)			**75**			**73**	**100.0%**	**-1.70 [-4.20, 0.80]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.33 (P = 0.18)								
4.2.2 Black family background								
Bazzano 2014	-6.6	7.817	40	-3.7	7.6843	36	100.0%	-2.90 [-6.39, 0.59]
Subtotal (95% CI)			**40**			**36**	**100.0%**	**-2.90 [-6.39, 0.59]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.63 (P = 0.10)								
4.2.3 White family background								
Bazzano 2014	-7	8.0248	34	-6.8	7.8966	33	100.0%	-0.20 [-4.01, 3.61]
Subtotal (95% CI)			**34**			**33**	**100.0%**	**-0.20 [-4.01, 3.61]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.10 (P = 0.92)								



Test for subgroup differences: Chi² = 1.05, df = 2 (P = 0.59), I² = 0%

Figure 80. % Change in HbA1c at 1 year from baseline

Study or Subgroup	Very low carb diet Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Moreno 2014	-0.01	0.66	27	0.37	0.34	26	100.0%	-0.38 [-0.66, -0.10]
Total (95% CI)			**27**			**26**	**100.0%**	**-0.38 [-0.66, -0.10]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.65 (P = 0.008)

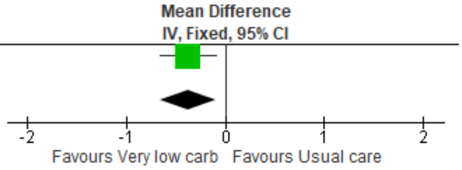


Figure 81. Adverse event: Hair loss at 1 year

Study or Subgroup	Very low carb diet Events	Total	Usual care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Foster 2010	29	153	19	154	97.5%	1.54 [0.90, 2.62]
Moreno 2014	2	26	0	27	2.5%	5.19 [0.26, 103.11]
Total (95% CI)		**179**		**181**	**100.0%**	**1.63 [0.97, 2.75]**
Total events	31		19			

Heterogeneity: Chi² = 0.62, df = 1 (P = 0.43); I² = 0%
Test for overall effect: Z = 1.83 (P = 0.07)

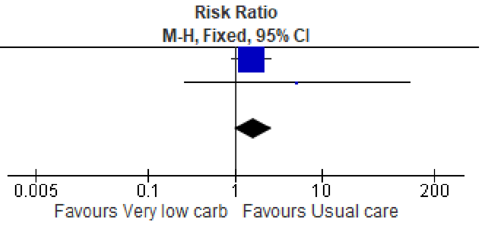


Figure 82. Adverse event: Constipation at 1 year

Study or Subgroup	Very low carb diet Events	Total	Usual care Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Moreno 2014	5	27	3	26	18.1%	1.60 [0.43, 6.05]
Foster 2010	53	153	33	154	46.7%	1.62 [1.11, 2.35]
Bazzano 2014	11	75	17	73	35.2%	0.63 [0.32, 1.25]
Total (95% CI)		**255**		**253**	**100.0%**	**1.16 [0.58, 2.31]**
Total events	69		53			

Heterogeneity: Tau² = 0.23; Chi² = 5.70, df = 2 (P = 0.06); I² = 65%
Test for overall effect: Z = 0.42 (P = 0.68)

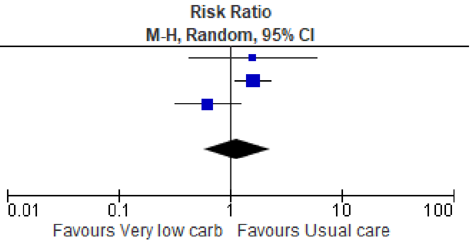


Figure 83. Change in weight (kg) at 2 years from baseline

Study or Subgroup	Very low carb diet Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Foster 2010	-6.34	10.7685	153	-7.37	10.867	154	100.0%	1.03 [-1.39, 3.45]
Total (95% CI)			**153**			**154**	**100.0%**	**1.03 [-1.39, 3.45]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.83 (P = 0.40)

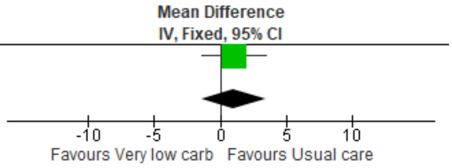


Figure 84. Adverse event: Hair loss at 2 years

Study or Subgroup	Very low carb diet Events	Total	Usual care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Foster 2010	23	153	15	154	100.0%	1.54 [0.84, 2.84]
Total (95% CI)		**153**		**154**	**100.0%**	**1.54 [0.84, 2.84]**
Total events	23		15			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.39 (P = 0.16)

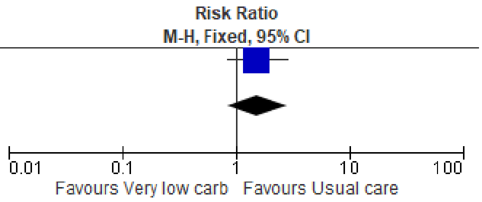
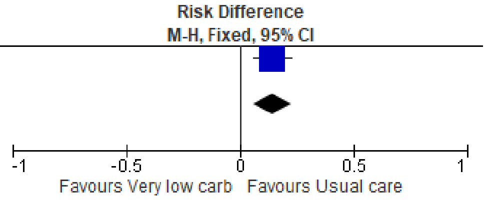


Figure 85. Adverse event: Constipation at 2 years

Study or Subgroup	Very low carb diet Events	Very low carb diet Total	Usual care Events	Usual care Total	Weight	Risk Difference M-H, Fixed, 95% CI
Foster 2010	39	153	17	154	100.0%	0.14 [0.06, 0.23]
Total (95% CI)		**153**		**154**	**100.0%**	**0.14 [0.06, 0.23]**
Total events	39		17			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.33 (P = 0.0009)

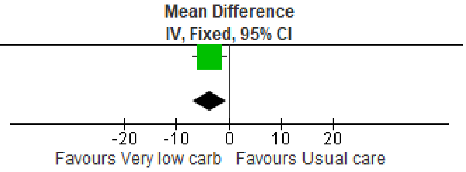


Very low carbohydrate diet + support vs No intervention

Figure 86. Change in weight (kg) at 15 months from baseline

Study or Subgroup	Very low carb diet Mean	Very low carb diet SD	Very low carb diet Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Lim 2010	-2.9	4.9	17	0.8	5	19	100.0%	-3.70 [-6.94, -0.46]
Total (95% CI)			**17**			**19**	**100.0%**	**-3.70 [-6.94, -0.46]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.24 (P = 0.03)



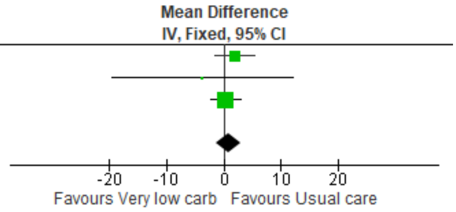
In people with type 2 diabetes

Very low carbohydrate diet + support bs Usual care (diet)+ support

Figure 87. Change in weight (kg) at 1 year from baseline

Study or Subgroup	Very low carb Mean	Very low carb SD	Very low carb Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Goldstein 2011	-3.4	4	14	-5.4	5.7	16	35.1%	2.00 [-1.49, 5.49]
Saslow 2017 (1)	92	22.82	15	95.8	20.71	14	1.7%	-3.80 [-19.64, 12.04]
Tay 2015	-9.8	6.0195	41	-10.1	5.6986	37	63.2%	0.30 [-2.30, 2.90]
Total (95% CI)			**70**			**67**	**100.0%**	**0.83 [-1.24, 2.89]**

Heterogeneity: Chi² = 0.92, df = 2 (P = 0.63); I² = 0%
Test for overall effect: Z = 0.78 (P = 0.43)



Footnotes
(1) End value at 12 months.

Figure 88. % Change in HbA1c at 1 year from baseline

Study or Subgroup	Very low carb Mean	Very low carb SD	Very low carb Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Goldstein 2011	1.5	1	14	1.1	1	16	14.4%	0.40 [-0.32, 1.12]
Iqbal 2010	-0.1	1.0583	28	-0.3	1.2649	40	24.2%	0.20 [-0.35, 0.75]
Saslow 2017	33.3	6.49	15	36	6.32	14	0.3%	-2.70 [-7.36, 1.96]
Tay 2015	-1	0.6336	41	-1	0.8998	37	61.0%	0.00 [-0.35, 0.35]
Total (95% CI)			**98**			**107**	**100.0%**	**0.10 [-0.18, 0.37]**

Heterogeneity: Chi² = 2.50, df = 3 (P = 0.48); I² = 0%
Test for overall effect: Z = 0.70 (P = 0.49)

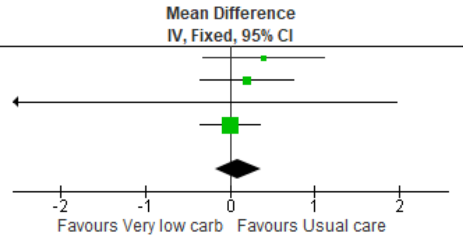


Figure 89. Change in WC (cm) at 1 year from baseline

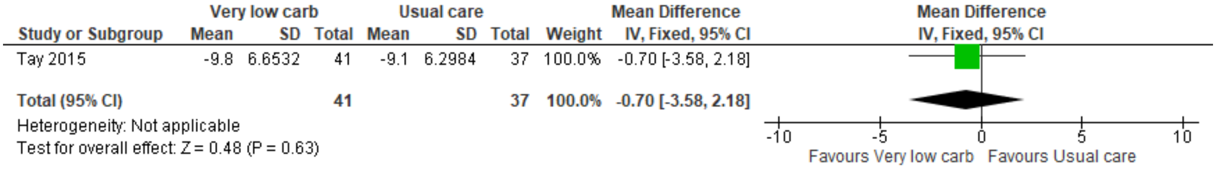


Figure 90. Adherence at 1 year

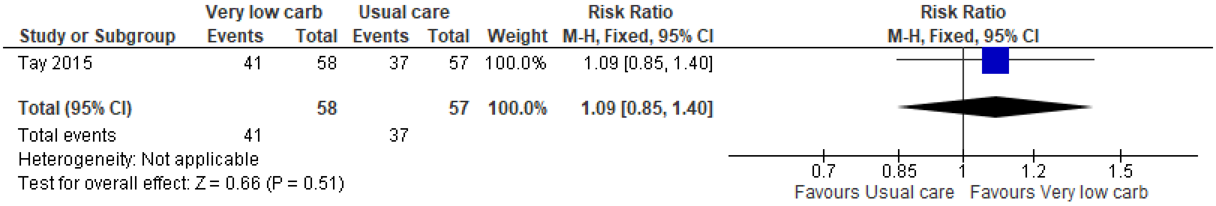


Figure 91. Serious AEs at 1 year

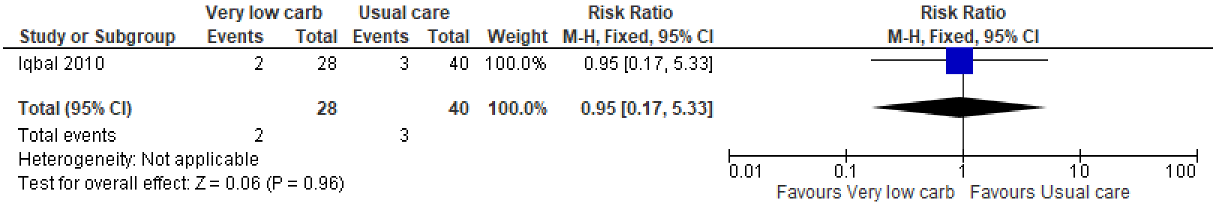


Figure 92. Change in weight (kg) at 2 years from baseline

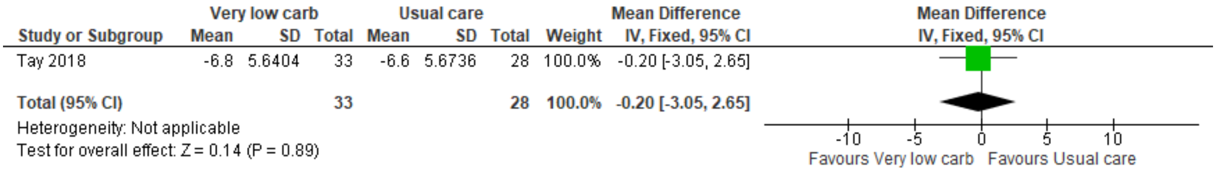


Figure 93. % Change in HbA1c at 2 years from baseline

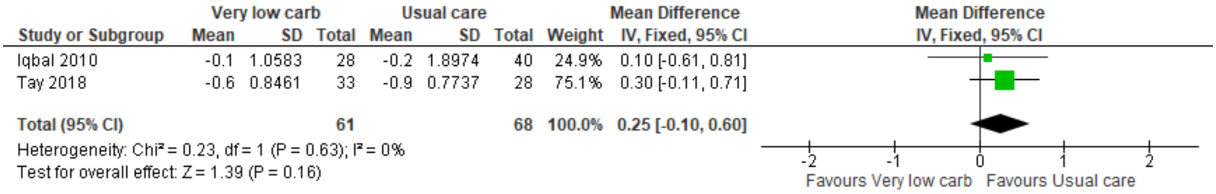


Figure 94. Adherence at 2 years

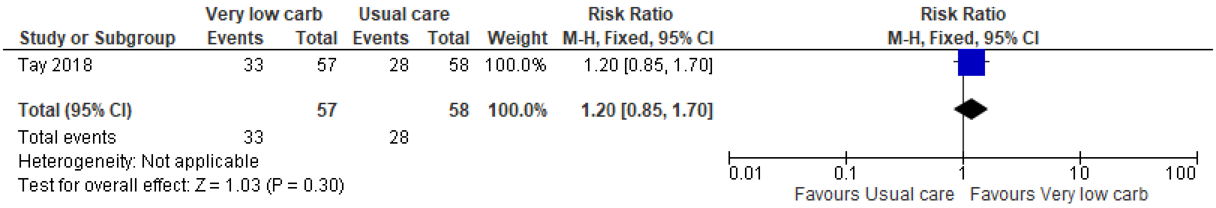


Figure 95. QoL (PAID questionnaire) Higher scores indicate higher distress at 1 year

Study or Subgroup	Very low carb Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Brinkworth 2016b	15.4	1.8	41	12.3	1.9	37	100.0%	3.10 [2.28, 3.92]
Total (95% CI)			**41**			**37**	**100.0%**	**3.10 [2.28, 3.92]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 7.38 (P < 0.00001)								

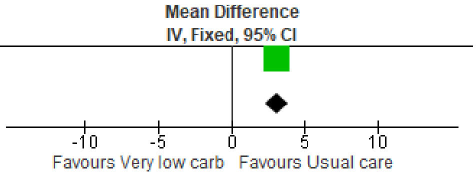


Figure 96. QoL (Diabetes-39 (Diabetes control)) Higher scores indicate greater impact on QoL at 1 year

Study or Subgroup	Very low carb Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Brinkworth 2016b	18.5	2.8	41	15.8	2.8	37	100.0%	2.70 [1.46, 3.94]
Total (95% CI)			**41**			**37**	**100.0%**	**2.70 [1.46, 3.94]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.25 (P < 0.0001)								

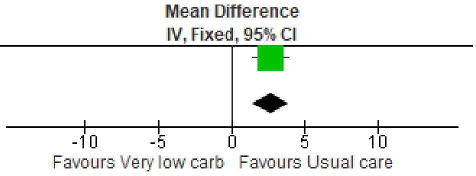


Figure 97. QoL (Diabetes-39 (Anxiety and worry)) Higher scores indicate greater impact on QoL at 1 year

Study or Subgroup	Very low carb Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Brinkworth 2016b	31.5	3.8	41	22.1	3.9	37	100.0%	9.40 [7.69, 11.11]
Total (95% CI)			**41**			**37**	**100.0%**	**9.40 [7.69, 11.11]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 10.76 (P < 0.00001)								

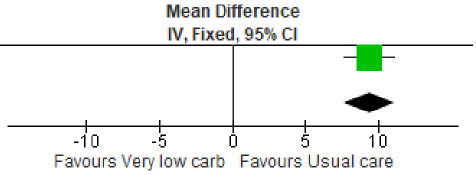


Figure 98. QoL (Diabetes-39 (Social burden)) Higher scores indicate greater impact on QoL at 1 year

Study or Subgroup	Very low carb Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Brinkworth 2016b	10.8	2.3	41	8.1	2.3	37	100.0%	2.70 [1.68, 3.72]
Total (95% CI)			**41**			**37**	**100.0%**	**2.70 [1.68, 3.72]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.18 (P < 0.00001)								

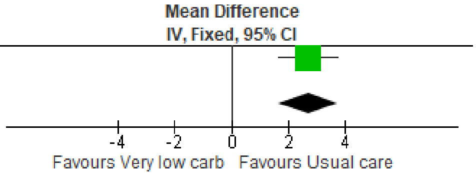


Figure 99. QoL (Diabetes-39 (Energy and Mobility)) Higher scores indicate greater impact on QoL at 1year

Study or Subgroup	Very low carb Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Brinkworth 2016b	19.3	2.3	41	12.5	2.3	37	100.0%	6.80 [5.78, 7.82]
Total (95% CI)			**41**			**37**	**100.0%**	**6.80 [5.78, 7.82]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 13.04 (P < 0.00001)								

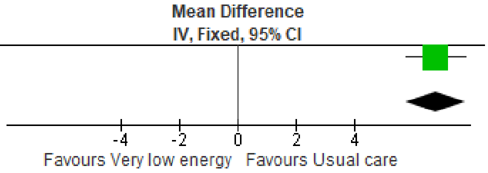


Figure 100. QoL (PAID questionnaire) Higher scores indicate higher distress at 2 years

Study or Subgroup	Very low carb Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Kakoschke 2021	13.87	2.03	33	14.19	2.15	28	100.0%	-0.32 [-1.38, 0.74]
Total (95% CI)			**33**			**28**	**100.0%**	**-0.32 [-1.38, 0.74]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.59 (P = 0.55)								

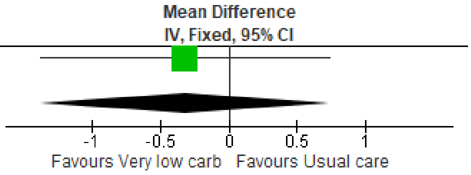


Figure 101. QoL (Diabetes-39 (Diabetes control)) Higher scores indicate greater impact on QoL at 2 years

Study or Subgroup	Very low carb Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Kakoschke 2021	17.3	2.64	33	12.94	2.8	28	100.0%	4.36 [2.99, 5.73]
Total (95% CI)			**33**			**28**	**100.0%**	**4.36 [2.99, 5.73]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 6.22 (P < 0.00001)								

Mean Difference IV, Fixed, 95% CI

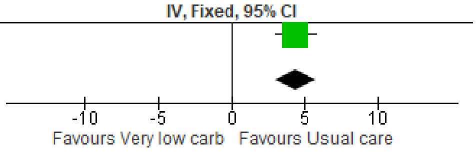


Figure 102. QoL (Diabetes-39 (Anxiety and worry)) Higher scores indicate greater impact on QoL at 2 years

Study or Subgroup	Very low carb Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Kakoschke 2021	32.8	3.54	33	23.1	3.73	28	100.0%	9.70 [7.86, 11.54]
Total (95% CI)			**33**			**28**	**100.0%**	**9.70 [7.86, 11.54]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 10.36 (P < 0.00001)								

Mean Difference IV, Fixed, 95% CI

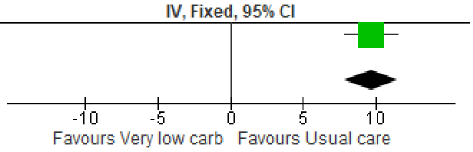


Figure 103. QoL (Diabetes-39 (Social burden)) Higher scores indicate greater impact on QoL at 2 years

Study or Subgroup	Very low carb Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Kakoschke 2021	8.38	2.17	33	6.39	2.3	28	100.0%	1.99 [0.86, 3.12]
Total (95% CI)			**33**			**28**	**100.0%**	**1.99 [0.86, 3.12]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.46 (P = 0.0005)								

Mean Difference IV, Fixed, 95% CI

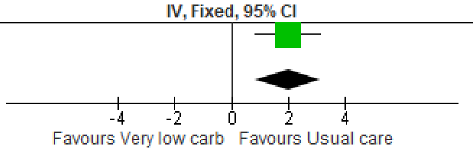
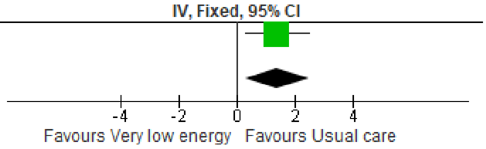


Figure 104. QoL (Diabetes-39 (Energy and Mobility)) Higher scores indicate greater impact on QoL at 2 years

Study or Subgroup	Very low carb Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Brinkworth 2016b	19.66	2.42	41	18.28	2.56	37	100.0%	1.38 [0.27, 2.49]
Total (95% CI)			**41**			**37**	**100.0%**	**1.38 [0.27, 2.49]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.44 (P = 0.01)								

Mean Difference IV, Fixed, 95% CI



Intermittent energy restriction (IER) – 5:2 Diet

Mixed population

IER (5:2 Diet) vs usual care

Figure 105. Change in weight (kg) at 1 year from baseline

Study or Subgroup	Intermittent ER Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Hajek 2021	-1.9	4.9	100	-1.8	5.7	100	100.0%	-0.10 [-1.57, 1.37]
Total (95% CI)			**100**			**100**	**100.0%**	**-0.10 [-1.57, 1.37]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.13 (P = 0.89)								

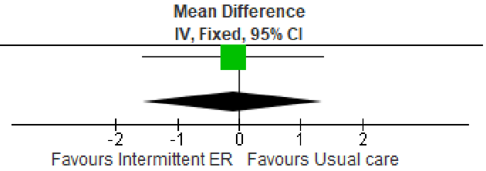
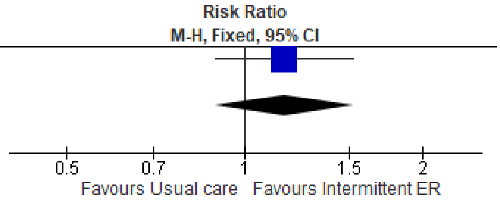


Figure 106. Adherence at 1 year

Study or Subgroup	Intermittent ER Events	Total	Usual care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hajek 2021 (1)	56	100	48	100	100.0%	1.17 [0.89, 1.53]
Total (95% CI)		**100**		**100**	**100.0%**	**1.17 [0.89, 1.53]**
Total events	56		48			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.13 (P = 0.26)						



Footnotes
(1) Study reported retention rates.

IER (5:2 diet) + support vs Usual care (advice)

Figure 107. Change in weight (kg) at 1 year from baseline

Study or Subgroup	Intermittent ER Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Hajek 2021	-2.6	4.6	100	-1.8	5.7	100	100.0%	-0.80 [-2.24, 0.64]
Total (95% CI)			**100**			**100**	**100.0%**	**-0.80 [-2.24, 0.64]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.09 (P = 0.27)								

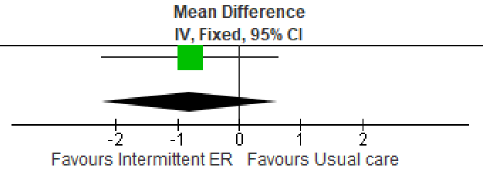
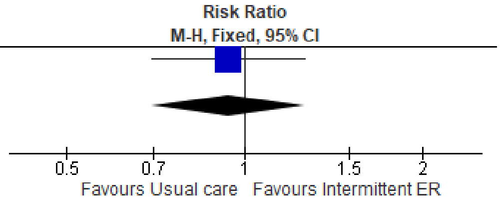


Figure 108. Adherence at 1 year

Study or Subgroup	Intermittent ER Events	Total	Usual care Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hajek 2021 (1)	45	100	48	100	100.0%	0.94 [0.70, 1.26]
Total (95% CI)		**100**		**100**	**100.0%**	**0.94 [0.70, 1.26]**
Total events	45		48			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.43 (P = 0.67)						



Footnotes
(1) Study reported retention rates.

IER (5:2 diet)+ support vs Usual care (advice)+ support

Figure 109. Change in weight (kg) at 1 year from baseline

Study or Subgroup	IER Mean	IER SD	IER Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Schubel 2018 (HELENA Trial)	-4.4	16.49	49	-1.5	13.72	52	100.0%	-2.90 [-8.83, 3.03]
Total (95% CI)			**49**			**52**	**100.0%**	**-2.90 [-8.83, 3.03]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.96 (P = 0.34)

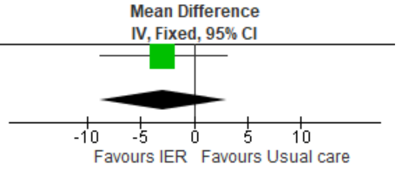
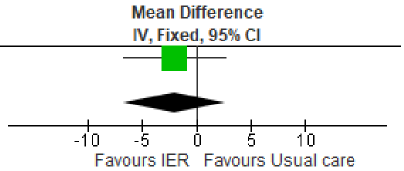


Figure 110. Change in WC (cm) at 1 year from baseline

Study or Subgroup	IER Mean	IER SD	IER Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Schubel 2018 (HELENA Trial)	-2.3	13	49	-0.3	11.07	52	100.0%	-2.00 [-6.72, 2.72]
Total (95% CI)			**49**			**52**	**100.0%**	**-2.00 [-6.72, 2.72]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.83 (P = 0.41)



Intermittent energy restriction (5:2 diet)+ support vs Usual care (diet)+ support

Figure 111. Change in weight (kg) at 1 year from baseline

Study or Subgroup	IER Mean	IER SD	IER Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Schubel 2018 (HELENA Trial)	-4.4	16.49	49	-4.6	14.96	49	14.0%	0.20 [-6.03, 6.43]
Sundfor 2018	-8	6.5	54	-9	7.1	58	86.0%	1.00 [-1.52, 3.52]
Total (95% CI)			**103**			**107**	**100.0%**	**0.89 [-1.45, 3.22]**

Heterogeneity: $Chi^2 = 0.05$, df = 1 (P = 0.82); $I^2 = 0\%$
Test for overall effect: Z = 0.75 (P = 0.46)

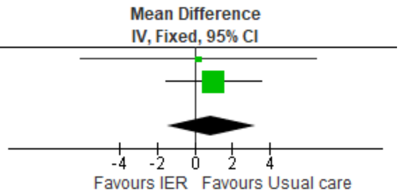
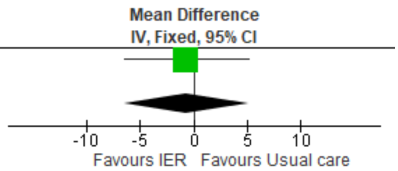


Figure 112. Change in weight (kg) at 2 years from baseline

Study or Subgroup	IER Mean	IER SD	IER Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Pannen 2021 (HELENA Trial) (1)	-5.7	16.7	32	-5	1.2	38	100.0%	-0.70 [-6.50, 5.10]
Total (95% CI)			**32**			**38**	**100.0%**	**-0.70 [-6.50, 5.10]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.24 (P = 0.81)

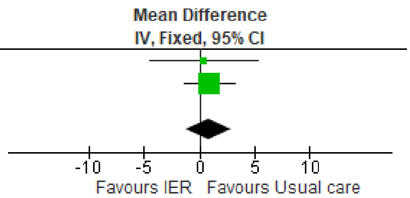


Footnotes
(1) Weight change according to self-reported continuation of diets

Figure 113. Change in WC (cm) at 1 year from baseline

Study or Subgroup	IER Mean	IER SD	IER Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Schubel 2018 (HELENA Trial)	-2.3	13	49	-2.7	12.1	52	17.5%	0.40 [-4.51, 5.31]
Sundfor 2018	-8.7	5.9	54	-9.6	6.3	58	82.5%	0.90 [-1.36, 3.16]
Total (95% CI)			**103**			**110**	**100.0%**	**0.81 [-1.24, 2.86]**

Heterogeneity: $Chi^2 = 0.03$, df = 1 (P = 0.86); $I^2 = 0\%$
Test for overall effect: Z = 0.78 (P = 0.44)



In people with type 2 diabetes

IER (5:2 diet)+ support vs Usual care (diet)+ support

Figure 114. Change in weight (kg) at 1 year from baseline

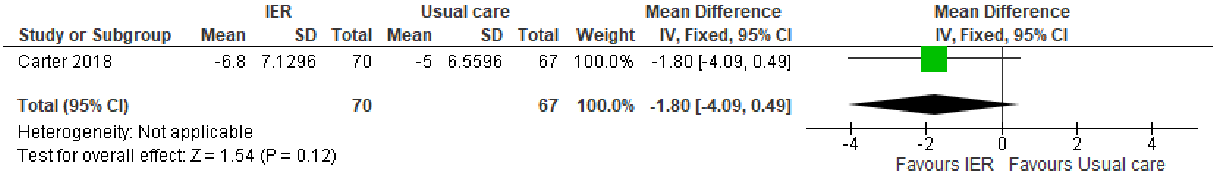


Figure 115. Change in weight (kg) at 2 years from baseline

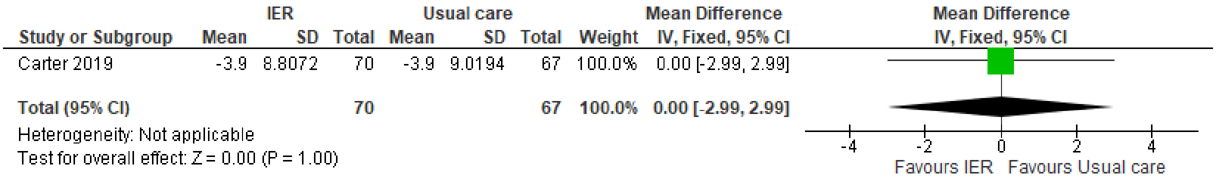


Figure 116. % change in HbA1c at 1 year from baseline

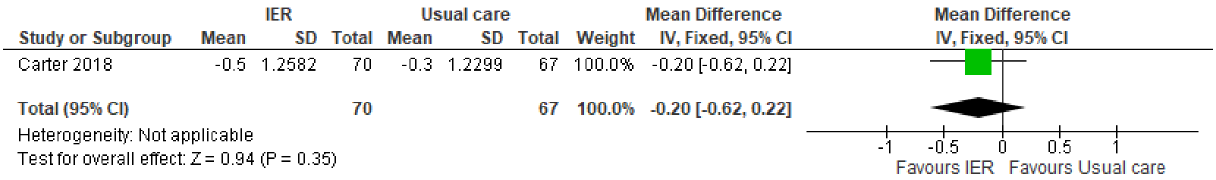
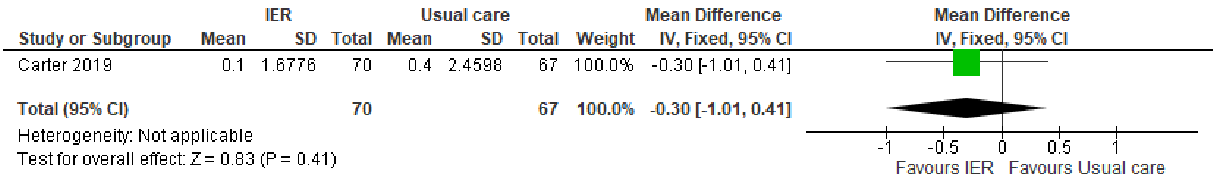


Figure 117. % change in HbA1c at 2 years from baseline



IER (5:2 diet) + support vs Low energy TOTAL MR + support

Figure 118. Change in weight (kg) at 1 year from baseline

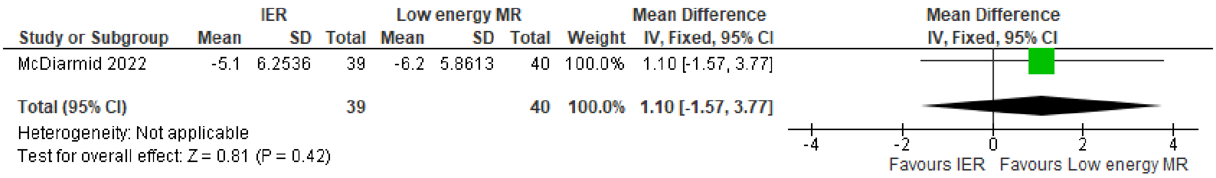


Figure 119. Change in HbA1c at 1 year from baseline

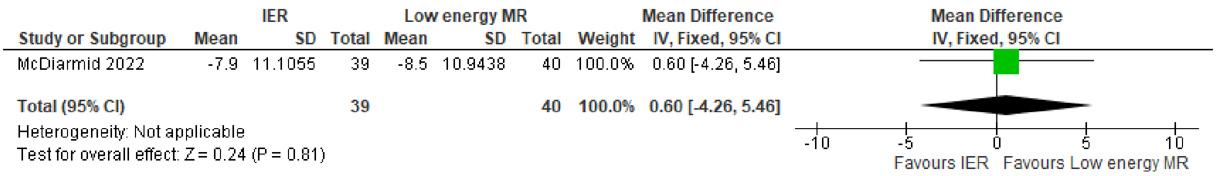


Figure 120. Serious AEs at 1 year from baseline

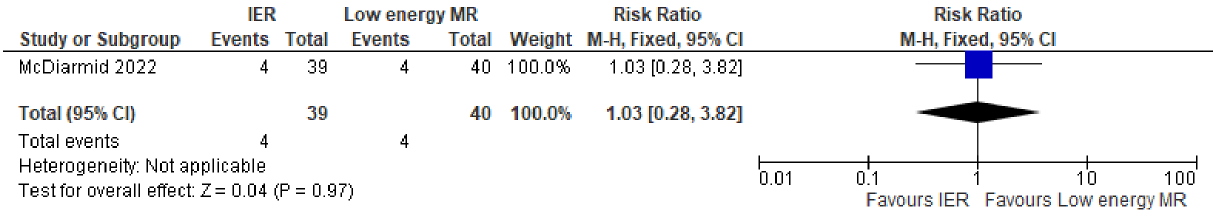
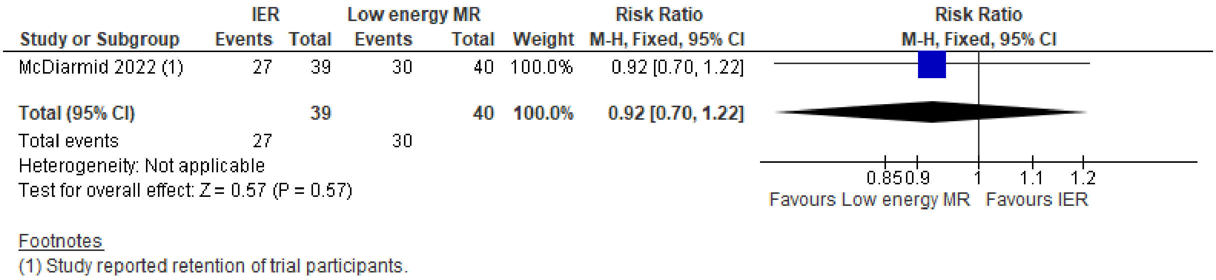


Figure 121. Adherence at 1 year from baseline

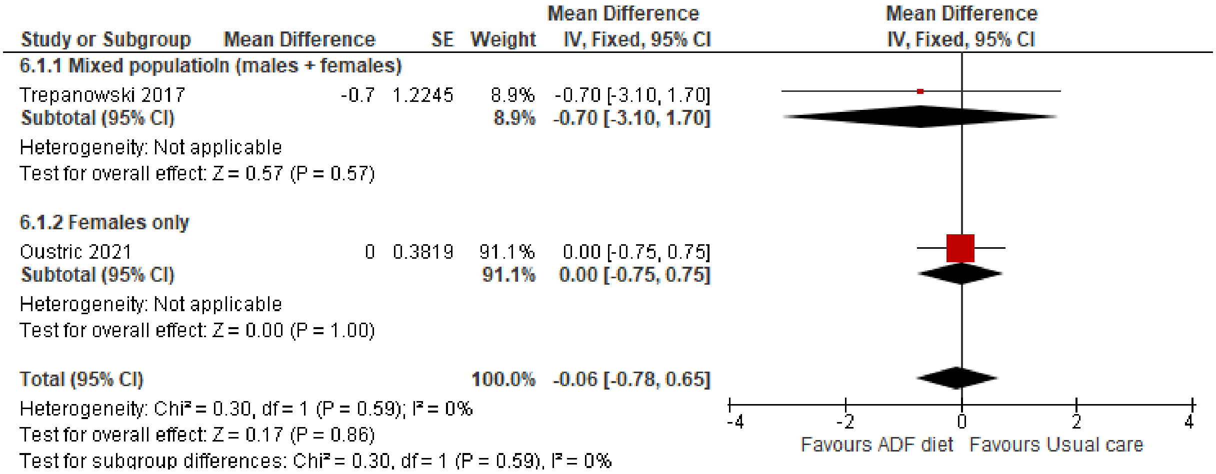


Intermittent energy restriction (IER) – Alternate day fasting (ADF) Diet

Mixed population

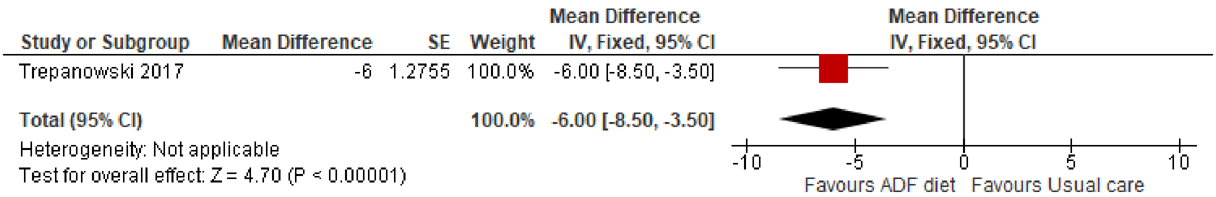
Intermittent energy restriction (ADF diet)+ support vs Usual care (diet)+ support

Figure 122. % Change in weight from baseline at 1 year



Intermittent energy restriction (ADF diet)+ support vs No intervention

Figure 123. % Change in weight from baseline at 1 year



Intermittent energy restriction – Time restricted eating

Mixed population

Intermittent energy restriction (TRE) + support vs Usual care (diet) + support

Figure 124. Change in weight (kg) from end of baseline to 1 year

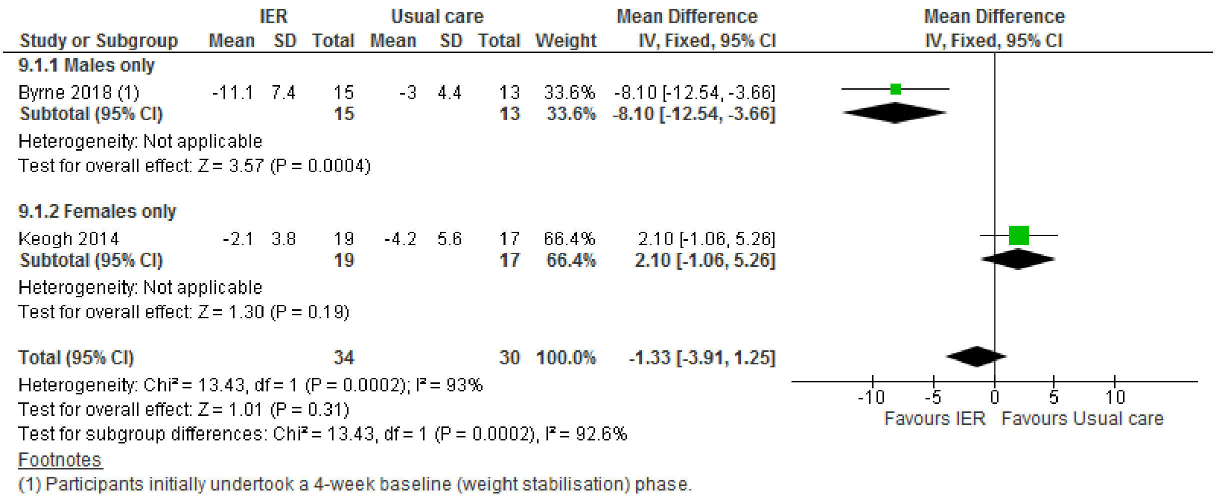
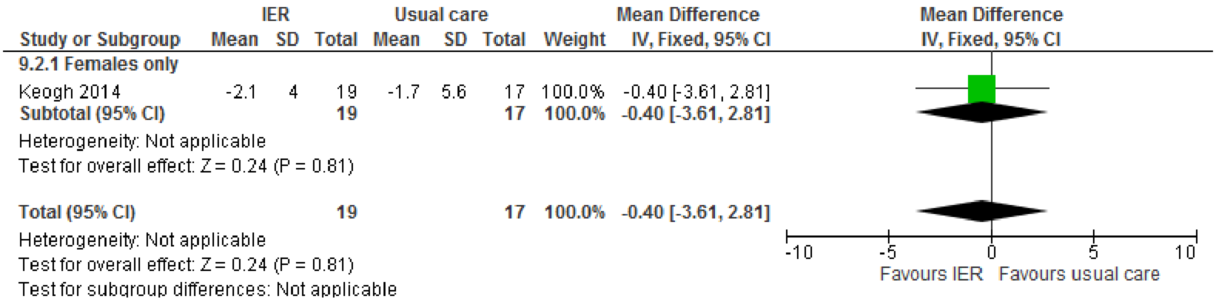


Figure 125. Change in waist circumference (cm) from end of baseline to 1 year



Intermittent energy restriction: intermittent fasting

Mixed population

Intermittent energy restriction: intermittent fasting vs standard care (advice)

Figure 126. HbA1c % change from baseline – 18 months

Study or Subgroup	iTRE Mean	iTRE SD	iTRE Total	Standard Care Mean	Standard Care SD	Standard Care Total	Weight	Mean Difference IV, Fixed, 95% CI
Teong 2023	-0.07	0.2318	85	-0.01	0.2535	41	100.0%	-0.06 [-0.15, 0.03]
Total (95% CI)			**85**			**41**	**100.0%**	**-0.06 [-0.15, 0.03]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.28 (P = 0.20)

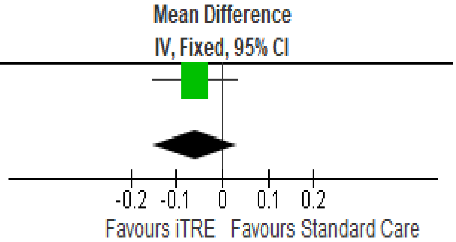


Figure 127. Body weight (kg) - change from baseline at 18 months

Study or Subgroup	iTRE Mean [kg]	iTRE SD [kg]	iTRE Total	Standard Care Mean [kg]	Standard Care SD [kg]	Standard Care Total	Weight	Mean Difference IV, Fixed, 95% CI
Teong 2023	-4.36	8.3451	85	-2.64	8.1739	41	100.0%	-1.72 [-4.79, 1.35]
Total (95% CI)			**85**			**41**	**100.0%**	**-1.72 [-4.79, 1.35]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.10 (P = 0.27)

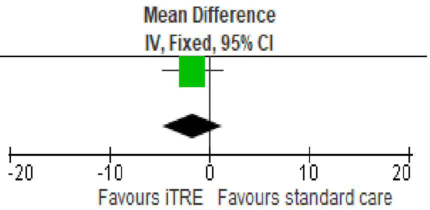


Figure 128. Number with at least one serious adverse event

Study or Subgroup	iTRE Events	iTRE Total	Standard Care Events	Standard Care Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Teong 2023	2	85	0	41	100.0%	2.44 [0.12, 49.73]
Total (95% CI)		**85**		**41**	**100.0%**	**2.44 [0.12, 49.73]**
Total events	2		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.58 (P = 0.56)

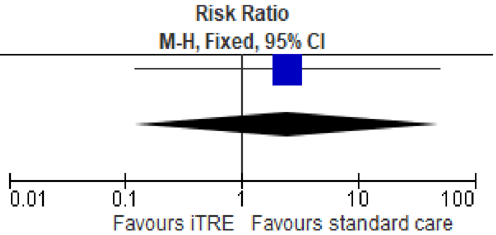


Figure 129. Number with at least one adverse event

Study or Subgroup	iTRE Events	iTRE Total	Standard Care Events	Standard Care Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Teong 2023	31	85	6	41	100.0%	2.49 [1.13, 5.50]
Total (95% CI)		**85**		**41**	**100.0%**	**2.49 [1.13, 5.50]**
Total events	31		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.26 (P = 0.02)

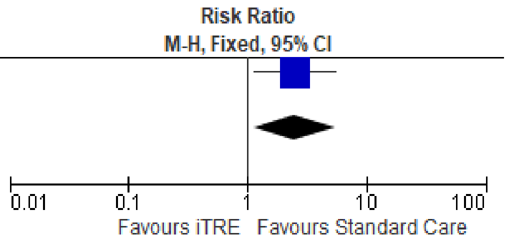
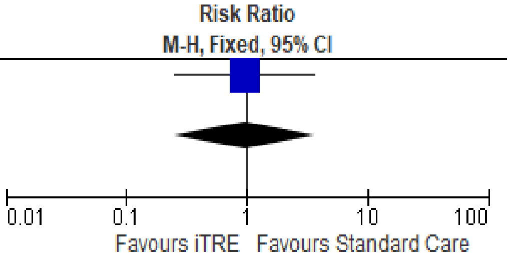


Figure 130. Adverse event: Constipation

Study or Subgroup	iTRE Events	iTRE Total	Standard Care Events	Standard Care Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Teong 2023	6	85	3	41	100.0%	0.96 [0.25, 3.67]
Total (95% CI)		**85**		**41**	**100.0%**	**0.96 [0.25, 3.67]**
Total events	6		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.05 (P = 0.96)						



Intermittent energy restriction: intermittent fasting vs Usual care (diet)

Figure 131. Weight change: from baseline at 12 months (kg)

Study or Subgroup	TRE Mean [kg]	TRE SD [kg]	TRE Total	Habitual meal timing Mean [kg]	Habitual meal timing SD [kg]	Habitual meal timing Total	Weight	Mean Difference IV, Fixed, 95% CI
Wei 2023	-8.4	6.3242	45	-7.8	6.1738	43	100.0%	-0.60 [-3.21, 2.01]
Total (95% CI)			**45**			**43**	**100.0%**	**-0.60 [-3.21, 2.01]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.45 (P = 0.65)								

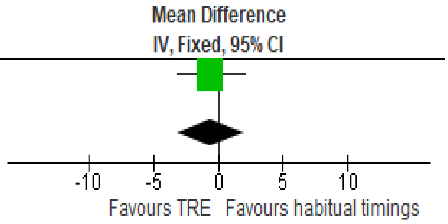


Figure 132. Waist circumference: change from baseline at 12 months (cm)

Study or Subgroup	TRE Mean [cm]	TRE SD [cm]	TRE Total	Habitual meal timing Mean [cm]	Habitual meal timing SD [cm]	Habitual meal timing Total	Weight	Mean Difference IV, Fixed, 95% CI
Wei 2023	-9.3	6.9899	45	-8.2	6.4987	43	100.0%	-1.10 [-3.92, 1.72]
Total (95% CI)			**45**			**43**	**100.0%**	**-1.10 [-3.92, 1.72]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.76 (P = 0.44)								

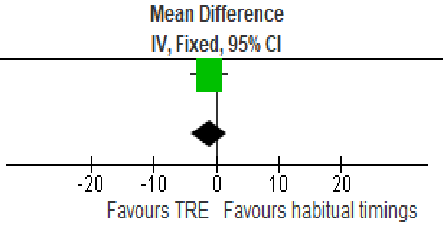
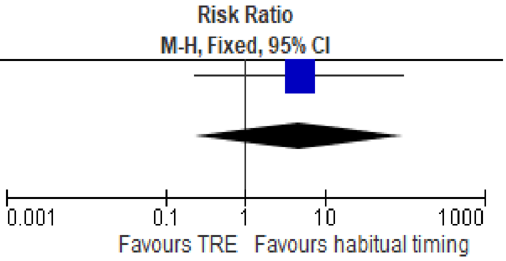


Figure 133. Constipation at 12 months

Study or Subgroup	TRE Events	TRE Total	Habitual meal timing Events	Habitual meal timing Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Wei 2023	2	45	0	43	100.0%	4.78 [0.24, 96.84]
Total (95% CI)		**45**		**43**	**100.0%**	**4.78 [0.24, 96.84]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.02 (P = 0.31)						



Appendix F – GRADE tables

Low energy diet - TOTAL meal replacement

Mixed population

Table 1. Low energy TOTAL MR + support vs Usual care (conventional diet) + support

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Low energy TOTAL MR + support	Control	Relative (95% CI)	Absolute		
% Change in weight at 1 year from baseline. MID = 5% (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	135	138	-	MD 5 lower (5.14 to 4.86 lower)	⊕OOO VERY LOW	CRITICAL
Change in WC (cm) at 1 year from baseline. MID = 4.65 (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	135	138	-	MD 4.7 lower (7.26 to 2.14 lower)	⊕OOO VERY LOW	IMPORTANT
Serious adverse events at 1 year from baseline. MID 0.8 to 1.25 (follow-up 12 months). Better indicated by lower values												
1[1]	randomised trials	very serious[2]	no serious inconsistency[3]	serious[5]	very serious[6]	None	7/155 (4.5%)	3/150 (2%)	RR 2.26 (0.59 to 8.57)	25 more per 1000 (from 8 fewer to 151 more)	⊕OOO VERY LOW	CRITICAL
Adherence at 1 year from baseline. MID 0.8 to 1.25 (follow-up 12 months). Better indicated by higher values												

1[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	95/135 (70.4%)	94/138 (68.1%)	RR 1.03 (0.88 to 1.21)	20 more per 1000 (from 82 fewer to 143 more)	⊕⊕OO LOW	IMPORTANT

[1] Ard 2019
[2] Downgraded twice for high risk of bias due to no detail provided on the randomisation procedure or allocation concealment; 17% loss to follow up; and potential effect of not blinding the assessment of subjective outcomes
[3] Single study; inconsistency not applicable
[4] Downgraded once as 95%CI crosses one line of the calculated MID
[5] Downgraded once for indirectness because all serious adverse events were grouped together and not all were relevant to the intervention (e.g. concussion due to a vehicle accident)
[6] Downgraded twice as 95%CI crosses two clinical decision thresholds (0.8 and 1.25)

Table 2. Low energy TOTAL MR + support vs Usual care (advice)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Low energy TOTAL MR + support**	**Usual care (advice)**	**Relative (95% CI)**	**Absolute**		
Change in weight (kg) at 1 year from baseline. MID = 3.5 (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	104	95	-	MD 7.6 lower (9.92 to 5.28 lower)	⊕⊕⊕O MODERATE	CRITICAL
Change in WC (cm) at 1 year from baseline. MID = 3.25 (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	99	91	-	MD 5 lower (7.24 to 2.76 lower)	⊕⊕OO LOW	IMPORTANT
Change in HbA1c (mmol/mol) at 1 year from baseline. MID = 5 mmol/mol (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	91	75	-	MD 2.2 lower (4.71 lower to 0.31 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Change in QoL (EQ-5D Index) at year 1 from baseline. MID = 0.07 (follow-up 12 months; Better indicated by higher values)												

1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	100	93	-	MD 0.02 higher (0.02 lower to 0.06 higher)	⊕⊕⊕O MODERATE	CRITICAL
Change in QoL (EQ-5D VAS) at year 1 from baseline. MID = 8.5 (Better indicated by higher values)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	101	96	-	MD 3.8 higher (1.19 lower to 8.79 higher)	⊕⊕OO LOW	CRITICAL
Change in QoL (OWL-QOL) at year 1 from baseline. MID = 8.35 (follow-up 12 months; Better indicated by higher values)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	99	94	-	MD 3 higher (2.32 lower to 8.32 higher)	⊕⊕⊕O MODERATE	CRITICAL
Serious AEs at 1 year from baseline. MID 0.8 to 1.25 (follow-up 12 months). Better indicated by lower values												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	serious[5]	very serious[6]	none	15/138 (10.9%)	17/140 (12.1%)	RR 0.9 (0.47 to 1.72)	12 fewer per 1000 (from 64 fewer to 87 more)	⊕OOO VERY LOW	CRITICAL
Adverse event: constipation at 1 year from baseline. MID 0.8 to 1.25 (follow-up 12 months). Better indicated by lower values.												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	no serious	none	20/138 (14.5%)	0/140 (0%)	RR 41.59 (2.54 to 680.93)	Not calculable*	⊕⊕⊕O MODERATE	CRITICAL
Change in weight (kg) at 3 years from baseline. MID = 3.85 (follow-up 3 years; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	96	83	-	MD 3.6 lower (6.06 to 1.14 lower)	⊕⊕OO LOW	CRITICAL
Change in WC (cm) at 3 years from baseline. MID = 3.65 (follow-up 3 years; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	77	70	-	MD 5 lower (7.66 to 2.34 lower)	⊕⊕OO LOW	IMPORTANT
Change in HbA1c (mmol/mol) at 3 years from baseline. MID = 5 mmol/mol (follow-up 3 years; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	71	61	-	MD 3.9 higher (1.11 to 6.69 higher)	⊕⊕OO LOW	IMPORTANT

Change in quality of life (EQ-5D index) at 3 years from baseline. MID = 0.008 (follow-up 3 years; Better indicated by higher values)											
1[6]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	very serious[7]	none	67	70	-	MD 0.02 higher (0.02 lower to 0.06 higher)	⊕OOO VERY LOW	CRITICAL
Change in quality of life at 3 years (EQ-5D VAS). MID = 57.55 (follow-up 3 years; Better indicated by higher values)											
1[8]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	79	70	-	MD 16 lower (43.32 lower to 11.32 higher)	⊕⊕⊕O MODERATE	CRITICAL
Change in quality of life at 3 years (OWL-QOL). MID = 7.35 (follow-up 3 years; Better indicated by higher values)											
1[8]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	77	70	-	MD 1.4 higher (3.6 lower to 6.4 higher)	⊕⊕⊕O MODERATE	CRITICAL

[1] Astbury 2018 (DROPLET)
[2] Downgraded once due to missing data and the potential effects of not blinding participants or outcome assessors
[3] Single study; inconsistency not applicable
[4] Downgraded once as 95%CI crosses one line of the calculated MID
[5] Downgraded once for indirectness because study reports composite score for moderate or severe adverse events (severe AEs could not be separated)
[6] Downgraded twice as 95%CI crosses two clinical decision thresholds (0.8 and 1.25)
[7] Downgraded twice as 95%CI crosses two lines of the calculated MID
[8] Astbury 2021 (DROPLET)
* Could not be calculated due to zero events in the control arm.

In people with type 2 diabetes

Table 3. Low energy TOTAL MR + support vs Usual care (advice)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**T2DM Low energy TOTAL MR + support**	**Usual care (advice)**	**Relative (95% CI)**	**Absolute**		
Change in weight (kg) at 1 year from baseline. MID= 2.65 (follow-up 12 months; Better indicated by lower values)												

3[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	225	242	-	MD 8.67 lower (9.91 to 7.42 lower)	⊕⊕OO LOW	CRITICAL
Change in WC (cm) at 1 year from baseline. MID = 2.92 (follow-up 12 months; Better indicated by lower values)												
2[4]	randomised trials	serious[5]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	86	94	-	MD 7.19 lower (9.61 to 4.77 lower)	⊕⊕⊕O MODERATE	IMPORTANT
Change in HbA1c (mmol/mol) at 1 year from baseline. MID = 5 mmol/mol (follow-up 12 months; Better indicated by lower values)												
3[1]	randomised trials	very serious[2]	serious[6]	no serious indirectness	no serious imprecision	none	346	365	-	MD 7.98 lower (10.28 to 5.69 lower)	⊕OOO VERY LOW	IMPORTANT
Change in QoL (EQ-5D VAS) at 1 year from baseline. MID = 8 (follow-up 12 months; Better indicated by higher values)												
2[7]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	serious[16]	none	208	225	-	MD 6.06 higher (2.86 to 9.25 higher)	⊕OOO VERY LOW	CRITICAL
Change in QoL (EQ-5D Health utility score) at 1 year from baseline MID = 0.101 (follow-up 12 months; Better indicated by higher values)												
1[8]	randomised trials	very serious[9]	no serious inconsistency[10]	no serious indirectness	no serious imprecision	none	138	148	-	MD 0.03 higher (0.02 lower to 0.07 higher)	⊕⊕OO LOW	CRITICAL
Serious AEs at 1 year from baseline. MID 0.8 to 1.25 (follow-up 12 months). Better indicated by lower values												
2[7]	randomised trials	very serious[2]	very serious[12]	no serious indirectness	very serious[13]	none	7/227 (3.1%)	6/226 (2.7%)	RR 1.16 (0.40 to 3.36)	5 fewer per 1000 (from 26 fewer to 543 more)	⊕OOO VERY LOW	CRITICAL
Adherence at 1 year from baseline. MID 0.8 to 1.25 (follow-up 12 months). Better indicated by higher values												
1[8]	randomised trials	very serious[9]	no serious inconsistency[10]	no serious indirectness	serious[14]	none	117/143 (81.8%)	115/115 (100%)	RR 0.82 (0.76 to 0.89)	180 fewer per 1000 (from 110 fewer to 240 fewer)	⊕OOO VERY LOW	IMPORTANT
Change in weight (kg) at 2 years from baseline. MID = 2.6 (follow-up 2 years; Better indicated by lower values)												

1[15]	randomised trials	very serious[9]	no serious inconsistency[10]	no serious indirectness	no serious imprecision	none	129	143	-	MD 5.43 lower (6.87 to 3.99 lower)	⊕⊕OO LOW	CRITICAL
Change in HbA1c (mmol/mol) at 2 years from baseline. MID = 5 mmol/mol (follow-up 2 years; Better indicated by lower values)												
1[15]	randomised trials	very serious[9]	no serious inconsistency[10]	no serious indirectness	serious[16]	none	129	143	-	MD 4.82 lower (8.28 to 1.36 lower)	⊕OOO VERY LOW	IMPORTANT
Change in QoL (EQ-5D VAS) at 2 years from baseline. MID = 7.55 (follow-up 2 years; Better indicated by higher values)												
1[15]	randomised trials	very serious[9]	no serious inconsistency[10]	no serious indirectness	serious[14]	none	129	143	-	MD 4.64 higher (0.39 to 8.89 higher)	⊕OOO VERY LOW	CRITICAL
Change in QoL (EQ-5D Health utility score) at 2 years from baseline. MID = 0.097 (follow-up 2 years; Better indicated by higher values)												
1[15]	randomised trials	very serious[9]	no serious inconsistency[10]	no serious indirectness	no serious imprecision	none	129	143	-	MD 0.02 higher (0.02 lower to 0.07 higher)	⊕⊕OO LOW	CRITICAL
Serious Adverse events at 2 years from baseline. MID 0.8 to 1.25 (follow-up 2 years). Better indicated by lower values												
1[15]	randomised trials	very serious[9]	no serious inconsistency[10]	no serious indirectness	serious[14]	none	11/157 (7%)	19/149 (12.8%)	RR 0.55 (0.27 to 1.12)	57 fewer per 1000 (from 93 fewer to 15 more)	⊕OOO VERY LOW	CRITICAL
Change in weight (kg) at 3 years from baseline. MID = 2.55 (follow-up 3 years; Better indicated by lower values)												
1[17]	randomised trials	serious[18]	no serious inconsistency[10]	no serious indirectness	serious[16]	none	19	17	-	MD 3.5 lower (8.65 lower to 1.65 higher)	⊕⊕OO LOW	CRITICAL
Change in WC (cm) at 3 years from baseline. MID = 3.75 (follow-up 3 years; Better indicated by lower values)												
1[17]	randomised trials	serious[18]	no serious inconsistency[10]	no serious indirectness	serious[16]	none	15	14	-	MD 3.8 lower (10.86 lower to 3.26 higher)	⊕⊕OO LOW	IMPORTANT
Change in HbA1c (mmol/mol) at 3 years from baseline. MID = 5mmol/mol (follow-up 3 years; Better indicated by lower values)												

1[17]	randomised trials	serious[18]	no serious inconsistency[10]	no serious indirectness	serious[16]	none	16	17	-	MD 8.3 higher (0.47 lower to 17.07 higher)	⊕⊕OO LOW	IMPORTANT

[1] Astbury 2018 (DROPLET); Lean 2018 (DIRECT); Taheri (2020)
[2] Downgraded twice as greater than 33.3% of the weight in the meta-analysis came from studies at high risk of bias (Lean 2018 – high RoB due to no random sequence generation, no allocation concealment, and lack of blinding of participants and personnel)
[3] No inconsistency; I2 = 0%
[4] Astbury 2018 (DROPLET); Taheri 2020
[5] Downgraded once as greater than 33.3% of the weight in the meta-analysis came from studies at moderate risk of bias
[6] Downgraded once as I2 was between 33.3% and 66.7% (I2 = 43%)
[7] Lean 2018 (DIRECT); Taheri 2020
[8] Lean 2018 (DIRECT)
[9] Downgraded twice for high risk of bias due to no information on random sequence generation, allocation concealment, and lack of blinding of participants and study personnel
[10] Single study; inconsistency not applicable
[12] Downgraded twice as I2 was greater than 66.7% (I2 = 75%)
[13] Downgraded twice as 95%CI crosses two clinical decision thresholds (0.8 and 1.25)
[14] Downgraded once as 95%CI crosses one clinical decision threshold (0.8)
[15] Lean 2019 (DIRECT)
[16] Downgraded once as 95%CI crosses one calculated MID
[17] Astbury 2018 (DROPLET)
[18] Downgraded once for moderate risk of bias due to missing data and the potential effects of not blinding participants or outcome assessors

Table 4. Low energy TOTAL MR + support vs Usual care (conventional diet) + support

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**T2DM Low energy TOTAL MR + support**	**Usual care + support**	**Relative (95% CI)**	**Absolute**		
Change in weight (kg) at 1 year from baseline. MID = 3.05 (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	45	45	-	MD 4.2 lower (6.49 to 1.91 lower)	⊕OOO VERY LOW	CRITICAL
Change in WC at 1 year from baseline. MID = 7.0 (follow-up 12 months; Better indicated by lower values)												

1[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	45	45	-	MD 10.4 lower (15.65 to 5.15 lower)	⊕OOO VERY LOW	IMPORTANT
% change in HbA1c at 1 year from baseline. MID = 5% (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	45	45	-	MD 0.34 lower (0.9 lower to 0.22 higher)	⊕⊕OO LOW	IMPORTANT
Change in QoL at 1 year from baseline (EQ-5D). MID = 9.7 (follow-up 12 months; Better indicated by higher values)												
1[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	45	45	-	MD 10.39 higher (1.86 to 18.92 higher)	⊕OOO VERY LOW	CRITICAL
Serious AEs at 1 year from baseline. MID 0.8 to 1.25 (follow-up 12 months). Better indicated by lower values												
1[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	very serious[5]	none	5/45 (11.1%)	9/45 (20%)	RR 0.56 (0.2 to 1.53)	88 fewer per 1000 (from 160 fewer to 106 more)	⊕OOO VERY LOW	CRITICAL

[1] Brown 2020
[2] Downgraded twice for high risk of bias due to no blinding of participants and personnel, and unclear risk of bias due to incomplete outcome data
[3] Single study; inconsistency not applicable
[4] Downgraded once as 95%CI crosses one calculated MID
[5] Downgraded twice as 95%CI crosses two clinical decision thresholds (0.8 and 1.25)

Table 5. Low energy TOTAL MR + support vs Intermittent energy restriction (5:2 diet) + support

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	T2DM Low energy TOTAL MR + support	IER (5:2 diet) + support	Relative (95% CI)	Absolute		
Change in weight (kg) at 1 year from baseline. MID = 3.1 (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	40	39	-	MD 1.1 lower (3.77 lower to 1.57 higher)	⊕⊕OO LOW	CRITICAL

Change in HbA1c at 1 year from baseline. MID = 5 mmol/mol (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	40	39	-	MD 0.6 lower (5.46 lower to 4.26 higher)	⊕⊕OO LOW	IMPORTANT
Serious AEs at 1 year from baseline. MID 0.8 to 1.25 (follow-up 12 months). Better indicated by lower values												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	very serious[5]	none	4/40 (10%)	4/39 (10.3%)	RR 0.98 (0.26 to 3.63)	2 fewer per 1000 (from 76 fewer to 270 more)	⊕OOO VERY LOW	CRITICAL
Adherence at 1 year from baseline. MID 0.8 to 1.25 (follow-up 12 months). Better indicated by higher values.												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	30/40 (75%)	27/39 (69.2%)	RR 1.08 (0.82 to 1.43)	55 more per 1000 (from 125 fewer to 298 more)	⊕⊕OO LOW	IMPORTANT

[1] McDiarmid 2022
[2] Downgraded once for moderate risk of bias due to high number of drop outs from the trial
[3] Single study; inconsistency not applicable
[4] Downgraded once as 95%CI crosses one calculated MID
[5] Downgraded twice as 95%CI crosses two clinical decision thresholds (0.8 and 1.25)
[6] Downgraded once as 95%CI crosses one clinical decision threshold (1.25)

Low energy diet – PARTIAL meal replacement

Mixed population

Table 6. Low energy PARTIAL MR + support vs Usual care (conventional diet) + support

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Low energy PARTIAL MR + support	Usual care (conventional diet) + support	Relative (95% CI)	Absolute		
Change in weight (kg) at 1 year from baseline. MID = 3.35 (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	35	35	-	MD 1.1 higher (1.65 lower to 3.85 higher)	⊕⊕OO LOW	CRITICAL
Change in WC (cm) at 1 year from baseline. MID = 3.5 (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	35	35	-	MD 1.2 higher (1.57 lower to 3.97 higher)	⊕⊕OO LOW	IMPORTANT

[1] Ashley 2007
[2] Downgraded once for moderate risk of bias due to concerns over sequence generation and allocation concealment
[3] Single study; inconsistency not applicable
[4] Downgraded once as 95%CI crosses once calculated MID

Table 7. Low energy PARTIAL MR + support vs Usual care (advice + conventional diet)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Low energy PARTIAL MR + support	Usual care (advice/diet)	Relative (95% CI)	Absolute		
Change in weight (kg) at 1 year from baseline. MID = 3.5 (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency[2]	no serious indirectness	serious[3]	none	57	56	-	MD 2.8 lower (5.38 to 0.22 lower)	⊕⊕⊕O MODERATE	CRITICAL
Change in WC (cm) at 1 year from baseline. MID = 2.6 (follow-up 12 months; Better indicated by lower values)												

1[1]	randomised trials	no serious risk of bias	no serious inconsistency[2]	no serious indirectness	serious[3]	none	57	56	-	MD 1.4 lower (3.3 lower to 0.5 higher)	⊕⊕⊕O MODERATE	IMPORTANT

[1] Shikany 2013
[2] Single study; inconsistency not applicable
[3] Downgraded once as 95%CI crosses one calculated MID

In people with type 2 diabetes

Table 8. Low energy PARTIAL MR vs Usual care (conventional diet)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**T2DM Low energy PARTIAL MR**	**Usual care**	**Relative (95% CI)**	**Absolute**		
Change in weight (kg) at 1 year from baseline. MID = 2.6 (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	very serious[4]	none	19	12	-	MD 0.6 lower (4.06 lower to 2.86 higher)	⊕OOO VERY LOW	CRITICAL
Change in WC at 1 year from baseline. MID = 1.84 (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	serious[5]	none	19	12	-	MD 3.4 lower (5.88 to 0.92 lower)	⊕⊕OO LOW	IMPORTANT

[1] Khoo 2011
[2] Downgraded once for moderate risk of bias due to unclear sequence generation and allocation concealment
[3] Single study; inconsistency not applicable
[4] Downgraded twice as 95%CI crosses two calculated MIDs
[5] Downgraded once as 95%CI crosses one calculated MID

Very low energy diet – TOTAL meal replacement

Mixed population

Table 9. Very low energy TOTAL MR + support vs Usual care (conventional diet) + support

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Very low energy TOTAL MR + support	Usual care (advice/conventional diet)+ support	Relative (95% CI)	Absolute		
Change in weight at 1 year from baseline. MID = 3.39 (follow-up 12 months; Better indicated by lower values)												
2[1]	randomised trials	serious[2]	very serious[3]	no serious indirectness	very serious[4]	none	143	142	-	MD 2.45 lower (10.75 lower to 5.85 higher)	⊕OOO VERY LOW	CRITICAL
Change in weight at 1 year from baseline - Mixed population (Males and females). MID = 2.15 (follow-up 12 months; Better indicated by lower values)												
1[5]	randomised trials	no serious risk of bias	no serious inconsistency[6]	no serious indirectness	serious[7]	none	97	103	-	MD 1.58 higher (0.15 to 3.01 higher)	⊕⊕⊕O MODERATE	CRITICAL
Change in weight at 1 year from baseline - Only females. MID = 4.6 (follow-up 12 months; Better indicated by lower values)												
1[8]	randomised trials	serious[9]	no serious inconsistency[6]	no serious indirectness	serious[7]	none	46	39	-	MD 6.9 lower (10.88 to 2.92 lower)	⊕⊕OO LOW	CRITICAL
Change in WC at 1 year from baseline. MID = 4.9 (follow-up 12 months; Better indicated by lower values)												

1[8]	randomised trials	serious[9]	no serious inconsistency[6]	no serious indirectness	serious[7]	none	46	38	-	MD 7.4 lower (11.65 to 3.15 lower)	⊕⊕OO LOW	IMPORTANT
Change in weight at 2 years from baseline. MID = 3.7 (follow-up 2 years; Better indicated by lower values)												
2[1]	randomised trials	no serious risk of bias	no serious inconsistency[10]	no serious indirectness	serious[7]	none	142	134	-	MD 1.73 lower (3.19 to 0.27 lower)	⊕⊕⊕O MODERATE	CRITICAL
Change in weight at 2 years from baseline - Mixed population (Males and females). MID = 2.35 (follow-up 2 years; Better indicated by lower values)												
1[5]	randomised trials	no serious risk of bias	no serious inconsistency[6]	no serious indirectness	serious[7]	none	97	103	-	MD 1.5 lower (3.03 lower to 0.03 higher)	⊕⊕⊕O MODERATE	CRITICAL
Change in weight at 2 years from baseline - Only females. MID = 5 (follow-up 2 years; Better indicated by lower values)												
1[8]	randomised trials	serious[9]	no serious inconsistency[6]	no serious indirectness	serious[7]	none	45	31	-	MD 4 lower (8.79 lower to 0.79 higher)	⊕⊕OO LOW	CRITICAL
Change in WC at 2 years from baseline. MID = 5 (follow-up 2 years; Better indicated by lower values)												
1[8]	randomised trials	serious[9]	no serious inconsistency[6]	no serious indirectness	serious[7]	none	45	31	-	MD 4.3 lower (9.09 lower to 0.49 higher)	⊕⊕OO LOW	IMPORTANT
Change in weight at 3 years from baseline. MID = 4.35 (follow-up 3 years; Better indicated by lower values)												
2[1]	randomised trials	no serious risk of bias	no serious inconsistency[11]	no serious indirectness	no serious imprecision	none	102	74	-	MD 0.51 lower (2.96 lower to 1.93 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Change in weight at 3 years from baseline - Mixed population (Males and females). MID = 3.25 (follow-up 3 years; Better indicated by lower values)												
1[5]	randomised trials	no serious risk of bias	no serious inconsistency[6]	no serious indirectness	no serious imprecision	none	61	43	-	MD 0.2 higher (2.56 lower to 2.96 higher)	⊕⊕⊕⊕ HIGH	CRITICAL

Change in weight at 3 years from baseline - Only females. MID = 5.05 (follow-up 3 years; Better indicated by lower values)												
1[8]	randomised trials	serious[9]	no serious inconsistency[6]	no serious indirectness	serious[7]	none	41	31	-	MD 3.1 lower (8.35 lower to 2.15 higher)	⊕⊕OO LOW	CRITICAL
Change in WC at 3 years from baseline. MID = 4.7 (follow-up 3 years; Better indicated by lower values)												
2[1]	randomised trials	no serious risk of bias	no serious inconsistency[10]	no serious indirectness	no serious imprecision	none	102	74	-	MD 1.13 lower (3.81 lower to 1.55 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Change in WC at 3 years from baseline - Mixed population (Males and females). MID = 4.22 (follow-up 3 years; Better indicated by lower values)												
1[5]	randomised trials	no serious risk of bias	no serious inconsistency[6]	no serious indirectness	no serious imprecision	none	61	43	-	MD 0.3 lower (3.5 lower to 2.9 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Change in WC at 3 years from baseline - Only females. MID = 5.15 (follow-up 3 years; Better indicated by lower values)												
1[8]	randomised trials	serious[9]	no serious inconsistency[6]	no serious indirectness	serious[7]	none	41	31	-	MD 3.1 lower (8.02 lower to 1.82 higher)	⊕⊕OO LOW	IMPORTANT

[1] Purcell 2014; Seimon 2019 (TEMPO)
[2] Downgraded once as greater than 33.3% of the weight in the meta-analysis came from a study at moderate risk of bias (Seimon 2019; moderate RoB due to substantial missing data at 1-year and 3-year follow-ups)
[3] Downgraded twice for very serious inconsistency due to I2 greater than 66.7% (I2 = 94%)
[4] Downgraded twice as 95%CI crosses two calculated MIDs
[5] Purcell 2014
[6] Single study; inconsistency not applicable
[7] Downgraded once as 95%CI crosses one calculated MID
[8] Seimon 2019 (TEMPO)
[9] Downgraded once due to substantial missing data at 1-year and 3-year follow-ups
[10] No inconsistency; I2 = 0%
[11] I2 < 33.35%; not downgraded

Table 10. Very low energy TOTAL MR + support vs Usual care (advice)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Very low energy TOTAL MR + support	Usual care (advice)	Relative (95% CI)	Absolute		
Change in weight at 1 year from baseline. MID = 2.8 (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	35	37	-	MD 8.3 lower (11.11 to 5.49 lower)	⊕⊕⊕O MODERATE	CRITICAL
Change in WC at 1 year from baseline. MID = 3 (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	35	37	-	MD 8.6 lower (11.52 to 5.68 lower)	⊕⊕⊕O MODERATE	IMPORTANT
Change in weight at 2 years from baseline. MID = 3.75 (follow-up 2 years; Better indicated by lower values)												
1[4]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	serious[5]	none	35	36	-	MD 4.4 lower (7.66 to 1.14 lower)	⊕⊕OO LOW	CRITICAL
Change in WC at 2 years from baseline. MID = 3.65 (follow-up 2 years; Better indicated by lower values)												
1[4]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	serious[5]	none	35	36	-	MD 4.2 lower (7.46 to 0.94 lower)	⊕⊕OO LOW	IMPORTANT

[1] Tuomilehto 2009
[2] Downgraded once due to selective reporting
[3] Single study; inconsistency not applicable

[4] Tuomilehto 2010
[5] Downgraded once as 95%CI crosses one calculated MID

Low carbohydrate diet

Mixed population

Table 11. Low carbohydrate diet + support vs Usual care (diet) + support

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Low carb diet + support	Usual care + support	Relative (95% CI)	Absolute		
Change in weight (kg) at 1 year from baseline. MID = 3.03 (follow-up 12 months; Better indicated by lower values)												
6[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	336	349	-	MD 0.81 lower (1.77 lower to 0.15 higher)	⊕⊕OO LOW	CRITICAL
Change in weight (kg) at 1 year from baseline - Mixed population (males and females). MID = 3.07 (follow-up 12 months; Better indicated by lower values)												
3[5]	randomised trials	very serious[2]	no serious inconsistency[6]	no serious indirectness	no serious imprecision	none	236	239	-	MD 0.65 lower (1.69 lower to 0.4 higher)	⊕⊕OO LOW	CRITICAL
Change in weight (kg) at 1 year from baseline - Only females. MID = 2.8 (follow-up 12 months; Better indicated by lower values)												
2[7]	randomised trials	very serious[2]	no serious inconsistency[8]	serious indirectness[23]	serious[9]	none	43	49	-	MD 1.79 lower (4.8 lower to 1.22 higher)	⊕OOO VERY LOW	CRITICAL
Change in weight (kg) at 1 year from baseline - Only males. MID = 5.45 (follow-up 12 months; Better indicated by lower values)												
1[10]	randomised trials	very serious[11]	no serious inconsistency[12]	no serious indirectness	no serious imprecision	none	57	61	-	MD 1.4 lower (5.28 lower to 2.48 higher)	⊕⊕OO LOW	CRITICAL

Change in weight (kg) at 2 years from baseline. MID = 3.35 (follow-up 2 years; Better indicated by lower values)												
1[13]	randomised trials	very serious[11]	no serious inconsistency[12]	no serious indirectness	no serious imprecision	none	201	204	-	MD 0.6 higher (0.77 lower to 1.97 higher)	⊕⊕OO LOW	CRITICAL
Change in BMI at 1 year from baseline. MID = 1.2 (follow-up 12 months; Better indicated by lower values)												
1[14]	randomised trials	very serious[11]	no serious inconsistency[3]	no serious indirectness	very serious[15]	none	21	19	-	MD 0.23 lower (1.8 lower to 1.34 higher)	⊕OOO VERY LOW	CRITICAL
Change in BMI at 2 years from baseline. MID = 0.8 (follow-up 2 years; Better indicated by lower values)												
1[16]	randomised trials	very serious[11]	no serious inconsistency[12]	serious indirectness[23]	serious[9]	none	27	22	-	MD 1 lower (2.04 lower to 0.04 higher)	⊕OOO VERY LOW	CRITICAL
Change in WC (cm) at 1 year from baseline. MID = 3.98 (follow-up 12 months; Better indicated by lower values)												
4[17]	randomised trials	very serious[11]	serious[18]	no serious indirectness	no serious imprecision	none	293	298	-	MD 1.37 lower (3.36 lower to 0.61 higher)	⊕OOO VERY LOW	IMPORTANT
Change in WC (cm) at 1 year from baseline - Mixed population (males and females). MID = 5.01 (follow-up 12 months; Better indicated by lower values)												
2[19]	randomised trials	very serious[11]	very serious[20]	no serious indirectness	no serious imprecision	none	200	202	-	MD 0.3 lower (4.31 lower to 3.7 higher)	⊕OOO VERY LOW	IMPORTANT
Change in WC (cm) at 1 year from baseline - Only males. MID = 3.5 (follow-up 12 months; Better indicated by lower values)												
1[10]	randomised trials	very serious[11]	no serious inconsistency[12]	no serious indirectness	serious[9]	none	57	61	-	MD 1.3 lower (3.72 lower to 1.12 higher)	⊕OOO VERY LOW	IMPORTANT
Change in WC (cm) at 1 year from baseline - Only females. MID = 1.9 (follow-up 12 months; Better indicated by lower values)												

1[21]	randomised trials	very serious[11]	no serious inconsistency[12]	serious indirectness[23]	serious[9]	none	36	35	-	MD 3.5 lower (6.39 to 0.61 lower)	⊕OOO VERY LOW	IMPORTANT
% Change in HbA1c at 1 year from baseline. MID = 5% (follow-up 12 months; Better indicated by lower values)												
1[22]	randomised trials	very serious[11]	no serious inconsistency[12]	no serious indirectness	no serious imprecision	none	100	100	-	MD 0 higher (0.06 lower to 0.06 higher)	⊕⊕OO LOW	IMPORTANT

[1] Ebbeling 2007; Frisch 2009; Klemsdal 2010; Foraker 2014; Griffin 2013; Wycherley 2012
[2] Downgraded twice as greater than 33.3% of the weight in the meta-analysis came from studies at high risk of bias
[3] I2 = 0%; no inconsistency
[5] Ebbeling 2007; Frisch 2009; Klemsdal 2010
[6] I2 < 33.3% (I2 = 19%); not downgraded
[7] Foraker 2014; Griffin 2013
[8] I2 < 33.3% (I2 = 23%); not downgraded
[9] Downgraded once as 95%CI crosses one calculated MID
[10] Wycherley 2012
[11] Downgraded twice for high risk of bias
[12] Single study; inconsistency not applicable
[13] Sacks 2009
[14] Calleja-Fernandez 2012 (in people with insulin resistance) and Calleja-Fernandez 2012 (in people without insulin resistance)
[15] Downgraded twice as 95%CI crosses two calculated MIDs
[16] Mellberg 2014
[17] Frisch 2009; Klemsdal 2010; Wycherley 2012; Griffin 2013
[18] Downgraded once as I2 was between 33.3% and 66.7% (I2 = 57%)
[19] Frisch 2009; Klemsdal 2010
[20] Downgraded twice as I2 > 66.7% (I2 = 79%)
[21] Griffin 2013
[22] Frisch 2009
[23] Downgraded once for partial indirectness.

In people with type 2 diabetes

Table 12. Low carbohydrate diet vs Usual care (diet)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**T2DM Low carb diet**	**Usual care**	**Relative (95% CI)**	**Absolute**		
Weight (kg) at 1 year from baseline. MID = 9.2 (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	31	33	-	MD 2.3 lower (11.59 lower to 6.99 higher)	⊕OOO VERY LOW	CRITICAL
% Change in HbA1c at 1 year from baseline. MID = 5% (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	21	24	-	MD 0.1 lower (2.91 lower to 2.71 higher)	⊕⊕OO LOW	IMPORTANT

[1] Pedersen 2014
[2] Downgraded twice for high risk of bias
[3] Single study; inconsistency not applicable
[4] Downgraded once as 95%CI crosses one calculated MID

Table 13. Low carbohydrate diet + support vs Usual care (diet) + support

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**T2DM Low carb diet + support**	**Usual care + support**	**Relative (95% CI)**	**Absolute**		
Change in weight (kg) at 1 year from baseline. MID = 7.47 (follow-up 12 months; Better indicated by lower values)												

4[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	351	352	-	MD 0.27 lower (1.65 lower to 1.1 higher)	⊕⊕OO LOW	CRITICAL
Change in weight (kg) at 2 years from baseline. MID = 9.9 (follow-up 2 years; Better indicated by lower values)												
2[4]	randomised trials	serious[5]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	237	243	-	MD 1.97 higher (1.41 lower to 5.36 higher)	⊕⊕⊕O MODERATE	CRITICAL
Change in WC (cm) at 1 year from baseline. MID = 5.51 (follow-up 12 months; Better indicated by lower values)												
4[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	351	352	-	MD 0.19 lower (1.55 lower to 1.17 higher)	⊕⊕OO LOW	IMPORTANT
Change in WC (cm) at 2 years from baseline. MID = 6.85 (follow-up 2 years; Better indicated by lower values)												
2[4]	randomised trials	serious[5]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	237	243	-	MD 1.89 higher (0.55 lower to 4.32 higher)	⊕⊕⊕O MODERATE	IMPORTANT
% Change in HbA1c at 1 year from baseline. MID = 5% (follow-up 12 months; Better indicated by lower values)												
4[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	351	352	-	MD 0.03 higher (0.16 lower to 0.21 higher)	⊕⊕OO LOW	IMPORTANT
% Change in HbA1c at 2 years from baseline. MID = 5% (follow-up 2 years; Better indicated by lower values)												
2[4]	randomised trials	serious[5]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	237	243	-	MD 0 higher (0.26 lower to 0.26 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Change in QoL (SF-36 Physical component score (PCS) at 1 year from baseline. MID = 4.76 (follow-up 12 months; Better indicated by higher values)												
2[4]	randomised trials	serious[5]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	237	243	-	MD 1.02 higher (0.67 lower to 2.72 higher)	⊕⊕⊕O MODERATE	CRITICAL
Change in QoL (SF-36 Physical component score (PCS) at 2 years from baseline. MID = 4.9 (follow-up 2 years; Better indicated by higher values)												
2[4]	randomised trials	serious[5]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	237	243	-	MD 1.91 lower (3.64 to 0.18 lower)	⊕⊕⊕O MODERATE	CRITICAL
Change in QoL (SF-36 Mental component score (MCS) at 1 year from baseline. MID = 4.7 (follow-up 12 months; Better indicated by higher values)												

2[4]	randomised trials	serious[5]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	237	243	-	MD 1.22 higher (0.43 lower to 2.88 higher)	⊕⊕⊕O MODERATE	CRITICAL
Change in QoL (SF-36 Mental component score (MCS) at 2 years from baseline. MID = 4.97 (follow-up 2 years; Better indicated by higher values)												
2[4]	randomised trials	serious[5]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	237	243	-	MD 1.02 higher (0.71 lower to 2.74 higher)	⊕⊕⊕O MODERATE	CRITICAL

[1] Elhayany 2010; Guldbrand 2012; Krebs 2012; Larsen 2011
[2] Downgraded twice as greater than 33.3% of the weight in the meta-analysis came from studies at high risk of bias
[3] I2 = 0%; not downgraded
[4] Guldbrand 2012; Krebs 2012
[5] Downgraded once as greater than 33.3% of the weight in the meta-analysis came from studies at moderate risk of bias

Very low carbohydrate diet

Mixed population

Table 14. Very low carbohydrate diet + support vs Usual care (diet) + support

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Very low carb diet + support	Usual care + support	Relative (95% CI)	Absolute		
Change in weight (kg) at 1 year from baseline - Mixed population (Mixed family backgrounds). MID = 3.21 (follow-up 12 months; Better indicated by lower values)												
7[1]	randomised trials	very serious[2]	serious[3]	serious indirectness[17]	serious[4]	none	431	395	-	MD 2.38 lower (4.22 to 0.55 lower)	⊕OOO VERY LOW	CRITICAL
Change in weight (kg) at 1 year from baseline - Black family background. MID = 2.9 (follow-up 12 months; Better indicated by lower values)												

1[5]	randomised trials	serious[6]	no serious inconsistency[7]	serious indirectness[18]	serious[4]	none	40	36	-	MD 3.3 lower (5.97 to 0.63 lower)	⊕OOO VERY LOW	CRITICAL
Change in weight (kg) at 1 year from baseline - White family background. MID = 3.5 (follow-up 12 months; Better indicated by lower values)												
1[5]	randomised trials	serious[6]	no serious inconsistency[7]	serious indirectness[18]	serious[4]	none	34	33	-	MD 3.9 lower (7.3 to 0.5 lower)	⊕OOO VERY LOW	CRITICAL
Change in WC (cm) at 1 year from baseline - Mixed population (Mixed family backgrounds). MID = 3.85 (follow-up 12 months; Better indicated by lower values)												
1[5]	randomised trials	serious[6]	no serious inconsistency[7]	serious indirectness[18]	serious[4]	none	75	73	-	MD 1.7 lower (4.2 lower to 0.8 higher)	⊕OOO VERY LOW	IMPORTANT
Change in WC (cm) at 1 year from baseline - Black family background. MID = 3.8 (follow-up 12 months; Better indicated by lower values)												
1[5]	randomised trials	serious[6]	no serious inconsistency[7]	serious indirectness[18]	serious[4]	none	40	36	-	MD 2.9 lower (6.39 lower to 0.59 higher)	⊕OOO VERY LOW	IMPORTANT
Change in WC (cm) at 1 year from baseline - White family background. MID = 3.9 (follow-up 12 months; Better indicated by lower values)												
1[5]	randomised trials	serious[6]	no serious inconsistency[7]	serious indirectness[18]	serious[4]	none	34	33	-	MD 0.2 lower (4.01 lower to 3.61 higher)	⊕OOO VERY LOW	IMPORTANT
% Change in HbA1c at 1 year from baseline. MID = 5% (follow-up 12 months; Better indicated by lower values)												
1[9]	randomised trials	very serious[10]	no serious inconsistency[7]	no serious indirectness	no serious imprecision	none	27	26	-	MD 0.38 lower (0.66 to 0.1 lower)	⊕⊕OO LOW	IMPORTANT
Adverse event: Hair loss at 1 year. MID = 0.8 to 1.25 (follow-up 12 months). Better indicated by lower values)												
2[11]	randomised trials	very serious[2]	no serious inconsistency[12]	no serious indirectness	very serious[15]	none	31/179 (17.3%)	19/181 (10.5%)	RR 1.63 (0.97 to 2.75)	66 more per 1000 (from 3 fewer to 184 more)	⊕OOO VERY LOW	CRITICAL

Adverse event: Constipation at 1 year. MID = 0.8 to 1.25 (follow-up 12 months). Better indicated by lower values)												
3[13]	randomised trials	very serious[2]	serious[14]	serious indirectness[17]	serious[8]	none	69/255 (27.1%)	53/253 (20.9%)	RR 1.16 (0.58 to 2.31)	34 more per 1000 (from 88 fewer to 274 more)	⊕OOO VERY LOW	CRITICAL
Change in weight (kg) at 2 years from baseline. MID = 5.4 (follow-up 2 years; Better indicated by lower values)												
1[16]	randomised trials	very serious[10]	no serious inconsistency[7]	no serious indirectness	no serious imprecision	none	153	154	-	MD 1.03 higher (1.39 lower to 3.45 higher)	⊕⊕OO LOW	CRITICAL
Adverse event: Hair loss at 2 years. MID = 0.8 to 1.25 (follow-up 2 years). Better indicated by lower values)												
1[16]	randomised trials	very serious[10]	no serious inconsistency[7]	no serious indirectness	very serious[15]	none	23/153 (15%)	15/154 (9.7%)	RR 1.54 (0.84 to 2.84)	53 more per 1000 (from 16 fewer to 179 more)	⊕OOO VERY LOW	CRITICAL
Adverse event: Constipation at 2 years. MID = 0.8 to 1.25 (follow-up 2 years). Better indicated by lower values)												
1[16]	randomised trials	very serious[10]	no serious inconsistency[7]	no serious indirectness	no serious imprecision	none	39/153 (25.5%)	17/154 (11%)	See comment	145 more per 1000 (from 60 more to 230 more)	⊕⊕OO LOW	CRITICAL

[1] Bazzano 2014; Brinkworth 2016a; Foster 2010; Hu 2015; Layman 2009; Lim 2010; Moreno 2014
[2] Downgraded twice as greater than 33.3% of the weight in the meta-analysis came from studies at high risk of bias
[3] Downgraded once as I2 was between 33.3% and 66.7% (I2 = 62%)
[4] Downgraded once as 95%CI crosses one calculated MID
[5] Bazzano 2014
[6] Downgraded once for moderate risk of bias
[7] Single study; inconsistency not applicable
[8] Downgraded once as 95%CI crosses one clinical decision threshold (1.25)
[9] Moreno 2014
[10] Downgraded twice for high risk of bias
[11] Foster 2010; Moreno 2014
[12] I2 = 0%; not downgraded
[13] Moreno 2014; Foster 2010; Bazzano 2014
[14] Downgraded once as I2 was between 33.3% and 66.7% (I2 = 65%)
[15] Downgraded twice as 95%CI crosses two clinical decision thresholds (0.8 and 1.25)
[16] Foster 2010
[17] Downgraded twice as greater than 33.3% of the weight in the meta-analysis came from studies that were partially indirect.

[18] Downgraded once for partial indirectness.

Table 15. Very low carbohydrate diet + support vs No intervention

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Very low carb diet + support**	**No intervention**	**Relative (95% CI)**	**Absolute**		
Change in weight (kg) at 15 months from baseline. MID = 2.5 (follow-up 15 months; Better indicated by lower values)												
1[1]	randomised trials	very serious[2]	no serious inconsistency[3]	serious indirectness[5]	serious[4]	none	17	19	-	MD 3.7 lower (6.94 to 0.46 lower)	⊕OOO VERY LOW	CRITICAL

[1] Lim 2010
[2] Downgraded twice for high risk of bias
[3] Single study; inconsistency not applicable
[4] Downgraded once as 95%CI crosses one calculated MID
[5] Downgraded once for partial indirectness.

In people with type 2 diabetes

Table 16. Very low carbohydrate diet + support vs Usual care (diet) + support

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**T2DM Very low carb diet + support**	**Usual care + support**	**Relative (95% CI)**	**Absolute**		

Change in weight (kg) at 1 year from baseline. MID = 2.85 (follow-up 12 months; Better indicated by lower values)												
3[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	serious[9]	none	70	67	-	MD 0.83 higher (1.24 lower to 2.89 higher)	⊕OOO VERY LOW	CRITICAL
% Change HbA1c at 1 year from baseline. MID = 5% (follow-up 12 months; Better indicated by lower values)												
4[5]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	no serious inconsistency	none	98	107	-	MD 0.1 higher (0.18 lower to 0.37 higher)	⊕⊕OO LOW	IMPORTANT
Change in WC (cm) at 1 year from baseline. MID = 3.1 (follow-up 12 months; Better indicated by lower values)												
1[6]	randomised trials	serious[7]	no serious inconsistency[8]	no serious indirectness	serious[9]	none	41	37	-	MD 0.7 lower (3.58 lower to 2.18 higher)	⊕⊕OO LOW	IMPORTANT
Adherence at 1 yea. MID = 0.8 to 1.25 (follow-up 12 months)												
1[6]	randomised trials	serious[7]	no serious inconsistency[8]	no serious indirectness	very serious[10]	none	41/58 (70.7%)	37/57 (64.9%)	RR 1.09 (0.85 to 1.4)	58 more per 1000 (from 97 fewer to 260 more)	⊕OOO VERY LOW	IMPORTANT
Serious AEs at 1 year. MID = 0.8 to 1.25 (follow-up 12 months)												
1[11]	randomised trials	very serious[12]	no serious inconsistency[8]	no serious indirectness	very serious[10]	none	2/28 (7.1%)	3/40 (7.5%)	RR 0.95 (0.17 to 5.33)	4 fewer per 1000 (from 62 fewer to 325 more)	⊕OOO VERY LOW	CRITICAL
Change in weight (kg) at 2 years from baseline. MID = 2.8 (follow-up 2 years; Better indicated by lower values)												
1[13]	randomised trials	serious[7]	no serious inconsistency[8]	no serious indirectness	serious[9]	none	33	28	-	MD 0.2 lower (3.05 lower to 2.65 higher)	⊕⊕OO LOW	CRITICAL
% Change HbA1c at 2 years from baseline. MID = 5% (follow-up 2 years; Better indicated by lower values)												

2[14]	randomised trials	serious[15]	no serious inconsistency[3]	no serious indirectness	no serious inconsistency	none	61	68	-	MD 0.25 higher (0.1 lower to 0.6 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Adherence at 2 years. MID = 0.8 to 1.25 (follow-up 2 years)												
1[13]	randomised trials	serious[7]	no serious inconsistency[8]	no serious indirectness	very serious[10]	none	33/57 (57.9%)	28/58 (48.3%)	RR 1.2 (0.85 to 1.7)	97 more per 1000 (from 72 fewer to 338 more)	⊕OOO VERY LOW	IMPORTANCE
QoL (PAID questionnaire) Higher scores indicate higher distress at 1 year. MID = 0.95 (follow-up 12 months; Better indicated by lower values)												
1[16]	randomised trials	very serious[12]	no serious inconsistency[8]	no serious indirectness	no serious imprecision	none	41	37	-	MD 3.1 higher (2.28 to 3.92 higher)	⊕⊕OO LOW	CRITICAL
QoL (Diabetes-39 (Diabetes control)) Higher scores indicate greater impact on QoL at 1 year. MID = 1.4 (follow-up 12 months; Better indicated by lower values)												
1[16]	randomised trials	very serious[12]	no serious inconsistency[8]	no serious indirectness	no serious imprecision	none	41	37	-	MD 2.7 higher (1.46 to 3.94 higher)	⊕⊕OO LOW	CRITICAL
QoL (Diabetes-39 (Anxiety and worry)) Higher scores indicate greater impact on QoL at 1 year. MID = 1.95 (follow-up 12 months; Better indicated by lower values)												
1[16]	randomised trials	very serious[12]	no serious inconsistency[8]	no serious indirectness	no serious imprecision	none	41	37	-	MD 9.4 higher (7.69 to 11.11 higher)	⊕⊕OO LOW	CRITICAL
QoL (Diabetes-39 (Social burden)) Higher scores indicate greater impact on QoL at 1 year. MID = 1.15 (follow-up 12 months; Better indicated by lower values)												
1[16]	randomised trials	very serious[12]	no serious inconsistency[8]	no serious indirectness	no serious imprecision	none	41	37	-	MD 2.7 higher (1.68 to 3.72 higher)	⊕⊕OO LOW	CRITICAL
QoL (Diabetes-39 (Energy and Mobility)) Higher scores indicate greater impact on QoL at 1 year. MID = 1.15 (follow-up 12 months; Better indicated by lower values)												
1[16]	randomised trials	very serious[12]	no serious inconsistency[8]	no serious indirectness	no serious imprecision	none	41	37	-	MD 6.8 higher (5.78 to 7.82 higher)	⊕⊕OO LOW	CRITICAL

QoL (PAID questionnaire) Higher scores indicate higher distress at 2 years. MID = 1.07 (follow-up 2 years; Better indicated by lower values)												
1[17]	randomised trials	serious[7]	no serious inconsistency[8]	no serious indirectness	serious[9]	none	33	28	-	MD 0.32 lower (1.38 lower to 0.74 higher)	⊕⊕OO LOW	CRITICAL
QoL (Diabetes-39 (Diabetes control)) Higher scores indicate greater impact on QoL at 2 years. MID = 1.4 (follow-up 2 years; Better indicated by lower values)												
1[17]	randomised trials	serious[7]	no serious inconsistency[8]	no serious indirectness	no serious imprecision	none	33	28	-	MD 4.36 higher (2.99 to 5.73 higher)	⊕⊕⊕O MODERATE	CRITICAL
QoL (Diabetes-39 (Anxiety and worry)) Higher scores indicate greater impact on QoL at 2 years. MID = 1.86 (follow-up 2 years; Better indicated by lower values)												
1[17]	randomised trials	serious[7]	no serious inconsistency[8]	no serious indirectness	no serious imprecision	none	33	28	-	MD 9.7 higher (7.86 to 11.54 higher)	⊕⊕⊕O MODERATE	CRITICAL
QoL (Diabetes-39 (Social burden)) Higher scores indicate greater impact on QoL at 2 years. MID = 1.15 (follow-up 2 years; Better indicated by lower values)												
1[17]	randomised trials	serious[7]	no serious inconsistency[8]	no serious indirectness	serious[9]	none	33	28	-	MD 1.99 higher (0.86 to 3.12 higher)	⊕⊕OO LOW	CRITICAL
QoL (Diabetes-39 (Energy and Mobility)) Higher scores indicate greater impact on QoL at 2 years. MID = 1.28 (follow-up 2 years; Better indicated by lower values)												
1[16]	randomised trials	very serious[12]	no serious inconsistency[8]	no serious indirectness	serious[9]	none	41	37	-	MD 1.38 higher (0.27 to 2.49 higher)	⊕OOO VERY LOW	CRITICAL

[1] Goldstein 2011; Saslow 2017; Tay 2015
[2] Downgraded twice as greater than 33.3% of the weight in the meta-analysis came from studies at high risk of bias
[3] I2 = 0%; not downgraded
[5] Goldstein 2011; Iqbal 2010; Saslow 2017; Tay 2015
[6] Tay 2015
[7] Downgraded once for moderate risk of bias
[8] Single study; inconsistency not applicable
[9] Downgraded once as 95%CI crosses one calculated MID
[10] Downgraded twice as 95%CI crosses two clinical decision thresholds (0.8 and 1.25)
[11] Iqbal 2010

[12] Downgraded twice for high risk of bias
[13] Tay 2018
[14] Iqbal 2010; Tay 2018
[15] Downgraded once as greater than 33.3% of the weight in the meta-analysis came from studies at moderate risk of bias
[16] Brinkworth 2016b
[17] Kakoschke 2021

Intermittent energy restriction (IER) – 5:2 Diet

Mixed population

Table 17. IER (5:2 Diet) vs usual care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intermittent energy restriction (5:2 diet)	Usual care	Relative (95% CI)	Absolute		
Change in weight (kg) at 1 year from baseline. MID = 2.85 (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency[2]	no serious indirectness	no serious imprecision	none	100	100	-	MD 0.1 lower (1.57 lower to 1.37 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Adherence at 1 year. MID = 0.8 to 1.25 (follow-up 12 months)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency[2]	no serious indirectness	very serious[4]	none	56/100 (56%)	48/100 (48%)	RR 1.17 (0.89 to 1.53)	82 more per 1000 (from 53 fewer to 254 more)	⊕⊕OO LOW	IMPORTANT

[1] Hajek 2021
[2] Single study; inconsistency not applicable
[3] Downgraded twice as 95%CI crosses two clinical decision thresholds (0.8 and 1.25)

Table 18. IER (5:2 diet) + support vs Usual care (advice)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Intermittent energy restriction (5:2 diet) + support**	**Usual care (advice)**	**Relative (95% CI)**	**Absolute**		
Change in weight (kg) at 1 year from baseline. MID = 2.85 (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency[2]	no serious indirectness	no serious imprecision	none	100	100	-	MD 0.8 lower (2.24 lower to 0.64 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Adherence at 1 year. MID = 0.8 to 1.25 (follow-up 12 months)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency[2]	no serious indirectness	serious[4]	none	45/100 (45%)	48/100 (48%)	RR 0.94 (0.7 to 1.26)	29 fewer per 1000 (from 144 fewer to 125 more)	⊕⊕OO LOW	IMPORTANT

[1] Hajek 2021
[2] Single study; inconsistency not applicable
[3] Downgraded once as 95%CI crosses one clinical decision thresholds (1.25)

Table 19. IER (5:2 diet) + support vs Usual care (advice) + support

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Intermittent energy restriction (5:2 diet) + support**	**Usual care (advice) + support**	**Relative (95% CI)**	**Absolute**		
Change in weight (kg) at 1 year from baseline. MID = 6.86 (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	49	52	-	MD 2.9 lower (8.83 lower to 3.03 higher)	⊕⊕OO LOW	CRITICAL

Change in WC (cm) at 1 year from baseline. MID = 5.5 (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	49	52	-	MD 2 lower (6.72 lower to 2.72 higher)	⊕⊕OO LOW	IMPORTANT

[1] Schubel 2018 (HELENA Trial)
[2] Downgraded once for moderate risk of bias
[3] Single study; inconsistency not applicable
[4] Downgraded once as 95%CI crosses one calculated MID

Table 20. IER (5:2 diet) + support vs Usual care (diet) + support

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intermittent energy restriction (5:2 diet) + support	Usual care (diet) + support	Relative (95% CI)	Absolute		
Change in weight (kg) at 1 year from baseline. MID = 5.5 (follow-up 12 months; Better indicated by lower values)												
2[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	103	107	-	MD 0.89 higher (1.45 lower to 3.22 higher)	⊕⊕OO LOW	CRITICAL
Change in weight (kg) at 2 years from baseline. MID = 0.6 (follow-up 2 years; Better indicated by lower values)												
1[5]	randomised trials	serious[6]	no serious inconsistency[7]	no serious indirectness	very serious[8]	none	32	38	-	MD 0.7 lower (6.5 lower to 5.1 higher)	⊕OOO VERY LOW	CRITICAL
Change in WC (cm) at 1 year from baseline. MID = 4.6 (follow-up 12 months; Better indicated by lower values)												
2[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	103	110	-	MD 0.81 higher (1.24 lower to 2.86 higher)	⊕⊕OO LOW	IMPORTANT

[1] Schubel 2018 (HELENA Trial); Sundfor 2018
[2] Downgraded twice as greater than 33.3% of the weight in the meta-analysis came from studies at high risk of bias
[3] I2 = 0%; not downgraded
[5] Pannen 2021 (HELENA Trial)
[6] Downgraded once for moderate risk of bias
[7] Single study; inconsistency not applicable
[8] Downgraded twice as 95%CI crosses two calculated MIDs

In people with type 2 diabetes

Table 21. IER (5:2 diet) + support vs Usual care (diet) + support

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**T2DM Intermittent energy restriction (5:2 diet) + support**	**Usual care (diet) + support**	**Relative (95% CI)**	**Absolute**		
Change in weight (kg) at 1 year from baseline. MID = 3.28 (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	70	67	-	MD 1.8 lower (4.09 lower to 0.49 higher)	⊕OOO VERY LOW	CRITICAL
Change in weight (kg) at 2 years from baseline. MID = 4.5 (follow-up 2 years; Better indicated by lower values)												
1[5]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	70	67	-	MD 0 higher (2.99 lower to 2.99 higher)	⊕⊕OO LOW	CRITICAL
% change in HbA1c at 1 year from baseline. MID = 5% (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	70	67	-	MD 0.2 lower (0.62 lower to 0.22 higher)	⊕⊕OO LOW	IMPORTANT
% change in HbA1c at 2 years from baseline. MID = 5% (follow-up 2 years; Better indicated by lower values)												

1[5]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	70	67	-	MD 0.3 lower (1.01 lower to 0.41 higher)	⊕⊕OO LOW	IMPORTANT

[1] Carter 2018
[2] Downgraded twice for high risk of bias
[3] Single study; inconsistency not applicable
[4] Downgraded once as 95%CI crosses one calculated MID
[5] Carter 2019

Table 22. IER (5:2 diet) + support vs Low energy TOTAL MR + support

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**T2DM Intermittent energy restriction (5:2 diet) + support**	**Low energy TOTAL MR + support**	**Relative (95% CI)**	**Absolute**		
Change in weight (kg) at 1 year from baseline. MID = 2.9 (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	39	40	-	MD 1.1 higher (1.57 lower to 3.77 higher)	⊕⊕OO LOW	CRITICAL
Change in HbA1c at 1 year from baseline. MID = 5 mmol/mol (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	39	40	-	MD 0.6 higher (4.26 lower to 5.46 higher)	⊕⊕OO LOW	IMPORTANT
Serious AEs at 1 year from baseline. MID = 0.8 to 1.25 (follow-up 12 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	very serious[5]	none	4/39 (10.3%)	4/40 (10%)	RR 1.03 (0.28 to 3.82)	3 more per 1000 (from 72 fewer to 282 more)	⊕OOO VERY LOW	CRITICAL

Adherence at 1 year from baseline. MID = 0.8 to 1.25 (follow-up 12 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness	serious[6]	none	27/39 (69.2%)	30/40 (75%)	RR 0.92 (0.7 to 1.22)	60 fewer per 1000 (from 225 fewer to 165 more)	⊕⊕OO LOW	IMPORTANT

[1] McDiamid 2022
[2] Downgraded once for moderate risk of bias
[3] Single study; inconsistency not applicable
[4] Downgraded once as 95%CI crosses one calculated MID
[5] Downgraded twice as 95%CI crosses two clinical decision thresholds (0.8 and 1.25)
[6] Downgraded once as 95%CI crosses one clinical decision threshold (0.8)

Intermittent energy restriction (IER) – Alternate day fasting (ADF) Diet

Mixed population

Table 23. Intermittent energy restriction (ADF diet) + support vs Usual care (diet) + support

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intermittent energy restriction (ADF diet) + support	Usual care (diet) + support	Relative (95% CI)	Absolute		
% Change in weight from baseline at 1 year. MID = 5% (follow-up 12 months; Better indicated by lower values)												
2[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	no serious imprecision	none	46	49	-	MD 0.06 lower (0.78 lower to 0.65 higher)	⊕⊕OO LOW	CRITICAL
% Change in weight from baseline at 1 year - Mixed population (males + females). MID = 5% (follow-up 12 months; Better indicated by lower values)												
1[5]	randomised trials	very serious[6]	no serious inconsistency[7]	no serious indirectness	no serious imprecision	none	34	31	-	MD 0.7 lower (3.1 lower to 1.7 higher)	⊕⊕OO LOW	CRITICAL

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intermittent energy restriction	No intervention	Relative (95% CI)	Absolute	Quality	Importance
% Change in weight from baseline at 1 year - Females only. MID = 5% (follow-up 12 months; Better indicated by lower values)												
1[8]	randomised trials	very serious[6]	no serious inconsistency[7]	no serious indirectness	no serious imprecision	none	12	18	-	MD 0 higher (0.75 lower to 0.75 higher)	⊕⊕OO LOW	CRITICAL

[1] Trepanowski 2017; Oustric 2021
[2] Downgraded twice as greater than 33.3% of the weight in the meta-analysis came from studies at high risk of bias
[3] I2 = 0%; not downgraded
[5] Trepanowski 2017
[6] Downgraded twice for high risk of bias
[7] Single study; inconsistency not applicable
[8] Oustric 2021

Table 24. Intermittent energy restriction (ADF diet) + support vs No intervention

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Intermittent energy restriction (ADF diet) + support**	**No intervention**	**Relative (95% CI)**	**Absolute**		
% Change in weight from baseline at 1 year. MID = 5% (follow-up 12 months; Better indicated by lower values)												
1[1]	randomised trials	very serious[2]	no serious inconsistency[3]	no serious indirectness	serious[4]	none	34	31	-	MD 6 lower (8.5 to 3.5 lower)	⊕OOO VERY LOW	CRITICAL

[1] Trepanowski 2017
[2] Downgraded twice for high risk of bias
[3] Single study; inconsistency not applicable
[4] Downgraded once as 95%CI crosses one clinical decision threshold

Intermittent energy restriction (IER) – Time restricted eating (TRE)

Mixed population

Table 25. Intermittent energy restriction (TRE) + support vs Usual care (diet) + support

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intermittent energy restriction (TRE) + support	Usual care (diet) + support	Relative (95% CI)	Absolute		
Change in weight (kg) from end of baseline. MID = 2.5 (follow-up 12 months; Better indicated by lower values)												
2[1]	randomised trials	very serious[2]	very serious[3]	no serious indirectness	serious[4]	none	34	30	-	MD 1.33 lower (3.91 lower to 1.25 higher)	⊕OOO VERY LOW	CRITICAL
Change in weight (kg) from end of baseline - Males only. MID = 2.2 (follow-up 12 months; Better indicated by lower values)												
1[5]	randomised trials	very serious[6]	no serious inconsistency[7]	no serious indirectness	no serious imprecision	none	15	13	-	MD 8.1 lower (12.54 to 3.66 lower)	⊕⊕OO LOW	CRITICAL
Change in weight (kg) from end of baseline - Females only. MID = 2.8 (follow-up 12 months; Better indicated by lower values)												
1[8]	randomised trials	very serious[6]	no serious inconsistency[7]	no serious indirectness	serious[4]	none	19	17	-	MD 2.1 higher (1.06 lower to 5.26 higher)	⊕OOO VERY LOW	CRITICAL
Change in waist circumference (cm) from end of baseline to 1 year - Females only. MID = 2.8 (follow-up 12 months; Better indicated by lower values)												
1[8]	randomised trials	very serious[6]	no serious inconsistency[7]	no serious indirectness	very serious[9]	none	19	17	-	MD 0.4 lower (3.61 lower to 2.81 higher)	⊕OOO VERY LOW	IMPORTANT

[1] Byrne 2018; Keogh 2014
[2] Downgraded twice as greater than 33.3% of the weight in the meta-analysis came from studies at high risk of bias
[3] Downgraded twice as I2 > 66.7% (I2 = 93%)

[4] Downgraded once as 95%CI crosses one calculated MID
[5] Byrne 2018
[6] Downgraded twice for high risk of bias
[7] Single study; inconsistency not applicable
[8] Keogh 2014
[9] Downgraded twice as 95%CI crosses two calculated MIDs

Intermittent energy restriction (IER) – Intermittent fasting

Mixed population

Table 26. Intermittent energy restriction (iTRE): intermittent fasting vs standard care (weight loss booklet)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Intermittent energy restriction (iTRE): intermittent fasting**	**Habitual meal timings**	**Relative (95% CI)**	**Absolute**		
HbA1c % change from baseline – 18 months. MID = 5% (Better indicated by lower values)												
1[1]	randomised trials	Serious[6]	no serious inconsistency[2]	no serious indirectness	No serious imprecision	none	85	41	-	MD -0.06 lower (-0.15 lower to 0.03 higher)	⊕⊕⊕O MODERATE	Important
Body weight (kg) change from baseline – 18 months. MID = 4 (Better indicated by lower values)												
1[1]	randomised trials	Serious[6]	no serious inconsistency[2]	no serious indirectness	Serious imprecision[3]	none	85	41	-	MD -1.72 lower (-4.79 lower to 1.35 higher)	⊕⊕OO LOW	Critical

Number with at least one serious adverse event. MID = 0.8 to 1.25 (18 month follow up)												
1[1]	randomised trials	Serious[6]	no serious inconsistency[2]	no serious indirectness	Very serious imprecision[4]	none	2/85 (2.4%)	0/41 (0%)	RR 2.44 (0.12, 49.73)		⊕OOO VERY LOW	Critical
Number with at least one adverse event. MID = 0.8 to 1.25 (18 month follow up)												
1[1]	randomised trials	Serious[6]	no serious inconsistency[2]	no serious indirectness	Serious imprecision[5]	none	31/85 (36%)	6/41 (14.6%)	RR 2.49 (1.13, 5.50)		⊕⊕OO LOW	Critical
Constipation. MID = 0.8 to 1.25 (18 month follow up)												
1[1]	randomised trials	Serious[6]	no serious inconsistency[2]	no serious indirectness	Very serious imprecision[4]	none	6/85 (7.1%)	3/41 (7.3%)	RR 0.96 (0.25, 3.67)		⊕OOO VERY LOW	Critical

1. Teong 2023
2. Single study; inconsistency not applicable
3. Downgraded once as 95%CI crosses one calculated MID
4. Downgraded twice as 95%CI crosses two clinical decision thresholds (0.8 and 1.25)
5. Downgraded twice as 95%CI crosses one clinical decision thresholds (1.25)
6. Downgraded once due to moderate risk of bias

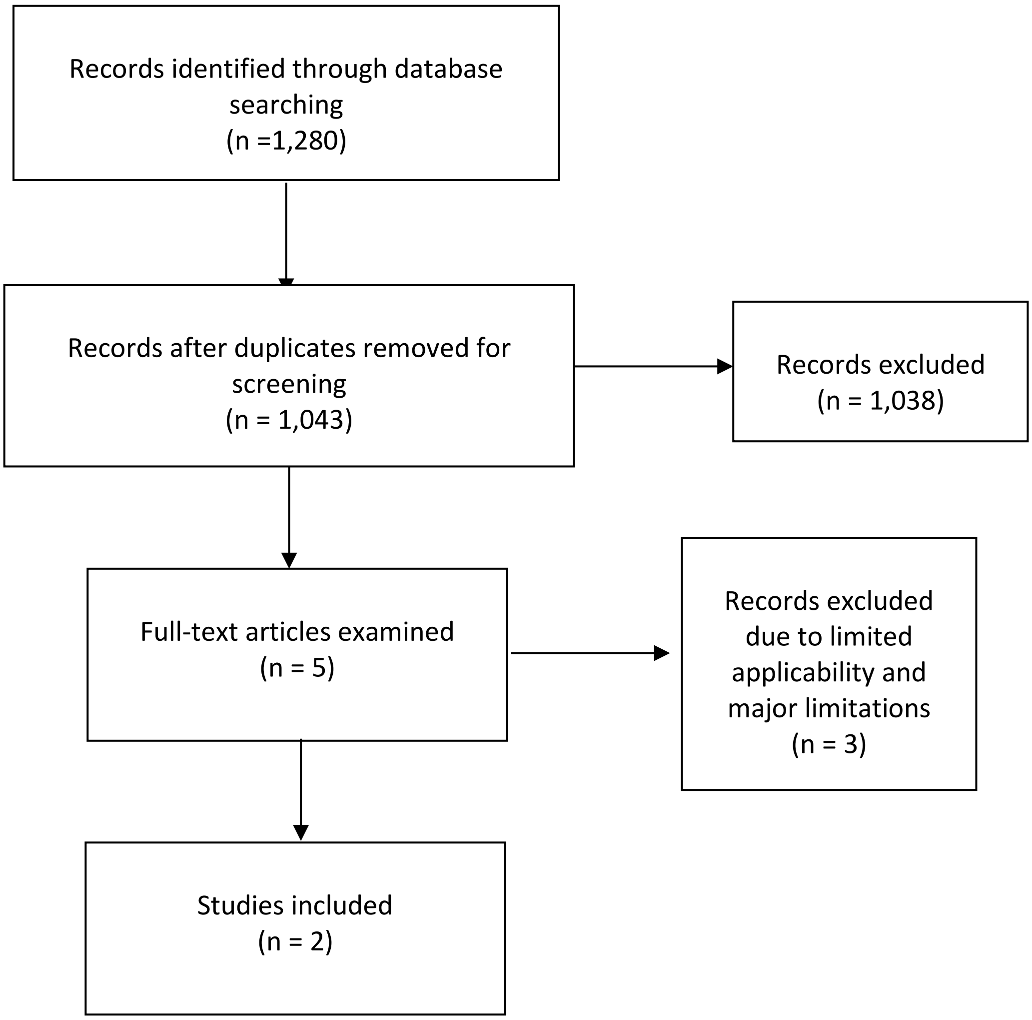
Table 27. Intermittent energy restriction (iTRE): intermittent fasting vs habitual meal timings

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Intermittent energy restriction (iTRE): intermittent fasting**	**Standard care (weight loss booklet)**	**Relative (95% CI)**	**Absolute**		
Weight change from baseline to 12 months (kg) MID = 3 (Better indicated by lower values)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency[2]	no serious indirectness	Serious imprecision[3]	None	45	43	-	MD -0.60 -3.21 lower to 2.01 higher)	⊕⊕⊕O MODERATE	Critical

Waist circumference from baseline to 12 months (cm) MID = 3.2 (Better indicated by lower values)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency[2]	no serious indirectness	Serious imprecision[3]	None	45	43	-	MD -1.10 (-3.92 lower to 1.72 higher)	⊕⊕⊕O MODERATE	Important
Constipation at 12 months. MID = 0.8 – 1.25 (Better indicated by lower values)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency[2]	no serious indirectness	Very serious imprecision[4]	None	2/45 (4.4%)	0/43 (0%)	RR 4.78 (0.24-96.84)		⊕⊕OO LOW	Critical

1. Wei 2023
2. Single study; inconsistency not applicable
3. Downgraded once as 95%CI crosses one calculated MID
4. Downgraded twice as 95%CI crosses two clinical decision thresholds (0.8 and 1.25)

Appendix G - Economic evidence study selection



Appendix H Economic evidence tables

Table 1: Xin et al. (2020)

Xin et al. (2020). Type 2 diabetes remission: 2 year within-trial and lifetime-horizon cost-effectiveness of the Diabetes Remission Clinical Trial (DiRECT)/Counterweight-Plus weight management programme	
Study details	**Analysis:** Cost-effectiveness and cost-utility analysis **Approach to analysis:** The cost-effectiveness analysis was a within-trial analysis based on the 2 years follow-up data from the DiRECT trial using intervention costs and healthcare resource use measured during the time of the study. The cost-utility analysis was a lifetime analysis developed by predicting time to relapse among those in remission at 2 years and applying mean management costs of diabetes. **Complications considered:** Type 2 diabetes **Time horizon:** 2 years and lifetime **Discounting:** Costs: 3.5%; Outcomes: 3.5% **Setting:** UK NHS health care perspective
Interventions	**Intervention 1:** Counterweight-plus intervention – total diet replacement (TDS), food reintroduction (FR), weight loss maintenance (WLM) behavioural therapy and anti-obesity medication **Intervention 2:** Standard Care (in accordance with guidelines)
Population	**Population:** Adults living with overweight or obesity (BMI = 27 - 45kg/m²) with type 2 diabetes**.** Mean age: 54; Mean BMI: 34.7 kg/m²; 41% females
Data sources	**Baseline/natural history:** Baseline natural history was informed from the DiRECT study. Mortality in people with diabetes was estimated using a population-based observational study conducted in Scotland. **Incidence of long-term conditions:** The proportion of people remaining in remission was estimated based on the rate of relapse observed in year 2. By year 10, all people were assumed to have relapsed. **Effectiveness:** Effectiveness was based on the 2 years data from DiRECT. The trial found the 35.6% of people who received the intervention achieved remission at 2 years compared to 3.4% in the control group.

Xin et al. (2020). Type 2 diabetes remission: 2 year within-trial and lifetime-horizon cost-effectiveness of the Diabetes Remission Clinical Trial (DiRECT)/Counterweight-Plus weight management programme	
	Resource use & Costs: The cost of the intervention, including training, low-energy formula, monitoring appointment and workbooks, was calculated using trial resource use and UK unit costs. The cost of diabetes-related healthcare was compiled from the measured costs for the first 2 years of DiRECT and includes: medication, primary and secondary care attendance, and hospitalisation. Long-term diabetes-related healthcare costs were assumed to increase linearly with duration of diabetes until 15 years after the study. **QoL:** QALYs in people in remission were calculated by applying standard UK age-dependent EQ-5D-5L utility population norms (Ara & Brazier 2010). For people not in remission, age-dependent health state utilities were reduced using a constant multiplier based on Sullivan et al. (2011)
Base-case results	(see table below)
Sensitivity analyses	**Deterministic:** Several scenario analyses with different assumptions on relapses, time-horizon, remission rates, QoL reduction, mortality and long-term costs. Moreover, the model was run for men and women separately. In all scenarios, the intervention remained dominant. **Probabilistic:** A probabilistic sensitivity analysis using Monte Carlo simulation was conducted. In the two-year time horizon, the intervention costs £4,212 per remission using the upper confidence interval (95%) and was dominant using the lower confidence interval (95%). For a lifetime horizon, the intervention was dominant in all the simulations.

Base-case results:

Intervention	Absolute		Incremental		
Within-trial analysis (2-year time horizon)	**Costs (£)**	**Proportion of remission (%)**	**Costs (£)**	**Proportion of remission, %**	**ICER (£)**
Standard Care	2,420	3.4	-	-	-
TDR (Counterweight-Plus intervention)	3,036	35.6	616	32.3	1,907 per remission
Lifetime time horizon	**Costs (£)**	**QALYs**	**Costs (£)**	**QALYs**	**ICER (£)**
Standard Care	34,283	11.22	-	-	-
TDR (Counterweight-Plus intervention)	32,947	11.27	-1,337	0.06	Dominant

Xin et al. (2020). Type 2 diabetes remission: 2 year within-trial and lifetime-horizon cost-effectiveness of the Diabetes Remission Clinical Trial (DiRECT)/Counterweight-Plus weight management programme	
Comments	**Source of funding:** Direct trial is funded by Diabetes UK with support provided by Cambridge Weigh Plan to Counterweright Ltd. The economic analysis was funded by a separate project gran from Diabetes UK. **Limitations:** Minor limitations (Table 7)
	Overall applicability: Directly applicable **Overall quality:** Potentially serious limitations

Table 2: Kent et al. (2019)

Kent et al. (2021). Is Doctor Referral to a Low-Energy Total Diet Replacement Program Cost-Effective for the Routine Treatment of Obesity?	
Study details	**Analysis:** Cost-utility analysis **Approach to analysis:** A cost-utility analysis based on data from the DROPLET trial. Data from the DROPLET trial was incorporated into an adapted version of the PRIMEtime Cost-Effectiveness Obesity model. PRIMEtime is a population-based, proportional multistate life table model which links BMI to mortality and related diseases. **BMI related complications considered:** Type 2 diabetes, coronary heart disease, stroke, and cancers of the breast, colon, liver, kidney, and pancreas **Time horizon:** Lifetime **Discounting: C**osts: 1.5%; Outcomes: 1.5% **Setting:** UK NHS health care perspective
Interventions	**Intervention 1:** Nurse-led behavioural support program **Intervention 2:** Total diet replacement (TDR)
Population	**Population:** A hypothetical cohort of adults with obesity, age and sex distribution matching the DROPLET study: Mean age of 47 (SD 13) in men and 50 (SD 13) in women. Mean BMI of 37.2 (SD 5.4).
Data sources	**Baseline/natural history:** Baseline natural history was informed from the DROPLET study. Additionally, prevalence was generated as detailed below using DISMOD II to generate internally consistent results. BMI distributions were from the Health Survey of England 2014. **Incidence of long-term conditions:** DISMOD II was used to generate internally consistent estimates of baseline disease prevalence, disease incidence, and case-fatality by sex and 1-year age intervals. Data for coronary heart disease was from Hospital Episode Statistics (HES), ONS mortality statistics and data from the OXVASC study. Stroke incidence was from the OXVASC study and general practice

Kent et al. (2021). Is Doctor Referral to a Low-Energy Total Diet Replacement Program Cost-Effective for the Routine Treatment of Obesity?	
	research datalink. Type-2 diabetes data was sources from the clinical practice research datalink (CPRD) and national diabetes audit. Cirrhosis data was sourced from CPRD data and HES. Finally, cancer incidence was sourced from cancer registration statistics. **Effectiveness:** Effectiveness of the TDR program comes from the DROPLET trial. At 12 months, TDR versus a nurse-led behavioural support program had a weight reduction presented in the form of a mean difference in BMI of 2.3 kg/m^2 in men and 2.7 kg/m^2 in women. Data from the DROPLET trial was limited to twelve months, therefore authors present 2 weight regain scenarios: 1) weight returns to baseline in a linear fashion from 1-5 years for those in treatment arms; 2) a 1-kg weight loss relative to baseline weight is maintained beyond 5 years for those in the TDR arm and weight reaches these levels from 12 months in an approximately linear fashion. **Resource use & Costs:** NHS costs per prevalent case of disease are estimate from Programme Budgeting Returns (PBR) for coronary heart disease, stroke, type-2 diabetes, breast cancer, colon cancer, liver cancer, kidney cancer and pancreatic cancer. These are calculated by dividing total expenditure by disease category by estimated age-standardized disease prevalence in the UK population. For TDR, intervention costs were based upon the average number of sessions attended and average number of products dispensed which in turn were used to calculate a mean total cost. For nurse-led behavioural support, intervention costs were based upon the cost of time with a general practitioner and 4 attendances with a nurse practitioner over 12 weeks. **QoL:** EQ-5D-5L utility was modelled as a function of age, sex, and disease incidence and prevalence, based on estimates presented in Sullivan et al (2011).
Base-case results	(see table below)

Intervention	Absolute		Incremental		
	Costs (£)	QALYs	Costs (£)	QALYs	ICER (£)
Nurse-led behavioural support program	£7,425	23.19	-	-	-
Total diet replacement (TDR)	£8,090	23.26	£665	0.065	£12,955

Kent et al. (2021). Is Doctor Referral to a Low-Energy Total Diet Replacement Program Cost-Effective for the Routine Treatment of Obesity?	
Sensitivity analyses	**Deterministic:** Scenario analyses were performed for different combinations of the rate of weight regain, total diet replacement program costs, discount rates, adding further health care costs, modelling a direct effect on weight loss EQ-5D-5L utility values, and applying the treatment to the general UK population. Total diet replacement remained cost-effective in all the above scenarios at a threshold of £20,000 per QALY **Probabilistic:** A probabilistic sensitivity analysis using Monte Carlo simulation was conducted. The 95% confidence intervals around the ICER ranged from £8,082 to £17,827 per QALY gained.
Comments	**Source of funding:** This study was funded through a research grant from Cambridge Weight Plan UK Ltd. to the University of Oxford and was also supported by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care Oxford at Oxford Health National Health Service (NHS) Foundation Trust. All authors are supported by the Oxford NIHR Biomedical Research Centre. **Limitations:** Minor limitations (Table 7)
	Overall applicability: Directly applicable **Overall quality:** Potentially serious limitations

Table 4: Applicability checklist

Study	1.1 Is the study population appropriate for the review question?	1.2 Are the interventions appropriate for the review question?	1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	1.4 Is the perspective for costs appropriate for the review question?	1.5 Is the perspective for outcomes appropriate for the review question?	1.6 Are all future costs and outcomes discounted appropriately?	1.7 Are QALYs, derived using NICE's preferred methods, or an appropriate social care-related equivalent used as an outcome?	1.8 Overall judgement
Xin et al. (2020)	Yes: subgroup analysis on people with type 2 diabetes.	Yes: low-energy formula diet, monitoring and education	Yes: UK	Yes (UK based study with an NHS perspective)	Yes	Yes: 3.5%	Yes: UK EQ-5D scores	Directly applicable

Study	1.1 Is the study population appropriate for the review question?	1.2 Are the interventions appropriate for the review question?	1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	1.4 Is the perspective for costs appropriate for the review question?	1.5 Is the perspective for outcomes appropriate for the review question?	1.6 Are all future costs and outcomes discounted appropriately?	1.7 Are QALYs, derived using NICE's preferred methods, or an appropriate social care-related equivalent used as an outcome?	1.8 Overall judgement
Kent et al. (2019)	Yes	Yes	Yes: UK	Yes (UK based study with an NHS perspective)	Yes	Yes (Discounted at 1.5%. A discount rate of 3.5% was used in sensitivity analysis)	Yes: UK EQ-5D scores	Directly applicable

Table 5: Limitations checklist

Study	2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	2.3 Are all important and relevant outcomes included?	2.4 Are the estimates of baseline outcomes from the best available source?	2.5 Are the estimates of relative intervention effects from the best available source?	2.6 Are all important and relevant costs included?	2.7 Are the estimates of resource use from the best available source?	2.8 Are the unit costs of resources from the best available source?	2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	2.11 Has no potential financial conflict of interest been declared?	2.12 Overall assessment
Xin et al. (2020)	Yes	Yes (Lifetime)	Partly (the analysis focused on	Partly (sourced from the trial)	Partly (sourced from the trial. 2 year	Partly (only diabetes-related	Yes (trial and UK sources)	Yes (UK specific sources	Yes	Yes	Yes	Potentially serious limitations

Study	2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	2.3 Are all important and relevant outcomes included?	2.4 Are the estimates of baseline outcomes from the best available source?	2.5 Are the estimates of relative intervention effects from the best available source?	2.6 Are all important and relevant costs included?	2.7 Are the estimates of resource use from the best available source?	2.8 Are the unit costs of resources from the best available source?	2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	2.11 Has no potential financial conflict of interest been declared?	2.12 Overall assessment
			diabetes events only and did not include all obesity-related outcomes)		data may not be enough to estimate lifetime risk of relapse, remission or weight regain)	outcomes. Not all outcomes included.)		have been used)				
Kent et al. (2019)	Yes	Yes (Lifetime)	Yes	Yes	Partly (The model relies on assumptions around weight regain. It is possible that different trajectories could lead to different outcomes).	Yes	Yes	Yes	Yes	Yes	Yes	Potentially serious limitations

Appendix I Economic model

See the economic report on evidence review F.

Appendix J – Excluded studies

Clinical studies

Excluded systematic reviews

Study	Reason
Abboud, M., Alanouti, F., Georgaki, E. et al. (2021) Effect of ketogenic diet on quality of life in adults with chronic disease: A systematic review of randomized controlled trials. Nutrients 13(12): 4463	- Incorrect population *Adults with chronic disease rather than people necessarily living with overweight ot obesity and no meta-analysis performed*
Abe, T., Song, J.S., Bell, Z.W. et al. (2022) Comparisons of calorie restriction and structured exercise on reductions in visceral and abdominal subcutaneous adipose tissue: a systematic review. European Journal of Clinical Nutrition 76(2): 184-195	- Study does not contain a relevant intervention *This study looked more broadly at diet through calorie restriction rather than the diet categories utilised in this current review*
Alarim, RA, Alasmre, FA, Alotaibi, HA et al. (2020) Effects of the Ketogenic Diet on Glycemic Control in Diabetic Patients: Meta-Analysis of Clinical Trials. Cureus 12(10): e10796	- More appropriate systematic review included for this diet *Only 4 studies were included*
Alexandraki, I.; Palacio, C.; Mooradian, A.D. (2015) Relative merits of low-carbohydrate versus low-fat diet in managing obesity. Southern Medical Journal 108(7): 401-416	- More recent systematic review included that covers the same topic
Alhamdan, B.A., Garcia-Alvarez, A., Alzahrnai, A.H. et al. (2016) Alternate-day versus daily energy restriction diets: which is more effective for weight loss? A systematic review and meta-analysis. Obesity Science and Practice 2(3): 293-302	- More recent systematic review included that covers the same topic
Allaf, M., Elghazaly, H., Mohamed, O.G. et al. (2021) Intermittent fasting for the prevention of cardiovascular disease. Cochrane Database of Systematic Reviews 2021(1): cd013496	- Incorrect population *Purpose of the study is prevention of cardiovascular disease and the populations in*

Study	Reason
	the included studies were not limited to people living with overweight or obesity. Studies checked for inclusion in this review.
American College of Cardiology/American Heart Association Task Force on Practice Guidelines, Obesity Expert Panel, 2013 (2014) Executive summary: Guidelines (2013) for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Obesity Society published by the Obesity Society and American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Based on a systematic review from the The Obesity Expert Panel, 2013. Obesity (Silver Spring, Md.) 22suppl2: 5-39	- Not a relevant study design *Summary and rationale of US guidelines on management of overweight and obesity in adults*
Amini, M.R., Aminianfar, A., Naghshi, S. et al. (2021) The effect of ketogenic diet on body composition and anthropometric measures: A systematic review and meta-analysis of randomized controlled trials. Critical reviews in food science and nutrition: 1-14	- Incorrect population *Half of the included studies were not necessarily in people living with overweight or obesity*
Amiri, M., Karabegovic, I., van Westing, A.C. et al. (2022) Whole-diet interventions and cardiovascular risk factors in postmenopausal women: A systematic review of controlled clinical trials. Maturitas 155: 40-53	- Incorrect population *Broad mix of diets often in people living without overweight and obesity. No meta-analysis undertaken for this systematic review.*
Anton, S.D., Hida, A., Heekin, K. et al. (2017) Effects of popular diets without specific calorie targets on weight loss outcomes: Systematic review of findings from clinical trials. Nutrients 9(8): 822	- Study does not contain a relevant intervention *Diets without specific calories restrictions were evaluated. No meta-analysis undertaken for this systematic review.*
Apekey, Tanefa A, Maynard, Maria J, Kittana, Monia et al. (2022) Comparison of the Effectiveness of Low Carbohydrate Versus Low Fat Diets, in Type 2 Diabetes: Systematic Review and Meta-Analysis of Randomized Controlled Trials. Nutrients 14(20)	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
Ashtary-Larky, D, Bagheri, R, Tinsley, GM et al. (2021) Effects of intermittent fasting combined with resistance training on body composition: a	- Incorrect population *Populations in the included studies do not live with overweight or obesity*

Study	Reason
systematic review and meta-analysis. Physiology & behavior 237: 113453	
Atallah, R., Filion, K.B., Wakil, S.M. et al. (2014) Long-term effects of 4 popular diets on weight loss and cardiovascular risk factors: A systematic review of randomized controlled trials. Circulation: Cardiovascular Quality and Outcomes 7(6): 815-827	- More recent systematic review included that covers the same topic *No meta-analysis undertaken for this systematic review.*
Austin, G.; Ferguson, J.J.A.; Garg, M.L. (2021) Effects of plant-based diets on weight status in type 2 diabetes: A systematic review and meta-analysis of randomised controlled trials. Nutrients 13(11): 4099	- Study does not contain a relevant intervention *The plant based diets mainly do not include a calorie deficit*
Barnard, N.D.; Levin, S.M.; Yokoyama, Y. (2015) A systematic review and meta-analysis of changes in body weight in clinical trials of vegetarian diets. Journal of the Academy of Nutrition and Dietetics 115(6): 954-969	- Incorrect population *4 studies were included in the meta-analysis and 2 were in people with Rheumatoid Arthritis who may not be living with overweight or obesity. In addition, few of the vegetarian diets appeared to have a calorie deficit*
Bendall, C.L., Mayr, H.L., Opie, R.S. et al. (2018) Central obesity and the Mediterranean diet: A systematic review of intervention trials. Critical reviews in food science and nutrition 58(18): 3070-3084	- More recent systematic review included that covers the same topic *No meta-analysis undertaken*
Berild, A; Holven, KB; Ulven, SM (2017) Recommended Nordic diet and risk markers for cardiovascular disease. Tidsskrift for den Norske laegeforening : tidsskrift for praktisk medicin, ny raekke 137(10): 721-726	- Study does not contain a relevant intervention *Nordic diet*
Borgundvaag, E.; Mak, J.; Kramer, C.K. (2021) Metabolic Impact of Intermittent Fasting in Patients with Type 2 Diabetes Mellitus: A Systematic Review and Meta-analysis of Interventional Studies. Journal of Clinical Endocrinology and Metabolism 106(3): 902-911	- Systematic review used as source of primary studies
Bruinsma, T.J., Dyer, A.-M., Rogers, C.J. et al. (2021) Effects of diet and exercise-induced weight loss on biomarkers of inflammation in breast cancer survivors: A systematic review	- Incorrect outcomes *Dieting linked to breast cancer recurrence rather than weight loss for people with overweight or obesity*

Study	Reason
and meta-analysis. Cancer Epidemiology Biomarkers and Prevention 30(6): 1048-1062	
Caristia, S., De Vito, M., Sarro, A. et al. (2020) Is caloric restriction associated with better healthy aging outcomes? A systematic review and meta- analysis of randomized controlled trials. Nutrients 12(8): 1-19	- Study does not contain a relevant intervention *Diet linked to calorie restriction with no total or partial replacement. The population included in each included study was not specified to be living with overweight or obesity*
Carter, P., Achana, F., Troughton, J. et al. (2014) A Mediterranean diet improves HbA1c but not fasting blood glucose compared to alternative dietary strategies: a network meta-analysis. Journal of human nutrition and dietetics : the official journal of the British Dietetic Association 27(3): 280-297	- Study does not contain a relevant intervention *Mediterranean diet*
Castellana, M., Conte, E., Cignarelli, A. et al. (2020) Efficacy and safety of very low calorie ketogenic diet (VLCKD) in patients with overweight and obesity: A systematic review and meta-analysis. Reviews in Endocrine and Metabolic Disorders 21(1): 5-16	- More recent systematic review included that covers the same topic
Chawla, S., Silva, F.T., Medeiros, S.A. et al. (2020) The effect of low-fat and low-carbohydrate diets on weight loss and lipid levels: A systematic review and meta-analysis. Nutrients 12(12): 1-21	- More recent systematic review included that covers the same topic
Chen, J.-H., Lu, L.W., Ge, Q. et al. (2021) Missing puzzle pieces of time-restricted-eating (TRE) as a long-term weight-loss strategy in overweight and obese people? A systematic review and meta-analysis of randomized controlled trials. Critical reviews in food science and nutrition: 1-17	- More appropriate systematic review included for this diet *Follow-up was often reported for less than 12 months after the intervention*
Chen, Weiyi, Liu, Xiaoli, Bao, Lei et al. (2023) Health effects of the time-restricted eating in adults with obesity: A systematic review and meta-analysis. Frontiers in nutrition 10: 1079250	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
Chew, Han Shi Jocelyn, Ang, Wei How Darryl, Tan, Zhen Yang Abel et al. (2022) Umbrella review of time-restricted eating on weight loss,	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.

Study	Reason
fasting blood glucose, and lipid profile. Nutrition reviews	
Cho, Y., Hong, N., Kim, K.-W. et al. (2019) The effectiveness of intermittent fasting to reduce body mass index and glucose metabolism: A systematic review and meta-analysis. Journal of Clinical Medicine 8(10): 1645	- More recent systematic review included that covers the same topic *Length of follow-up was unclear*
Choi, Y.J.; Jeon, S.-M.; Shin, S. (2020) Impact of a ketogenic diet on metabolic parameters in patients with obesity or overweight and with or without type 2 diabetes: A meta-analysis of randomized controlled trials. Nutrients 12(7): 1-19	- Incorrect analysis *Combines VLCD with LCD*
Churuangsuk, C., Hall, J., Reynolds, A. et al. (2022) Diets for weight management in adults with type 2 diabetes: an umbrella review of published meta-analyses and systematic review of trials of diets for diabetes remission. Diabetologia 65(1): 14-36	- Incorrect analysis *Review of reviews - included reviews checked for inclusion in this review*
Churuangsuk, C., Kherouf, M., Combet, E. et al. (2018) Low-carbohydrate diets for overweight and obesity: a systematic review of the systematic reviews. Obesity Reviews 19(12): 1700-1718	- Incorrect study design *Review of reviews*
Cioffi, I., Evangelista, A., Ponzo, V. et al. (2018) Intermittent versus continuous energy restriction on weight loss and cardiometabolic outcomes: A systematic review and meta-analysis of randomized controlled trials. Journal of Translational Medicine 16(1): 371	- Systematic review used as source of primary studies
Clark, J.K. (2015) Diet, exercise or diet with exercise: Comparing the effectiveness of treatment options for weight-loss and changes in fitness for adults (18-65 years old) who are overfat, or obese; systematic review and meta-analysis. Journal of Diabetes and Metabolic Disorders 14(1): 31	- Study does not contain a relevant intervention *No single diet assessed*
Correia, J.M., Santos, I., Pezarat-Correia, P. et al. (2020) Effects of intermittent fasting on specific exercise performance outcomes: A	- Incorrect analysis *Many included studies were uncontrolled and those that were included were not using diet to*

Study	Reason
systematic review including meta-analysis. Nutrients 12(5): 1390	*address overweight or obesity. The main outcomes were linked to exercise performance.*
Correia, Joana M, Santos, Ines, Pezarat-Correia, Pedro et al. (2020) Effects of Ramadan and Non-ramadan Intermittent Fasting on Body Composition: A Systematic Review and Meta-Analysis. Frontiers in nutrition 7: 625240	- Incorrect analysis *Many included studies were uncontrolled and those that were included were not using diet to address overweight or obesity. The main outcomes were linked to exercise performance.*
Corrêa P, Rafaela and Cardoso de AP, Michel (2019) Ketogenic diets in weight loss: a systematic review under physiological and biochemical aspects of nutrition. Rev. chil. nutr 46(5): 606-613	- Incorrect analysis *Many uncontrolled studies included in the review and no meta-analysis was undertaken.*
Cui, Yuanshan, Cai, Tong, Zhou, Zhongbao et al. (2020) Health Effects of Alternate-Day Fasting in Adults: A Systematic Review and Meta-Analysis. Frontiers in nutrition 7: 586036	- Incorrect population *The populations in the included studies were often not living with overweight or obesity*
Das, JK, Salam, RA, Mahmood, SB et al. (2019) Food fortification with multiple micronutrients: impact on health outcomes in general population. The Cochrane database of systematic reviews 12: cd011400	- Study does not contain a relevant intervention *This review investigates food fortification with micronutrients rather than a formal low carbohydrate or very low carbohydrate diet.*
Davis, C.S., Clarke, R.E., Coulter, S.N. et al. (2016) Intermittent energy restriction and weight loss: A systematic review. European Journal of Clinical Nutrition 70(3): 292-299	- More recent systematic review included that covers the same topic *No meta-analysis conducted*
Dyson, P. (2020) Very low carbohydrate ketogenic diets and diabetes. Practical Diabetes 37(4): 121-126	- Incorrect analysis *2 RCTs were included in this review and this does not appear to fully span the evidence base*
Eglseer, Doris, Traxler, Mariella, Embacher, Stefan et al. (2023) Nutrition and exercise interventions to improve body composition for persons with overweight or obesity near retirement age: A systematic review and network meta-analysis of randomised controlled trials. Advances in nutrition (Bethesda, Md.)	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
El Ghoch, M.; Calugi, S.; Grave, R.D. (2016) The effects of low-carbohydrate diets on psychosocial outcomes in obesity/overweight: A	- Review article but not a systematic review *Not meta-analysis conducted*

Study	Reason
systematic review of randomized, controlled studies. Nutrients 8(7): 402	
Emadian, A, Andrews, RC, England, CY et al. (2015) The effect of macronutrients on glycaemic control: a systematic review of dietary randomised controlled trials in overweight and obese adults with type 2 diabetes in which there was no difference in weight loss between treatment groups. The British journal of nutrition 114(10): 1-11	- Study does not contain a relevant intervention *This review does not investigate a relevant diet*
Enriquez Guerrero, A., San Mauro Martin, I., Garicano Vilar, E. et al. (2021) Effectiveness of an intermittent fasting diet versus continuous energy restriction on anthropometric measurements, body composition and lipid profile in overweight and obese adults: a meta-analysis. European Journal of Clinical Nutrition 75(7): 1024-1039	- More recent systematic review included that covers the same topic *Not meta-analysis conducted*
Esposito, K, Maiorino, MI, Bellastella, G et al. (2015) A journey into a Mediterranean diet and type 2 diabetes: a systematic review with meta-analyses. BMJ open 5(8): e008222	- Study does not contain a relevant intervention *Mediterranean diet*
Fan, Y., Di, H., Chen, G. et al. (2016) Effects of low carbohydrate diets in individuals with type 2 diabetes: Systematic review and meta-analysis. International Journal of Clinical and Experimental Medicine 9(6): 11166-11174	- More recent systematic review included that covers the same topic
Fechner, E., Smeets, E.T.H.C., Schrauwen, P. et al. (2020) The effects of different degrees of carbohydrate restriction and carbohydrate replacement on cardiometabolic risk markers in humans-a systematic review and meta-analysis. Nutrients 12(4): 991	- Incorrect population *2 included studies were in people who were not living with overweight or obesity*
Franz, M.J., Boucher, J.L., Rutten-Ramos, S. et al. (2015) Lifestyle weight-loss intervention outcomes in overweight and obese adults with type 2 diabetes: a systematic review and meta-analysis of randomized clinical trials. Journal of the Academy of Nutrition and Dietetics 115(9): 1447-1463	- Study does not contain a relevant intervention *Assessment of many different diets and lifestyle activities rather than an assessment of a single type of diet*

Study	Reason
Gaeini, Z.; Mirmiran, P.; Bahadoran, Z. (2021) Effects of Ramadan intermittent fasting on leptin and adiponectin: a systematic review and meta-analysis. Hormones 20(2): 237-246	- Incorrect population *Included papers are predominantly not in people living with overweight or obesity and no relevant outcomes presented*
Ganesan, Kavitha; Habboush, Yacob; Sultan, Senan (2018) Intermittent Fasting: The Choice for a Healthier Lifestyle. Cureus 10(7): e2947	- More recent systematic review included that covers the same topic *Not meta-analysis was conducted*
Garcêz, LS, Avelar, CR, Fonseca, NSS et al. (2021) Effect of dietary carbohydrate and lipid modification on clinical and anthropometric parameters in nonalcoholic fatty liver disease: a systematic review and meta-analysis. Nutrition reviews	- Study does not contain a relevant intervention *Unclear if the diets utilised in the included studies are low carbohydrate diets*
Ge, L., Sadeghirad, B., Ball, G.D.C. et al. (2020) Comparison of dietary macronutrient patterns of 14 popular named dietary programmes for weight and cardiovascular risk factor reduction in adults: Systematic review and network meta-analysis of randomised trials. The BMJ 369: m696	- Study does not contain a relevant intervention *Review does not specifically address diets named in the protocol for this review*
Genel, F., Kale, M., Pavlovic, N. et al. (2020) Health effects of a low-inflammatory diet in adults with arthritis: A systematic review and meta-analysis. Journal of Nutritional Science 9: e37	- Incorrect population *Review population not necessarily living with overweight or obesity and the diet specified do not match those in this review's protocol.*
Ghadimi, M., Mohammadi, R., Daneshzad, E. et al. (2021) Effectiveness of dietary interventions on cardio-metabolic risk factors in patients with nonalcoholic fatty liver disease: A systematic review and meta-analysis of randomized controlled trials. Annals of Gastroenterology 34(3): 415-423	- Study does not contain a relevant intervention
Gjuladin-Hellon, T., Davies, I.G., Penson, P. et al. (2019) Effects of carbohydrate-restricted diets on low-density lipoprotein cholesterol levels in overweight and obese adults: A systematic review and meta-analysis. Nutrition Reviews 77(3): 161-180	- Incorrect outcomes *This review does not report on outcomes specified in this review's protocol.*

Study	Reason
Goldenberg, Joshua Z, Day, Andrew, Brinkworth, Grant D et al. (2021) Efficacy and safety of low and very low carbohydrate diets for type 2 diabetes remission: systematic review and meta-analysis of published and unpublished randomized trial data. BMJ (Clinical research ed.) 372: m4743	- Incorrect analysis *VLCK and LCD analysed together*
Groenendijk, I, den Boeft, L, van Loon, LJC et al. (2019) High Versus low Dietary Protein Intake and Bone Health in Older Adults: a Systematic Review and Meta-Analysis. Computational and structural biotechnology journal 17: 1101-1112	- Study does not contain a relevant intervention *Diet linked to protein intake*
Gu, Lihu, Fu, Rongrong, Hong, Jiaze et al. (2022) Effects of Intermittent Fasting in Human Compared to a Non-intervention Diet and Caloric Restriction: A Meta-Analysis of Randomized Controlled Trials. Frontiers in nutrition 9: 871682	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
Harris, L., Hamilton, S., Azevedo, L.B. et al. (2018) Intermittent fasting interventions for treatment of overweight and obesity in adults: A systematic review and meta-analysis. JBI Database of Systematic Reviews and Implementation Reports 16(2): 507-547	- More recent systematic review included that covers the same topic
Harris, L., McGarty, A., Hutchison, L. et al. (2018) Short-term intermittent energy restriction interventions for weight management: a systematic review and meta-analysis. Obesity Reviews 19(1): 1-13	- More recent systematic review included that covers the same topic
Harris, Rebecca A, Fernando, Hamish A, Seimon, Radhika V et al. (2022) Effects of total diet replacement programs on mental well-being: A systematic review with meta-analyses. Obesity reviews : an official journal of the International Association for the Study of Obesity 23(11): e13465	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
He, S., Wang, J., Zhang, J. et al. (2021) Intermittent Versus Continuous Energy Restriction for Weight Loss and Metabolic Improvement: A Meta-Analysis and Systematic Review. Obesity 29(1): 108-115	- More recent systematic review included that covers the same topic

Study	Reason
	The follow-up for the weight loss outcome did not appear to be 12 months or more after the intervention
Headland, M., Clifton, P.M., Carter, S. et al. (2016) Weight-loss outcomes: A systematic review and meta-analysis of intermittent energy restriction trials lasting a minimum of 6 months. Nutrients 8(6): 354	- More recent systematic review included that covers the same topic
Herrington, G.J., Peterson, J.J., Cheng, L. et al. (2022) The use of very low-calorie diets in subjects with obesity complicated with nonalcoholic fatty liver disease: A scoping review. Obesity Science and Practice	- Study does not contain a relevant intervention *The diets investigated in this review are very low calorie diets and this is a broader definition of diet than that utilised in this review's protocol*
Horne, Benjamin D; Muhlestein, Joseph B; Anderson, Jeffrey L (2015) Health effects of intermittent fasting: hormesis or harm? A systematic review. The American journal of clinical nutrition 102(2): 464-70	- Data not reported in an extractable format *No meta-analysis of relevant outcomes reported in this review.*
Houttu, Veera, Csader, Susanne, Nieuwdorp, Max et al. (2021) Dietary Interventions in Patients With Non-alcoholic Fatty Liver Disease: A Systematic Review and Meta-Analysis. Frontiers in nutrition 8: 716783	- Incorrect analysis *A number of the diet studies utilised in this meta-analysis are not relevant for this review*
Hu, J., Wang, Z., Lei, B. et al. (2021) Effects of a low-carbohydrate high-fat diet combined with high-intensity interval training on body composition and maximal oxygen uptake: A systematic review and meta-analysis. International Journal of Environmental Research and Public Health 18(20): 10740	- Study does not contain a relevant intervention *Diet combined with high-intensity interval training*
Huang, Lu, Chen, Yan, Wen, Shu et al. (2023) Is time-restricted eating (8/16) beneficial for body weight and metabolism of obese and overweight adults? A systematic review and meta-analysis of randomized controlled trials. Food science & nutrition 11(3): 1187-1200	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
Huang, R.-Y., Huang, C.-C., Hu, F.B. et al. (2016) Vegetarian Diets and Weight Reduction: a Meta-Analysis of Randomized Controlled	- Study does not contain a relevant intervention *Over half of the included vegetarian trials did not include a calorie deficit*

Study	Reason
Trials. Journal of General Internal Medicine 31(1): 109-116	
Huang, Y.S., Zheng, Q., Yang, H. et al. (2020) Efficacy of Intermittent or Continuous Very Low-Energy Diets in Overweight and Obese Individuals with Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analyses. Journal of Diabetes Research 2020: 4851671	- Study does not contain a relevant intervention *Very low energy diets not necessarily combined with meal replacement*
Huntriss, R; Campbell, M; Bedwell, C (2018) The interpretation and effect of a low-carbohydrate diet in the management of type 2 diabetes: a systematic review and meta-analysis of randomised controlled trials. European journal of clinical nutrition 72(3): 311-325	- More recent systematic review included that covers the same topic
Huo, R., Du, T., Xu, Y. et al. (2015) Effects of Mediterranean-style diet on glycemic control, weight loss and cardiovascular risk factors among type 2 diabetes individuals: A meta-analysis. European Journal of Clinical Nutrition 69(11): 1200-1208	- Study does not contain a relevant intervention *Mediterranean-style diet*
Infante, M., Moriconi, E., Armani, A. et al. (2019) Very-low-calorie ketogenic diet (VLCKD) in the management of metabolic diseases: systematic review and consensus statement from the Italian Society of Endocrinology (SIE). Journal of Endocrinological Investigation 42(11): 1365-1386	- Review article but not a systematic review *Paper from the Italian Society of Endocrinology (SIE) on recommendations they have made linked to diets in adults*
Ismail, Suriani; Manaf, Rosliza Abdul; Mahmud, Aidalina (2019) Comparison of time-restricted feeding and Islamic fasting: a scoping review. Eastern Mediterranean health journal = La revue de sante de la Mediterranee orientale = al-Majallah al-sihhiyah li-sharq al-mutawassit 25(4): 239-245	- Not a relevant study design *Scoping review with little data or study details presented*
Jacob, E. and Avery, A. (2021) Energy-restricted interventions are effective for the remission of newly diagnosed type 2 diabetes: A systematic review of the evidence base. Obesity Science and Practice 7(5): 606-618	- Study does not contain a relevant intervention *The diets included in this review often went beyond dieting into full lifestyle interventions and the diets themselves did not always match those detailed in our protocol. No meta-analysis was conducted*

Study	Reason
Jahrami, HA, Alsibai, J, Clark, CCT et al. (2020) A systematic review, meta-analysis, and meta-regression of the impact of diurnal intermittent fasting during Ramadan on body weight in healthy subjects aged 16 years and above. European journal of nutrition 59(6): 2291-2316	- Incorrect analysis *No RCTs were included in this systematic review*
Kahathuduwa, C.N., Binks, M., Martin, C.K. et al. (2017) Extended calorie restriction suppresses overall and specific food cravings: a systematic review and a meta-analysis. Obesity Reviews 18(10): 1122-1135	- Study does not contain a relevant intervention *This studies utilised in this review are those with a calorie restriction intervention and this is too broad for this review*
Kang, J., Ratamess, N.A., Faigenbaum, A.D. et al. (2021) Effect of Time-Restricted Feeding on Anthropometric, Metabolic, and Fitness Parameters: A Systematic Review. Journal of the American College of Nutrition	- Incorrect population *A number of the studies were in people living with normal weight*
Kashyap, Anjali, Mackay, Alexander, Carter, Ben et al. (2022) Investigating the Effectiveness of Very Low-Calorie Diets and Low-Fat Vegan Diets on Weight and Glycemic Markers in Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis. Nutrients 14(22)	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
Kemalasari, I., Fitri, N.A., Sinto, R. et al. (2022) Effect of calorie restriction diet on levels of C reactive protein (CRP) in obesity: A systematic review and meta-analysis of randomized controlled trials. Diabetes and Metabolic Syndrome: Clinical Research and Reviews 16(3): 102388	- Study does not contain a relevant intervention *This studies utilised in this review are those with a calorie restriction intervention and this is too broad for this review*
Kloecker, D.E., Zaccardi, F., Baldry, E. et al. (2019) Efficacy of low- and very-low-energy diets in people with type 2 diabetes mellitus: A systematic review and meta-analysis of interventional studies. Diabetes, Obesity and Metabolism 21(7): 1695-1705	- Incorrect analysis *This is not a review comparing different diet types*
Korsmo-Haugen, HK, Brurberg, KG, Mann, J et al. (2019) Carbohydrate quantity in the dietary management of type 2 diabetes - a systematic review and meta-analysis. Diabetes, obesity & metabolism 21(1): 15-27	- More recent systematic review included that covers the same topic

Study	Reason
Lamberti, C. and Pagano, I. (2020) Ketogenic diet's effect on glycemic balance in patients with type 2 diabetes mellitus: A review. Pharmacologyonline 3specialissue: 79-83	- Review article but not a systematic review
Langeveld, M. and Devries, J.H. (2015) The long-term effect of energy restricted diets for treating obesity. Obesity 23(8): 1529-1538	- Study does not contain a relevant intervention *This study included all dietary interventions aimed to restrict energy intake and this did not meet any single diet type in our protocol*
Lee, H.S. and Lee, J. (2021) Effects of combined exercise and low carbohydrate ketogenic diet interventions on waist circumference and triglycerides in overweight and obese individuals: A systematic review and meta-analysis. International Journal of Environmental Research and Public Health 18(2): 1-15	- Incorrect comparison *This review investigated the effect of diet combined with exercise*
Lei, Lifu, Huang, Juan, Zhang, Longlong et al. (2022) Effects of low-carbohydrate diets versus low-fat diets on metabolic risk factors in overweight and obese adults: A meta-analysis of randomized controlled trials. Frontiers in nutrition 9: 935234	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
Leslie, W.S., Taylor, R., Harris, L. et al. (2017) Weight losses with low-energy formula diets in obese patients with and without type 2 diabetes: Systematic review and meta-analysis. International Journal of Obesity 41(1): 96-101	- Incorrect analysis *This review concentrates on a comparison of people living with or without type 2 diabetes rather than a comparison of diets*
Li, S.; Ding, L.; Xiao, X. (2021) Comparing the Efficacy and Safety of Low-Carbohydrate Diets with Low-Fat Diets for Type 2 Diabetes Mellitus Patients: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. International Journal of Endocrinology 2021: 8521756	- More recent systematic review included that covers the same topic
Lim, S, O'Reilly, S, Behrens, H et al. (2015) Effective strategies for weight loss in post-partum women: a systematic review and meta-analysis. Obesity reviews : an official journal of the International Association for the Study of Obesity 16(11): 972-87	- Study does not contain a relevant intervention *This study did not investigate the effectiveness of diets specified in the protocol of this review*

Study	Reason
Lima, C.H.R., Oliveira, I.K.F., de Macedo Goncalves Frota, K. et al. (2020) Impact of intermittent fasting on body weight in overweight and obese individuals. Revista da Associacao Medica Brasileira 66(2): 222-226	- More recent systematic review included that covers the same topic *This review looked at a relevant diet but presented very limited results from the studies and did not undertake meta-analysis*
Lin, Xiaoxiao, Guan, Yihong, Wu, Guomin et al. (2022) Time-restricted eating for patients with diabetes and prediabetes: A systematic review. Frontiers in nutrition 9: 1025919	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
Liu, Juanhong; Yi, Pan; Liu, Feng (2023) The Effect of Early Time-Restricted Eating vs. Later Time-Restricted Eating on Weight Loss and Metabolic Health: A Network Meta-Analysis of Randomized Controlled Trials. The Journal of clinical endocrinology and metabolism	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
Liu, Lili, Chen, Wei, Wu, Dan et al. (2022) Metabolic Efficacy of Time-Restricted Eating in Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. The Journal of clinical endocrinology and metabolism 107(12): 3428-3441	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
Liu, Y., Hong, F., Lebaka, V.R. et al. (2021) Calorie Restriction With Exercise Intervention Improves Inflammatory Response in Overweight and Obese Adults: A Systematic Review and Meta-Analysis. Frontiers in Physiology 12: 754731	- Study does not contain a relevant intervention *This review is broadly interested in the combination of a diet regimen with exercise*
Lopez-Espinoza, M.A., Chacon-Moscoso, S., Sanduvete-Chaves, S. et al. (2021) Effect of a ketogenic diet on the nutritional parameters of obese patients: A systematic review and meta-analysis. Nutrients 13(9): 2946	- Systematic review used as source of primary studies
Lu, M., Wan, Y., Yang, B. et al. (2018) Effects of low-fat compared with high-fat diet on cardiometabolic indicators in people with overweight and obesity without overt metabolic disturbance: A systematic review and meta-analysis of randomised controlled trials. British Journal of Nutrition 119(1): 96-108	- Study does not contain a relevant intervention *This review compares low fat to high fat diets and neither are included in this review protocol*

Study	Reason
Luo, Wei, Zhang, Jin, Xu, Dan et al. (2022) Low carbohydrate ketogenic diets reduce cardiovascular risk factor levels in obese or overweight patients with T2DM: A meta-analysis of randomized controlled trials. Frontiers in nutrition 9: 1092031	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
Mancini, J.G., Filion, K.B., Atallah, R. et al. (2016) Systematic Review of the Mediterranean Diet for Long-Term Weight Loss. American Journal of Medicine 129(4): 407	- Study does not contain a relevant intervention *Mediterranean diet*
Mansoor, N., Vinknes, K.J., Veierod, M.B. et al. (2016) Effects of low-carbohydrate diets v. low-fat diets on body weight and cardiovascular risk factors a meta-analysis of randomised controlled trials. British Journal of Nutrition 115(3): 466-479	- More recent systematic review included that covers the same topic
Maston, Gabrielle, Gibson, Alice A, Kahlaee, H Reza et al. (2019) Effectiveness and Characterization of Severely Energy-Restricted Diets in People with Class III Obesity: Systematic Review and Meta-Analysis. Behavioral sciences (Basel, Switzerland) 9(12)	- Incorrect analysis *This review included 10 papers of which only 1 was a randomised controlled trial*
Matiashova, L.; Shanker, A.; Isayeva, G. (2021) The effect of intermittent fasting on mortality in patients with type 2 diabetes and metabolic disease with high cardiovascular risk: A systematic review. Clinical Diabetology 10(3): 284-289	- More recent systematic review included that covers the same topic *Not meta-analysis conducted*
Mazidi, M, Rezaie, P, Chaudhri, O et al. (2015) The effect of Ramadan fasting on cardiometabolic risk factors and anthropometrics parameters: A systematic review. Pakistan journal of medical sciences 31(5): 1250-1255	- Incorrect analysis *This study concentrates alone on the non-comparative effects of Ramdan fasting rather than the comparative effect of intermittant fasting*
McGrice, M. and Porter, J. (2017) The effect of low carbohydrate diets on fertility hormones and outcomes in overweight and obese women: A systematic review. Nutrients 9(3): 204	- Incorrect population *The populations in the included studies most often suffered from polycystic ovary syndrome rather than necessarily living with overweight or obesity*

Study	Reason
Medawar, E., Huhn, S., Villringer, A. et al. (2019) The effects of plant-based diets on the body and the brain: a systematic review. Translational Psychiatry 9(1): 226	- Study does not contain a relevant intervention *This review included papers evaluating plant based diets but in many cases these diets did not have a calorie deficit and the population being studied was not necessarily living with overweight of obesity. No meta-analysis was undertaken*
Meng, Y., Bai, H., Wang, S. et al. (2017) Efficacy of low carbohydrate diet for type 2 diabetes mellitus management: A systematic review and meta-analysis of randomized controlled trials. Diabetes Research and Clinical Practice 131: 124-131	- More recent systematic review included that covers the same topic
Moon, S., Kang, J., Kim, S.H. et al. (2020) Beneficial effects of time-restricted eating on metabolic diseases: A systemic review and meta- analysis. Nutrients 12(5): 1267	- Incorrect population *This review included many studies in people who were not living with overweight or obesity*
Morales-Suarez-varela, M., Sanchez, E.C., Peraita-Costa, I. et al. (2021) Intermittent fasting and the possible benefits in obesity, diabetes, and multiple sclerosis: A systematic review of randomized clinical trials. Nutrients 13(9): 3179	- Incorrect study design *This is an overview of reviews*
Muscogiuri, G., El Ghoch, M., Colao, A. et al. (2021) European Guidelines for Obesity Management in Adults with a Very Low-Calorie Ketogenic Diet: A Systematic Review and Meta-Analysis. Obesity Facts 14(2): 222-245	- Review article but not a systematic review *Follow-up of included studies ranged from 3 weeks to 12 months*
Noronha, J.C., Nishi, S.K., Braunstein, C.R. et al. (2019) The effect of liquid meal replacements on cardiometabolic risk factors in overweight/obese individuals with type 2 diabetes: A Systematic Review and Meta-analysis of Randomized Controlled Trials. Diabetes Care 42(5): 767-776	- Systematic review used as source of primary studies
Oyabu, C., Hashimoto, Y., Fukuda, T. et al. (2016) Impact of low-carbohydrate diet on renal function: A meta-analysis of over 1000 individuals from nine randomised controlled trials. British Journal of Nutrition 116(4): 632-638	- More recent systematic review included that covers the same topic *No meta-analysis in relevant outcomes for this review was conducted*

Study	Reason
Pan, B., Wu, Y., Yang, Q. et al. (2019) The impact of major dietary patterns on glycemic control, cardiovascular risk factors, and weight loss in patients with type 2 diabetes: A network meta-analysis. Journal of Evidence-Based Medicine 12(1): 29-39	- Incorrect analysis *Network meta-analysis including diets which are not valid comparisons for this review*
Papadaki, A.; Nolen-Doerr, E.; Mantzoros, C.S. (2020) The effect of the mediterranean diet on metabolic health: A systematic review and meta-analysis of controlled trials in adults. Nutrients 12(11): 1-21	- Study does not contain a relevant intervention *Mediterranean diet*
Park, J., Seo, Y.-G., Paek, Y.-J. et al. (2020) Effect of alternate-day fasting on obesity and cardiometabolic risk: A systematic review and meta-analysis. Metabolism: Clinical and Experimental 111: 154336	- More appropriate systematic review included for this diet *Follow-up in included did not meet this review's inclusion criteria*
Patikorn, C., Roubal, K., Veettil, S.K. et al. (2021) Intermittent Fasting and Obesity-Related Health Outcomes: An Umbrella Review of Meta-analyses of Randomized Clinical Trials. JAMA Network Open 4(12): e2139558	- Incorrect study design *Review of reviews rather than a systematic review suitable for inclusion in this review*
Petersen, K.S., Clifton, P.M., Lister, N. et al. (2016) Effect of weight loss induced by energy restriction on measures of arterial compliance: A systematic review and meta-analysis. Atherosclerosis 247: 7-20	- Incorrect analysis *Review primarily investigating arterial compliance linked to weight loss*
Picasso, M.C., Lo-Tayraco, J.A., Ramos-Villanueva, J.M. et al. (2019) Effect of vegetarian diets on the presentation of metabolic syndrome or its components: A systematic review and meta-analysis. Clinical Nutrition 38(3): 1117-1132	- Study does not contain a relevant intervention *The plant-based diets did not mention any calorie deficits and the population did not appear to necessarily be living with overweight or obesity*
Rajpal, A. and Ismail-Beigi, F. (2020) Intermittent fasting and 'metabolic switch': Effects on metabolic syndrome, prediabetes and type 2 diabetes. Diabetes, Obesity and Metabolism 22(9): 1496-1510	- More recent systematic review included that covers the same topic *No meta-analysis in relevant outcomes for this review was conducted*
Ramezani-Jolfaie, N; Mohammadi, M; Salehi-Abargouei, A (2020) Effects of a healthy Nordic diet on weight loss in adults: a systematic review	- Study does not contain a relevant intervention *Nordic diet*

Study	Reason
and meta-analysis of randomized controlled clinical trials. Eating and weight disorders : EWD 25(5): 1141-1150	
Ramezani-Jolfaie, N; Mohammadi, M; Salehi-Abargouei, A (2019) The effect of healthy Nordic diet on cardio-metabolic markers: a systematic review and meta-analysis of randomized controlled clinical trials. European journal of nutrition 58(6): 2159-2174	- Study does not contain a relevant intervention *Nordic diet*
Rebic, N., Mirkovic, S., Mirkovic, M. et al. (2021) The effects of a low-carbohydrate diet on obesity and associated comorbidities. New Armenian Medical Journal 15(2): 92-101	- More recent systematic review included that covers the same topic *Not meta-analysis conducted*
Rehackova, L., Arnott, B., Araujo-Soares, V. et al. (2016) Efficacy and acceptability of very low energy diets in overweight and obese people with Type 2 diabetes mellitus: A systematic review with meta-analyses. Diabetic Medicine 33(5): 580-591	- Study does not contain a relevant intervention *Very low energy diets but most did not involve total or partial replacement*
Remde, A., DeTurk, S.N., Almardini, A. et al. (2021) Plant-predominant eating patterns - how effective are they for treating obesity and related cardiometabolic health outcomes? - a systematic review. Nutrition reviews	- Study does not contain a relevant intervention *Plant based diets that did not necessarily have calorie deficits. No meta-analysis was undertaken*
Roman, Y.M., Dominguez, M.C., Easow, T.M. et al. (2019) Effects of intermittent versus continuous dieting on weight and body composition in obese and overweight people: a systematic review and meta-analysis of randomized controlled trials. International Journal of Obesity 43(10): 2017-2027	- More recent systematic review included that covers the same topic
Ross, L.J., Byrnes, A., Hay, R.L. et al. (2021) Exploring the highs and lows of very low carbohydrate high fat diets on weight loss and diabetes- and cardiovascular disease-related risk markers: A systematic review. Nutrition & dietetics: the journal of the Dietitians Association of Australia 78(1): 41-56	- Incorrect population *Most of the studies included in this review are cohort studies. The population are losing weight in preparation for bariatric surgery. Not meta-analysis was undertaken.*
Ross, L.J., Wallin, S., Osland, E.J. et al. (2016) Commercial Very Low Energy Meal Replacements for Preoperative Weight Loss in	- Incorrect study design

Study	Reason
Obese Patients: a Systematic Review. Obesity Surgery 26(6): 1343-1351	*Most of the studies included in this review are cohort studies. The population are losing weight in preparation for bariatric surgery and no meta-analysis was undertaken.*
Sackner-Bernstein, J.; Kanter, D.; Kaul, S. (2015) Dietary intervention for overweight and obese adults: comparison of low- carbohydrate and low-fat diets. a meta- analysis. PLoS ONE 10(10): e0139817	- More recent systematic review included that covers the same topic
Salehi-Abargouei, A.; Izadi, V.; Azadbakht, L. (2015) The Effect of Low Calorie Diet on Adiponectin Concentration: A Systematic Review and Meta-Analysis. Hormone and Metabolic Research 47(8): 549-555	- Study does not contain a relevant intervention *This review included low energy diets but not necessarily with total or partial replacement. The outcome reported was not relevant for this review.*
Sanchez-Sanchez, M.L., Garcia-Vigara, A., Hidalgo-Mora, J.J. et al. (2020) Mediterranean diet and health: A systematic review of epidemiological studies and intervention trials. Maturitas 136: 25-37	- Study does not contain a relevant intervention *Mediterranean diet*
Sandoval, C.; Santibanez, S.; Villagran, F. (2021) Effectiveness of intermittent fasting to potentiate weight loss or muscle gains in humans younger than 60 years old: a systematic review. International journal of food sciences and nutrition 72(6): 734-745	- Incorrect population *Half of the studies included in this review did not limit their population to people who were living with overweight or obesity, No meta-analysis was undertaken.*
Sanford, Mitchell A, Sanford, Tracy S, Campbell, K F et al. (2020) Do Adults Utilizing Intermittent Fasting Improve Lipids More Than Those Following a Restricted-Calorie Diet? A Clin-IQ. Journal of patient-centered research and reviews 7(3): 282-285	- Not a relevant study design *Not a systematic review*
Sarro, A, Payedimarri, AB, Concina, D et al. (2020) The efficacy of fasting regimens on health outcomes: a systematic overview. Minerva gastroenterologica e dietologica	- Incorrect analysis *Overview of reviews which concentrates on the effects of fasting on specific disease outcomes*
Seimon, R.V., Roekenes, J.A., Zibellini, J. et al. (2015) Do intermittent diets provide physiological benefits over continuous diets for weight loss? A systematic review of clinical	- More recent systematic review included that covers the same topic *Not meta-analysis conducted*

Study	Reason
trials. Molecular and Cellular Endocrinology 418: 153-172	
Sellahewa, L., Khan, C., Lakkunarajah, S. et al. (2017) A systematic review of evidence on the use of very low calorie diets in people with diabetes. Current Diabetes Reviews 13(1): 35-46	- Incorrect population *This study included a study in children. The diets included were broader than those utilised in this review's protocol as they were very low energy without necessarily including total or partial replacement. No meta-analysis was conducted.*
Semlitsch, Thomas, Krenn, Cornelia, Jeitler, Klaus et al. (2021) Long-term effects of weight-reducing diets in people with hypertension. The Cochrane database of systematic reviews 2: cd008274	- Study does not contain a relevant intervention *This concentrated on weight-reducing diets in general rather than the specific diets being compared in this review*
Silver, Derek T and Pekari, Timothy B (2023) A Review of Intermittent Fasting as a Treatment for Type 2 Diabetes Mellitus. Medical journal (Fort Sam Houston, Tex.): 65-71	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
Silverii, G.A., Botarelli, L., Dicembrini, I. et al. (2020) Low-carbohydrate diets and type 2 diabetes treatment: a meta-analysis of randomized controlled trials. Acta Diabetologica 57(11): 1375-1382	- More recent systematic review included that covers the same topic
Silverii, Giovanni Antonio, Cosentino, Claudia, Santagiuliana, Federica et al. (2022) Effectiveness of low-carbohydrate diets for long-term weight loss in obese individuals: A meta-analysis of randomized controlled trials. Diabetes, obesity & metabolism 24(8): 1458-1468	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
Steckhan, N., Hohmann, C.-D., Kessler, C. et al. (2016) Effects of different dietary approaches on inflammatory markers in patients with metabolic syndrome: A systematic review and meta-analysis. Nutrition 32(3): 338-348	- Incorrect population *The studies included were not necessarily in people living with overweight or obesity and only a small subset were relevant for this review*
Tagde, Priti, Tagde, Sandeep, Bhattacharya, Tanima et al. (2022) Multifaceted Effects of Intermittent Fasting on the Treatment and Prevention of Diabetes, Cancer, Obesity or	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.

Study	Reason
Other Chronic Diseases. Current diabetes reviews 18(9): e131221198789	
Termannsen, Anne-Ditte, Clemmensen, Kim Katrine Bjerring, Thomsen, Jonas Mark et al. (2022) Effects of vegan diets on cardiometabolic health: A systematic review and meta-analysis of randomized controlled trials. Obesity reviews : an official journal of the International Association for the Study of Obesity 23(9): e13462	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
Tobias, D.K., Chen, M., Manson, J.E. et al. (2015) Effect of low-fat diet interventions versus other diet interventions on long-term weight change in adults: A systematic review and meta-analysis. The Lancet Diabetes and Endocrinology 3(12): 968-979	- Study does not contain a relevant intervention *Low fat diet*
Toumpanakis, A; Turnbull, T; Alba-Barba, I (2018) Effectiveness of plant-based diets in promoting well-being in the management of type 2 diabetes: a systematic review. BMJ open diabetes research & care 6(1): e000534	- Study does not contain a relevant intervention *The plant-based diets included in this review did not necessarily include a calorie deficit. No meta-analysis was undertaken.*
Tran, E., Dale, H.F., Jensen, C. et al. (2020) Effects of plant-based diets on weight status: A systematic review. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 13: 3433-3448	- Study does not contain a relevant intervention *The plant-based diets included in this review did not necessarily include a calorie deficit. No meta-analysis was undertaken.*
Tsitsou, Sofia, Zacharodimos, Nikolaos, Poulia, Kalliopi-Anna et al. (2022) Effects of Time-Restricted Feeding and Ramadan Fasting on Body Weight, Body Composition, Glucose Responses, and Insulin Resistance: A Systematic Review of Randomized Controlled Trials. Nutrients 14(22)	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
Turton, JL; Raab, R; Rooney, KB (2018) Low-carbohydrate diets for type 1 diabetes mellitus: A systematic review. PloS one 13(3): e0194987	- Incorrect population *The population included in this review are not necessarily living with overweight or obesity*
Van Zuuren, E.J., Fedorowicz, Z., Kuijpers, T. et al. (2018) Effects of low-carbohydrate-compared with low-fat-diet interventions on metabolic control in people with type 2 diabetes: A systematic review including GRADE	- More recent systematic review included that covers the same topic

Study	Reason
assessments. American Journal of Clinical Nutrition 108(2): 300-331	
Viguiliouk, E., Kendall, C.W., Kahleova, H. et al. (2019) Effect of vegetarian dietary patterns on cardiometabolic risk factors in diabetes: A systematic review and meta-analysis of randomized controlled trials. Clinical Nutrition 38(3): 1133-1145	- Study does not contain a relevant intervention *The plant-based diets did not have any calorie restrictions*
Vitale, R. and Kim, Y. (2020) The Effects of Intermittent Fasting on Glycemic Control and Body Composition in Adults with Obesity and Type 2 Diabetes: A Systematic Review. Metabolic Syndrome and Related Disorders 18(10): 450-461	- More recent systematic review included that covers the same topic *Not meta-analysis conducted*
Wang, Weihao, Wei, Ran, Pan, Qi et al. (2022) Beneficial effect of time-restricted eating on blood pressure: a systematic meta-analysis and meta-regression analysis. Nutrition & metabolism 19(1): 77	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
Wang, X., Li, Q., Liu, Y. et al. (2021) Intermittent fasting versus continuous energy-restricted diet for patients with type 2 diabetes mellitus and metabolic syndrome for glycemic control: A systematic review and meta-analysis of randomized controlled trials. Diabetes Research and Clinical Practice 179: 109003	- More recent systematic review included that covers the same topic *Follow-up was unclear*
Wang, X., Yan, Q., Liao, Q. et al. (2020) Effects of intermittent fasting diets on plasma concentrations of inflammatory biomarkers: A systematic review and meta-analysis of randomized controlled trials. Nutrition 7980: 110974	- Incorrect population *A number of included studies recruited people who were not living with overweight or obesity. No meta-analysis in relevant outcomes for this review was conducted*
Welton, S., Minty, R., O'Driscoll, T. et al. (2020) Intermittent fasting and weight loss Systematic review. Canadian Family Physician 66(2): 117-125	- More recent systematic review included that covers the same topic *Not meta-analysis conducted*
Willems, A.E.M., Sura-De Jong, M., Van Beek, A.P. et al. (2021) Effects of macronutrient intake in obesity: A meta-analysis of low-carbohydrate and low-fat diets on markers of the metabolic syndrome. Nutrition Reviews 79(4): 429-444	- More recent systematic review included that covers the same topic *Not meta-analysis conducted*

Study	Reason
Xu, Yang, Mo, Guli, Yao, Yu et al. (2023) The effects of vegetarian diets on glycemia and lipid parameters in adult patients with overweight and obesity: a systematic review and meta-analysis. European journal of clinical nutrition	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
Yan, S., Wang, C., Zhao, H. et al. (2020) Effects of fasting intervention regulating anthropometric and metabolic parameters in subjects with overweight or obesity: a systematic review and meta-analysis. Food & function 11(5): 3781-3799	- More recent systematic review included that covers the same topic *Follow-up of included studies was not at least 12 months*
Yang, Fan, Liu, Can, Liu, Xu et al. (2021) Effect of Epidemic Intermittent Fasting on Cardiometabolic Risk Factors: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Frontiers in nutrition 8: 669325	- Incorrect population *Many included studies were in people living without overweight or obesity*
Yang, Q., Lang, X., Li, W. et al. (2022) The effects of low-fat, high-carbohydrate diets vs. low-carbohydrate, high-fat diets on weight, blood pressure, serum liquids and blood glucose: a systematic review and meta-analysis. European Journal of Clinical Nutrition 76(1): 16-27	- More recent systematic review included that covers the same topic *Naude 2022*
Yin, Cong, Li, Zihan, Xiang, Yulin et al. (2021) Effect of Intermittent Fasting on Non-Alcoholic Fatty Liver Disease: Systematic Review and Meta-Analysis. Frontiers in nutrition 8: 709683	- More recent systematic review included that covers the same topic *Also the follow-up of the included studies did not appear to match this review's protocol*
Yuan, X., Wang, J., Yang, S. et al. (2020) Effect of the ketogenic diet on glycemic control, insulin resistance, and lipid metabolism in patients with T2DM: a systematic review and meta-analysis. Nutrition and Diabetes 10(1): 38	- More recent systematic review included that covers the same topic
Yuan, Xiaojie, Wang, Jiping, Yang, Shuo et al. (2022) Effect of Intermittent Fasting Diet on Glucose and Lipid Metabolism and Insulin Resistance in Patients with Impaired Glucose and Lipid Metabolism: A Systematic Review and Meta-Analysis. International journal of endocrinology 2022: 6999907	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.

Study	Reason
Zafar, M I, Mills, K E, Zheng, J et al. (2019) Low glycaemic index diets as an intervention for obesity: a systematic review and meta-analysis. Obesity reviews : an official journal of the International Association for the Study of Obesity 20(2): 290-315	- Study does not contain a relevant intervention *This paper is primarily interested in low glycaemic index diets. In some cases the comparator trials are suitable for this review but no appropriate meta-analysis is presented.*
Zafar, MI, Mills, KE, Zheng, J et al. (2019) Low-glycemic index diets as an intervention for diabetes: a systematic review and meta-analysis. The American journal of clinical nutrition 110(4): 891-902	- Study does not contain a relevant intervention *This paper is primarily interested in low glycaemic index diets. In some cases the comparator trials are suitable for this review but no appropriate meta-analysis is presented.*
Zaki, Hany A, Iftikhar, Haris, Abdalrubb, Abeer et al. (2022) Clinical Assessment of Intermittent Fasting With Ketogenic Diet in Glycemic Control and Weight Reduction in Patients With Type II Diabetes Mellitus: A Systematic Review and Meta-Analysis. Cureus 14(10): e30879	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
Zaki, Hany A, Iftikhar, Haris, Bashir, Khalid et al. (2022) A Comparative Study Evaluating the Effectiveness Between Ketogenic and Low-Carbohydrate Diets on Glycemic and Weight Control in Patients With Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis. Cureus 14(5): e25528	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
Zhang, Qing, Zhang, Caishun, Wang, Haidan et al. (2022) Intermittent Fasting versus Continuous Calorie Restriction: Which Is Better for Weight Loss?. Nutrients 14(9)	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
Zhang, Xiaoshuai, Zheng, Yang, Guo, Yanan et al. (2019) The Effect of Low Carbohydrate Diet on Polycystic Ovary Syndrome: A Meta-Analysis of Randomized Controlled Trials. International Journal of Endocrinology 2019: 1-14	- Incorrect population *The participants in the included studies were not necessarily living with overweight or obesity*
Zhang, Y., Chen, X., Allison, D.B. et al. (2022) Efficacy and safety of a specific commercial high-protein meal-replacement product line in weight management: meta-analysis of randomized controlled trials. Critical reviews in food science and nutrition 62(3): 798-809	- Study does not contain a relevant intervention *This study investigated high protein meal replacement products which did not necessarily meet any of the diets specified in this review's protocol*

Study	Reason
Zhou, Chong, Wang, Meng, Liang, Jiling et al. (2022) Ketogenic Diet Benefits to Weight Loss, Glycemic Control, and Lipid Profiles in Overweight Patients with Type 2 Diabetes Mellitus: A Meta-Analysis of Randomized Controlled Trails. International journal of environmental research and public health 19(16)	- Identified through an updated search. SR already included for this diet. SR was checked for additional primary studies.
Zimorovat, A, Mohammadi, M, Ramezani-Jolfaie, N et al. (2020) The healthy Nordic diet for blood glucose control: a systematic review and meta-analysis of randomized controlled clinical trials. Acta diabetologica 57(1): 1-12	- Study does not contain a relevant intervention *Nordic diet*

Excluded primary studies

Study	Reason
, Pi-Sunyer X, Blackburn G et al. (2007) Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: one-year results of the look AHEAD trial. Diabetes care 30(6): 1374-1383	- Study does not contain a relevant intervention
Acharya, S.D., Brooks, M.M., Evans, R.W. et al. (2013) Weight Loss Is More Important Than the Diet Type in Improving Adiponectin Levels Among Overweight/Obese Adults. Journal of the American College of Nutrition 32(4): 264-271	- Insufficient follow up *Study included a 6 month follow up.*
Antoni, R., Johnston, K.L., Collins, A.L. et al. (2018) Intermittent v. continuous energy restriction: Differential effects on postprandial glucose and lipid metabolism following matched weight loss in overweight/obese participants. British Journal of Nutrition 119(5): 507-516	- Insufficient follow up *Unclear follow-up but appears to be no longer than 3 months*
Aronica, L., Rigdon, J., Offringa, L.C. et al. (2021) Examining differences between overweight women and men in 12-month weight loss study comparing healthy low-carbohydrate vs. low-fat diets. International Journal of Obesity 45(1): 225-234	- Study does not contain a relevant intervention *No defined carbohydrate prescription used for intervention*

Study	Reason
Asghari, Somayyeh, Rezaei, Mahsa, Rafraf, Maryam et al. (2022) Effects of Calorie Restricted Diet on Oxidative/Antioxidative Status Biomarkers and Serum Fibroblast Growth Factor 21 Levels in Nonalcoholic Fatty Liver Disease Patients: A Randomized, Controlled Clinical Trial. Nutrients 14(12)	- Insufficient follow up
Asle Mohammadi Zadeh, M., Kargarfard, M., Marandi, S.M. et al. (2018) Diets along with interval training regimes improves inflammatory & anti-inflammatory condition in obesity with type 2 diabetes subjects. Journal of Diabetes and Metabolic Disorders 17(2): 253-267	- Insufficient follow up *Followed 24 weeks from baseline*
Baldry, E.L., Aithal, G.P., Kaye, P. et al. (2017) Effects of short-term energy restriction on liver lipid content and inflammatory status in severely obese adults: Results of a randomized controlled trial using 2 dietary approaches. Diabetes, Obesity and Metabolism 19(8): 1179-1183	- Incorrect population *Diet prior to bariatric surgery*
Bales, C.W., Starr, K.N.P., Orenduff, M.C. et al. (2017) Influence of protein intake, race, and age on responses to a weight-reduction intervention in obese women. Current Developments in Nutrition 1(5): e000703	- Insufficient follow up *Followed 6 months from baseline*
Ballesteros-Pomar, M.D., Calleja-Fernandez, A.R., Vidal-Casariego, A. et al. (2009) Effectiveness of energy-restricted diets with different protein:carbohydrate ratios: the relationship to insulin sensitivity. Public Health Nutrition: 1-8	- Insufficient follow up *Followed 4 months from baseline*
Bantle, Anne E, Lau, Kheng Joe, Wang, Qi et al. (2023) Time-restricted eating did not alter insulin sensitivity or beta-cell function in adults with obesity: A randomized pilot study. Obesity (Silver Spring, Md.) 31suppl1: 108-115	- Insufficient follow up
Barnard, N.D., Levin, S.M., Gloede, L. et al. (2018) Turning the Waiting Room into a Classroom: Weekly Classes Using a Vegan or a Portion-Controlled Eating Plan Improve Diabetes Control in a Randomized Translational	- Incorrect population *Study included people with Type 2 diabetes. Unclear if they were living with overweight and obesity. Study did specify that people with BMI over 45 kg/m2.*

Study	Reason
Study. Journal of the Academy of Nutrition and Dietetics 118(6): 1072-1079	
Barnard, Neal D, Cohen, Joshua, Jenkins, David J A et al. (2009) A low-fat vegan diet and a conventional diabetes diet in the treatment of type 2 diabetes: a randomized, controlled, 74-wk clinical trial. The American journal of clinical nutrition 89(5): 1588s-1596s	- Study does not contain a relevant intervention *Intervention did not include calorie restriction/ calorie deficit.*
Barnosky, Adrienne, Kroeger, Cynthia M, Trepanowski, John F et al. (2017) Effect of alternate day fasting on markers of bone metabolism: An exploratory analysis of a 6-month randomized controlled trial. Nutrition and healthy aging 4(3): 255-263	- Insufficient follow up *No follow-up after 6 month diet intervention is completed*
Bartholomew, Ciera L, Muhlestein, Joseph B, May, Heidi T et al. (2021) Randomized controlled trial of once-per-week intermittent fasting for health improvement: the WONDERFUL trial. European heart journal open 1(2): oeab026	- Insufficient follow up
Basciani, S., Camajani, E., Contini, S. et al. (2020) Very-low-calorie ketogenic diets with whey, vegetable, or animal protein in patients with obesity: A randomized pilot study. Journal of Clinical Endocrinology and Metabolism 105(9): 2939-2949	- Incorrect comparison *Comparison of 2 very low carbohydrate diets*
Beaulieu, K., Casanova, N., Oustric, P. et al. (2021) An exploratory investigation of the impact of 'fast' and 'feed' days during intermittent energy restriction on free-living energy balance behaviours and subjective states in women with overweight/obesity. European Journal of Clinical Nutrition 75(3): 430-437	- Secondary publication of an excluded study *Errata paper linked to Beaulieu 2020*
Beaulieu, K., Casanova, N., Oustric, P. et al. (2020) Matched Weight Loss Through Intermittent or Continuous Energy Restriction Does Not Lead to Compensatory Increases in Appetite and Eating Behavior in a Randomized Controlled Trial in Women with Overweight and Obesity. Journal of Nutrition 150(3): 623-633	- Insufficient follow up *No follow-up after 12 week diet intervention*

Study	Reason
Benassi-Evans Bianca, B., Clifton, P., Noakes, M. et al. (2010) High-protein/high red meat and high-carbohydrate weight-loss diets do not differ in their effect on faecal water genotoxicity tested by use of the WIL2-NS cell line and with other biomarkers of bowel health. Mutation Research - Genetic Toxicology and Environmental Mutagenesis 703(2): 130-136	- Incorrect outcomes *Study concentrated on diet effects on faecal water genotoxicity*
Bergia, R.E., Giacco, R., Hjorth, T. et al. (2022) Differential Glycemic Effects of Low-versus High-Glycemic Index Mediterranean-Style Eating Patterns in Adults at Risk for Type 2 Diabetes: The MEDGI-Carb Randomized Controlled Trial. Nutrients 14(3): 706	- Incorrect comparison *Low carbohydrate diet versus low carbohydrate diet*
Bhardwaj, Swati, Misra, Anoop, Gulati, Seema et al. (2017) A randomized controlled trial to evaluate the effects of high Protein Complete (lActo) VEgetaRian (PACER) diet in non-diabetic obese Asian Indians in North India. Heliyon 3(12): e00472	- Insufficient follow up *Followed 3 months from baseline*
Bhutani, S., Klempel, M.C., Kroeger, C.M. et al. (2013) Alternate day fasting and endurance exercise combine to reduce body weight and favorably alter plasma lipids in obese humans. Obesity 21(7): 1370-1379	- Insufficient follow up *No follow-up after 12 week diet intervention*
Burgess, B.; Raynor, H.A.; Tepper, B.J. (2017) PROP Nontaster Women Lose More Weight Following a Low-Carbohydrate Versus a Low-Fat Diet in a Randomized Controlled Trial. Obesity 25(10): 1682-1690	- Insufficient follow up *Followed 6 months from baseline*
Burke, L.E., Choo, J., Music, E. et al. (2006) PREFER study: A randomized clinical trial testing treatment preference and two dietary options in behavioral weight management - Rationale, design and baseline characteristics. Contemporary Clinical Trials 27(1): 34-48	- Study does not contain a relevant intervention *Not a strict plant based diet.*
Burke, L.E., Hudson, A.G., Warziski, M.T. et al. (2007) Effects of a vegetarian diet and treatment preference on biochemical and dietary variables in overweight and obese adults: A randomized clinical trial. American Journal of Clinical Nutrition 86(3): 588-596	- Study does not contain a relevant intervention *Not a strict plant based diet.*

Study	Reason
Burke, L.E., Styn, M.A., Steenkiste, A.R. et al. (2006) A randomized clinical trial testing treatment preference and two dietary options in behavioral weight management: Preliminary results of the impact of diet at 6 months - PREFER Study. Obesity 14(11): 2007-2017	- Study does not contain a relevant intervention *Not a strict plant based diet.*
Burke, L.E., Warziski, M., Styn, M.A. et al. (2008) A randomized clinical trial of a standard versus vegetarian diet for weight loss: The impact of treatment preference. International Journal of Obesity 32(1): 166-176	- Study does not contain a relevant intervention *Not a strict plant based diet.*
Cai, H., Qin, Y.-L., Shi, Z.-Y. et al. (2019) Effects of alternate-day fasting on body weight and dyslipidaemia in patients with non-alcoholic fatty liver disease: A randomised controlled trial. BMC Gastroenterology 19(1): 219	- Insufficient follow up *Participants followed 12 weeks from baseline*
Carter, S.; Clifton, P.M.; Keogh, J.B. (2016) The effects of intermittent compared to continuous energy restriction on glycaemic control in type 2 diabetes; a pragmatic pilot trial. Diabetes Research and Clinical Practice 122: 106-112	- Insufficient follow up *No follow-up after 12 week diet intervention*
Castela, I., Rodrigues, C., Ismael, S. et al. (2022) Intermittent energy restriction ameliorates adipose tissue-associated inflammation in adults with obesity: A randomised controlled trial. Clinical Nutrition 41(8): 1660-1666	- Insufficient follow up
Catenacci, V.A., Pan, Z., Ostendorf, D. et al. (2016) A randomized pilot study comparing zero-calorie alternate-day fasting to daily caloric restriction in adults with obesity. Obesity 24(9): 1874-1883	- Insufficient follow up *Participants followed 30 weeks from baseline*
Chair, S.Y., Cai, H., Cao, X. et al. (2022) Intermittent Fasting in Weight Loss and Cardiometabolic Risk Reduction: A Randomized Controlled Trial. The journal of nursing research : JNR 30(1): e185	- Incorrect comparison *Intermittent energy restriction versus intermittent energy restriction*
Chaiyasoot, K., Sarasak, R., Pheungruang, B. et al. (2018) Evaluation of a 12-week lifestyle education intervention with or without partial	- Incorrect outcomes *Insufficient follow-up for relevant outcomes*

Study	Reason
meal replacement in Thai adults with obesity and metabolic syndrome: A randomised trial. Nutrition and Diabetes 8(1): 34	
Che, T, Yan, C, Tian, D et al. (2021) Time-restricted feeding improves blood glucose and insulin sensitivity in overweight patients with type 2 diabetes: a randomised controlled trial. Nutrition & metabolism 18(1): 88	- Insufficient follow up *No follow-up after 12 week diet intervention*
Chee, W.S.S., Singh, H.K.G., Hamdy, O. et al. (2017) Structured lifestyle intervention based on a trans-cultural diabetesspecific nutrition algorithm (tDNA) in individuals with type 2 diabetes: A randomized controlled trial. BMJ Open Diabetes Research and Care 5(1): e000384	- Study does not contain a relevant intervention
Cheng, Hoi Lun, Griffin, Hayley, Claes, Bri-Ellen et al. (2014) Influence of dietary macronutrient composition on eating behaviour and self-perception in young women undergoing weight management. Eating and weight disorders : EWD 19(2): 241-7	- Secondary publication of an included study that does not provide any additional relevant information
Cheskin, L.J., Mitchell, A.M., Jhaveri, A.D. et al. (2008) Efficacy of meal replacements versus a standard food-based diet for weight loss in type 2 diabetes: a controlled clinical trial. The Diabetes educator 34(1): 118-127	- Study does not contain a relevant intervention
Cho, A.-R., Moon, J.-Y., Kim, S. et al. (2019) Effects of alternate day fasting and exercise on cholesterol metabolism in overweight or obese adults: A pilot randomized controlled trial. Metabolism: Clinical and Experimental 93: 52-60	- Insufficient follow up *No follow-up after 8 week diet intervention*
Chow, L.S., Manoogian, E.N.C., Alvear, A. et al. (2020) Time-Restricted Eating Effects on Body Composition and Metabolic Measures in Humans who are Overweight: A Feasibility Study. Obesity 28(5): 860-869	- Insufficient follow up *No follow-up after 12 week diet intervention*
Cienfuegos, S, Gabel, K, Kalam, F et al. (2021) The effect of 4-h versus 6-h time restricted feeding on sleep quality, duration, insomnia severity and obstructive sleep apnea in adults	- Insufficient follow up *No follow-up after 8 week diet intervention*

Study	Reason
with obesity. Nutrition and health: 2601060211002347	
Cienfuegos, Sofia, Gabel, Kelsey, Kalam, Faiza et al. (2020) Effects of 4- and 6-h Time-Restricted Feeding on Weight and Cardiometabolic Health: A Randomized Controlled Trial in Adults with Obesity. Cell metabolism 32(3): 366-378e3	- Insufficient follow up *No follow-up after 8 week diet intervention*
Conley, M., Le Fevre, L., Haywood, C. et al. (2018) Is two days of intermittent energy restriction per week a feasible weight loss approach in obese males? A randomised pilot study. Nutrition & dietetics: the journal of the Dietitians Association of Australia 75(1): 65-72	- Insufficient follow up *Participants followed 6 months from baseline*
Corley, B T, Carroll, R W, Hall, R M et al. (2018) Intermittent fasting in Type 2 diabetes mellitus and the risk of hypoglycaemia: a randomized controlled trial. Diabetic medicine : a journal of the British Diabetic Association 35(5): 588-594	- Insufficient follow up *No follow-up after 12 week diet intervention*
Coutinho, Silvia Ribeiro, Halset, Eline Holli, Gasbakk, Sigrid et al. (2018) Compensatory mechanisms activated with intermittent energy restriction: A randomized control trial. Clinical nutrition (Edinburgh, Scotland) 37(3): 815-823	- Insufficient follow up *Participants followed 2 months from baseline*
Crosby, Lelia, Rembert, Emilie, Levin, Susan et al. (2022) Changes in Food and Nutrient Intake and Diet Quality on a Low-Fat Vegan Diet Are Associated with Changes in Body Weight, Body Composition, and Insulin Sensitivity in Overweight Adults: A Randomized Clinical Trial. Journal of the Academy of Nutrition and Dietetics 122(10): 1922-1939e0	- Insufficient follow up
Crose, A., Alvear, A., Singroy, S. et al. (2021) Time-restricted eating improves quality of life measures in overweight humans. Nutrients 13(5): 1430	- Insufficient follow up *No follow-up after 12 week diet intervention*
Cunha, G.M., Correa de Mello, L.L., Hasenstab, K.A. et al. (2020) MRI estimated changes in visceral adipose tissue and liver fat fraction in patients with obesity during a very low-calorie-	- Insufficient follow up

Study	Reason
ketogenic diet compared to a standard low-calorie diet. Clinical Radiology 75(7): 526-532	
Cunha, G.M., Guzman, G., Correa De Mello, L.L. et al. (2020) Efficacy of a 2-Month Very Low-Calorie Ketogenic Diet (VLCKD) Compared to a Standard Low-Calorie Diet in Reducing Visceral and Liver Fat Accumulation in Patients With Obesity. Frontiers in Endocrinology 11: 607	- Insufficient follow up *2 months*
Davis, L.M., Coleman, C., Kiel, J. et al. (2010) Efficacy of a meal replacement diet plan compared to a food-based diet plan after a period of weight loss and weight maintenance: a randomized controlled trial. Nutrition journal 9: 11	- Insufficient follow up
Davis, N.J., Tomuta, N., Schechter, C. et al. (2009) Comparative study of the effects of a 1-year dietary intervention of a low-carbohydrate diet versus a low-fat diet on weight and glycemic control in type 2 diabetes. Diabetes Care 32(7): 1147-1152	- Study does not contain a relevant intervention *Amount of carbohydrate prescribed in intervention arm not clearly defined.*
De Jonge, L., Bray, G.A., Smith, S.R. et al. (2012) Effect of diet composition and weight loss on resting energy expenditure in the POUNDS LOST study. Obesity 20(12): 2384-2389	- Secondary publication of an included study that does not provide any additional relevant information
De Luis, D.A., Aller, R., Izaola, O. et al. (2015) Effects of a High-Protein/Low-Carbohydrate Diet versus a Standard Hypocaloric Diet on Weight and Cardiovascular Risk Factors: Role of a Genetic Variation in the rs9939609 FTO Gene Variant. Journal of Nutrigenetics and Nutrigenomics 8(3): 128-136	- Insufficient follow up *Followed 9 months from baseline*
De Luis, D.A., Aller, R., Izaola, O. et al. (2015) Effects of a high-protein/low-carbohydrate versus a standard hypocaloric diet on adipocytokine levels and cardiovascular risk factors during 9 months, role of rs6923761 gene variant of glucagon-like peptide 1 receptor. Journal of Endocrinological Investigation 38(11): 1183-1189	- Insufficient follow up *Followed 9 months from baseline*

Study	Reason
De Luis, D.A., Izaola, O., Aller, R. et al. (2015) Effects of a high-protein/low carbohydrate versus a standard hypocaloric diet on adipocytokine levels and insulin resistance in obese patients along 9 months. Journal of Diabetes and its Complications 29(7): 950-954	- Insufficient follow up *Followed 9 months from baseline*
De Luis, D.A., Izaola, O., De La Fuente, B. et al. (2015) Role of fatty acid-binding protein 2 Ala54Thr genotype on weight loss and cardiovascular risk factors after a high-protein/low-carbohydrate versus a standard hypocaloric diet during 9 months. Annals of Nutrition and Metabolism 67(2): 81-86	- Insufficient follow up *Followed 9 months from baseline*
de Luis, D.A., Izaola, O., Primo, D. et al. (2020) A circadian rhythm-related MTNR1B genetic variant (rs10830963) modulate body weight change and insulin resistance after 9months of a high protein/low carbohydrate vs a standard hypocaloric diet. Journal of Diabetes and its Complications 34(4): 107534	- Insufficient follow up *Followed 9 months from baseline*
de Luis, D.A., Izaola, O., Primo, D. et al. (2019) Different effects of high-protein/low-carbohydrate versus standard hypocaloric diet on insulin resistance and lipid profile: Role of rs16147 variant of neuropeptide Y. Diabetes Research and Clinical Practice 156: 107825	- Insufficient follow up *Followed 9 months from baseline*
De Luis, DA, Aller, R, Izaola, O et al. (2016) [Not Available]. Nutricion hospitalaria 33(3): 267	- Conference abstract
de Oliveira Maranhao Pureza, Isabele Rejane, da Silva Junior, Andre Eduardo, Silva Praxedes, Dafiny Rodrigues et al. (2021) Effects of time-restricted feeding on body weight, body composition and vital signs in low-income women with obesity: A 12-month randomized clinical trial. Clinical nutrition (Edinburgh, Scotland) 40(3): 759-766	- Study conducted in a non OEDCD country
Dyson, P.A.; Beatty, S.; Matthews, D.R. (2007) A low-carbohydrate diet is more effective in reducing body weight than healthy eating in both diabetic and non-diabetic subjects. Diabetic Medicine 24(12): 1430-1435	- Insufficient follow up *Participants were followed 3 months from baseline*

Study	Reason
Dyson, PA; Beatty, S; Matthews, DR (2010) An assessment of low-carbohydrate or low-fat diets for weight loss at 2 year's follow-up. Diabetic medicine 27(3): 363-364	- Data not reported in an extractable format
Ebbeling, C.B., Bielak, L., Lakin, P.R. et al. (2020) Energy requirement is higher during weight-loss maintenance in adults consuming a low- compared with high-carbohydrate diet. Journal of Nutrition 150(8): 2009-2015	- Insufficient follow up *Followed 20 weeks from baseline*
Ebbeling, C.B., Feldman, H.A., Klein, G.L. et al. (2018) Effects of a low carbohydrate diet on energy expenditure during weight loss maintenance: Randomized trial. The BMJ 363: k4583	- Errata for paper not included
Ebbeling, C.B., Knapp, A., Johnson, A. et al. (2022) Effects of a low-carbohydrate diet on insulin-resistant dyslipoproteinemia-a randomized controlled feeding trial. The American journal of clinical nutrition 115(1): 154-162	- Insufficient follow up *Followed 20 weeks from baseline*
Evangelista, L.S., Jose, M.M., Sallam, H. et al. (2021) High-protein vs. standard-protein diets in overweight and obese patients with heart failure and diabetes mellitus: findings of the Pro-HEART trial. ESC Heart Failure 8(2): 1342-1348	- Insufficient follow up *Followed 3 months from baseline*
Evans, Ellen M, Mojtahedi, Mina C, Thorpe, Matthew P et al. (2012) Effects of protein intake and gender on body composition changes: a randomized clinical weight loss trial. Nutrition & metabolism 9(1): 55	- Secondary publication of an included study that does not provide any additional relevant information
Ezpeleta, Mark, Gabel, Kelsey, Cienfuegos, Sofia et al. (2023) Alternate-Day Fasting Combined with Exercise: Effect on Sleep in Adults with Obesity and NAFLD. Nutrients 15(6)	- Insufficient follow up
Fagundes, Gabriela Barbosa Pires, Tibaes, Jenneffer Rayane Braga, Silva, Mariele Lino et al. (2023) Metabolic and behavioral effects of time-restricted eating in women with overweight or obesity: Preliminary findings from a	- Insufficient follow up

Study	Reason
randomized study. Nutrition (Burbank, Los Angeles County, Calif.) 107: 111909	
Ferdowsian, H.R., Barnard, N.D., Hoover, V.J. et al. (2010) A multicomponent intervention reduces body weight and cardiovascular risk at a GEICO corporate site. American journal of health promotion : AJHP 24(6): 384-387	- Insufficient follow up *Study included a 22 week follow up.*
Flechtner-Mors, M., Boehm, B.O., Wittmann, R. et al. (2010) Enhanced weight loss with protein-enriched meal replacements in subjects with the metabolic syndrome. Diabetes/Metabolism Research and Reviews 26(5): 393-405	- Study does not contain a relevant intervention *Both groups received replacements and it was not low energy from the start*
Fudla, H; Mudjihartini, N; Khusun, H (2021) Effect of four weeks of 5: 2 intermittent fasting on energy intake and body mass index among obese male students aged 18-25. Obesity medicine 25	- Insufficient follow up *No follow-up after 4 week diet intervention*
Gardner, C.D., Kiazand, A., Alhassan, S. et al. (2007) Comparison of the atkins, zone, ornish, and LEARN diets for change in weight and related risk factors among overweight premenopausal women. The A to Z weight loss study: A randomized trial. Obstetrical and Gynecological Survey 62(7): 454-456	- Editorial comment
Gardner, C.D., Offringa, L.C., Hartle, J.C. et al. (2016) Weight loss on low-fat vs. low-carbohydrate diets by insulin resistance status among overweight adults and adults with obesity: A randomized pilot trial. Obesity 24(1): 79-86	- Insufficient follow up *Followed 6 months from baseline*
Gardner, C.D., Trepanowski, J.F., Gobbo, L.C.D. et al. (2018) Effect of low-fat VS low-carbohydrate diet on 12-month weight loss in overweight adults and the association with genotype pattern or insulin secretion the DIETFITS randomized clinical trial. JAMA - Journal of the American Medical Association 319(7): 667-679	- Study does not contain a relevant intervention *No defined carbohydrate prescription used for intervention*
Goday, A., Bellido, D., Sajoux, I. et al. (2016) Short-Term safety, tolerability and efficacy of a very low-calorie-ketogenic diet interventional	- Insufficient follow up *4 months*

Study	Reason
weight loss program versus hypocaloric diet in patients with type 2 diabetes mellitus. Nutrition and Diabetes 6(9): e230	
Goldenshluger, Ariela, Constantini, Keren, Goldstein, Nir et al. (2021) Effect of Dietary Strategies on Respiratory Quotient and Its Association with Clinical Parameters and Organ Fat Loss: A Randomized Controlled Trial. Nutrients 13(7)	- Insufficient follow up *Followed 6 months from baseline*
Goni, L., Riezu-Boj, J.I., Milagro, F.I. et al. (2018) Interaction between an ADCY3 genetic variant and two weight-lowering diets affecting body fatness and body composition outcomes depending on macronutrient distribution: A randomized trial. Nutrients 10(6): 789	- Insufficient follow up *Followed 6 months from baseline*
Goss, A.M., Gower, B., Soleymani, T. et al. (2020) Effects of weight loss during a very low carbohydrate diet on specific adipose tissue depots and insulin sensitivity in older adults with obesity: A randomized clinical trial. Nutrition and Metabolism 17(1): 64	- Insufficient follow up
Gram-Kampmann, E.M., Hansen, C.D., Hugger, M.B. et al. (2022) Effects of a 6-month, low-carbohydrate diet on glycaemic control, body composition, and cardiovascular risk factors in patients with type 2 diabetes: An open-label randomized controlled trial. Diabetes, Obesity and Metabolism	- Insufficient follow up *Followed 6 months from baseline*
Gulati, S, Misra, A, Tiwari, R et al. (2017) Effect of high-protein meal replacement on weight and cardiometabolic profile in overweight/obese Asian Indians in North India. British journal of nutrition 117(11): 1531-1540	- Insufficient follow up *No follow-up after diet phase completed*
Gulsin, G.S., Swarbrick, D.J., Athithan, L. et al. (2020) Effects of low-energy diet or exercise on cardiovascular function in working-age adults with type 2 diabetes: A prospective, randomized, open-label, blinded end point trial. Diabetes Care 43(6): 1300-1310	- Insufficient follow up *12 weeks*
Guo, X., Xu, Y., He, H. et al. (2018) Effects of a Meal Replacement on Body Composition and	- Insufficient follow up

Study	Reason
Metabolic Parameters among Subjects with Overweight or Obesity. Journal of Obesity 2018: 2837367	*No follow-up after diet phase completed*
Guo, Y, Luo, S, Ye, Y et al. (2021) Intermittent Fasting Improves Cardiometabolic Risk Factors and Alters Gut Microbiota in Metabolic Syndrome Patients. Journal of clinical endocrinology and metabolism 106(1): 64-79	- Insufficient follow up *No follow-up after 8 week diet intervention*
Gutierrez-Repiso, C., Hernandez-Garcia, C., Garcia-Almeida, J.M. et al. (2019) Effect of Synbiotic Supplementation in a Very-Low-Calorie Ketogenic Diet on Weight Loss Achievement and Gut Microbiota: A Randomized Controlled Pilot Study. Molecular nutrition & food research 63(19): e1900167	- Incorrect comparison *Assessment of synbiotic supplementation and not a comparison of diets*
Hall, K.D., Guo, J., Courville, A.B. et al. (2021) Effect of a plant-based, low-fat diet versus an animal-based, ketogenic diet on ad libitum energy intake. Nature Medicine 27(2): 344-353	- Incorrect study design *Crossover RCT*
Hansen, C.D., Gram-Kampmann, E.-M., Hansen, J.K. et al. (2023) Effect of Calorie-Unrestricted Low-Carbohydrate, High-Fat Diet Versus High-Carbohydrate, Low-Fat Diet on Type 2 Diabetes and Nonalcoholic Fatty Liver Disease. Annals of Internal Medicine 176(1): 10-22	- Conference abstract
Harvey, C.J.D.C., Schofield, G.M., Zinn, C. et al. (2019) Low-carbohydrate diets differing in carbohydrate restriction improve cardiometabolic and anthropometric markers in healthy adults: A randomised clinical trial. PeerJ 2019(2): e6273	- Incorrect population *Not in people living with overweight or obesity*
Harvie, M., Wright, C., Pegington, M. et al. (2013) The effect of intermittent energy and carbohydrate restriction v. daily energy restriction on weight loss and metabolic disease risk markers in overweight women. British Journal of Nutrition 110(8): 1534-1547	- Insufficient follow up *Participants followed 4 months from baseline*
Harvie, M.N., Pegington, M., Mattson, M.P. et al. (2011) The effects of intermittent or continuous energy restriction on weight loss and metabolic	- Insufficient follow up *Participants followed 6 months from baseline*

Study	Reason
disease risk markers: A randomized trial in young overweight women. International Journal of Obesity 35(5): 714-727	
Haufe, S., Engeli, S., Kast, P. et al. (2011) Randomized comparison of reduced fat and reduced carbohydrate hypocaloric diets on intrahepatic fat in overweight and obese human subjects. Hepatology 53(5): 1504-1514	- Insufficient follow up *Followed 6 months from baseline*
Haufe, S., Haas, V., Utz, W. et al. (2013) Long-lasting improvements in liver fat and metabolism despite body weight regain after dietary weight loss. Diabetes Care 36(11): 3786-3792	- Incorrect outcomes *Extended follow-up that does not provide relevant outcomes*
Haufe, S, Engeli, S, Kaminski, J et al. (2017) Branched-chain amino acid catabolism rather than amino acids plasma concentrations is associated with diet-induced changes in insulin resistance in overweight to obese individuals. Nutrition, metabolism, and cardiovascular diseases : NMCD 27(10): 858-864	- Insufficient follow up *Followed 6 months from baseline*
Haywood, C.J., Prendergast, L.A., Purcell, K. et al. (2017) Very Low Calorie Diets for Weight Loss in Obese Older Adults-A Randomized Trial. The journals of gerontology. Series A, Biological sciences and medical sciences 73(1): 59-65	- Insufficient follow up *No follow-up after the diet*
He, Chao-Jie, Fei, Ye-Ping, Zhu, Chun-Yan et al. (2021) Effects of Intermittent Compared With Continuous Energy Restriction on Blood Pressure Control in Overweight and Obese Patients With Hypertension. Frontiers in cardiovascular medicine 8: 750714	- Study does not contain a relevant intervention *Low energy diet without replacement*
He, M., Wang, J., Liang, Q. et al. (2022) Time-restricted eating with or without low-carbohydrate diet reduces visceral fat and improves metabolic syndrome: A randomized trial. Cell Reports Medicine 3(10): 100777	- Insufficient follow up
Headland, M.L.; Clifton, P.M.; Keogh, J.B. (2019) Effect of intermittent compared to continuous energy restriction on weight loss and weight maintenance after 12 months in healthy	- Incorrect comparison *Intermittent energy restriction versus intermittent energy restriction*

Study	Reason
overweight or obese adults. International Journal of Obesity 43(10): 2028-2036	
Heggen, E., Svendsen, M., Klemsdal, T.O. et al. (2016) Low carbohydrate and moderately fat-reduced diets similarly affected early weight gain in varenicline-treated overweight or obese smokers. Nicotine and Tobacco Research 18(6): 1440-1448	- Insufficient follow up *Followed 6 months from baseline*
Henke, C., Haufe, S., Ziehl, D. et al. (2021) Low-fat hypocaloric diet reduces neprilysin in overweight and obese human subjects. ESC Heart Failure 8(2): 938-942	- Insufficient follow up *Followed 6 months from baseline*
Hirsh, S.P., Pons, M., Joyal, S.V. et al. (2019) Avoiding holiday seasonal weight gain with nutrient-supported intermittent energy restriction: A pilot study. Journal of Nutritional Science	- Insufficient follow up *No follow-up after 52 day diet intervention*
Holmer, M., Lindqvist, C., Petersson, S. et al. (2021) Treatment of NAFLD with intermittent calorie restriction or low-carb high-fat diet - a randomised controlled trial. JHEP Reports 3(3): 100256	- Insufficient follow up *No follow-up after 8 week diet intervention*
Hu, T, Yao, L, Reynolds, K et al. (2016) The effects of a low-carbohydrate diet on appetite: A randomized controlled trial. Nutrition, metabolism, and cardiovascular diseases : NMCD 26(6): 476-88	- Secondary publication of an included study that does not provide any additional relevant information
Hutchison, A.T., Liu, B., Wood, R.E. et al. (2019) Effects of Intermittent Versus Continuous Energy Intakes on Insulin Sensitivity and Metabolic Risk in Women with Overweight. Obesity 27(1): 50-58	- Insufficient follow up *No follow-up after 8 week diet intervention*
Hwang, C.-L., Ranieri, C., Szczurek, M.R. et al. (2020) The effect of low-carbohydrate diet on macrovascular and microvascular endothelial function is not affected by the provision of caloric restriction in women with obesity: A randomized study. Nutrients 12(6): 1649	- Incorrect comparison *Low carbohydrate diet versus low carbohydrate diet*

Study	Reason
Isenmann, E.; Dissemond, J.; Geisler, S. (2021) The effects of a macronutrient-based diet and time-restricted feeding (16:8) on body composition in physically active individuals-a 14-week randomised controlled trial. Nutrients 13(9): 3122	- Insufficient follow up *Participants followed 16 weeks from baseline*
Ismael, Sherzad Ali (2021) Effects of low carbohydrate diet compared to low fat diet on reversing the metabolic syndrome, using NCEP ATP III criteria: a randomized clinical trial. BMC nutrition 7(1): 62	- Insufficient follow up *Followed 6 months from baseline*
Izaola, O., Primo, D., Gomez Hoyos, E. et al. (2020) Association of rs670 variant of APOA1 gene with lipid profile and insulin resistance after 9 months of a high protein/low carbohydrate vs a standard hypocaloric diet. Clinical Nutrition 39(4): 988-993	- Insufficient follow up *Followed 9 months from baseline*
Jakše, B, Pinter, S, Jakše, B et al. (2017) Effects of an Ad Libitum Consumed Low-Fat Plant-Based Diet Supplemented with Plant-Based Meal Replacements on Body Composition Indices. BioMed research international 2017: 9626390	- Incorrect study design *Not an RCT*
Jamshed, Humaira, Steger, Felicia L, Bryan, David R et al. (2022) Effectiveness of Early Time-Restricted Eating for Weight Loss, Fat Loss, and Cardiometabolic Health in Adults With Obesity: A Randomized Clinical Trial. JAMA internal medicine 182(9): 953-962	- Insufficient follow up
Jansen, Lisa T, Yang, Nianlan, Wong, Julia M W et al. (2022) Prolonged Glycemic Adaptation Following Transition From a Low- to High-Carbohydrate Diet: A Randomized Controlled Feeding Trial. Diabetes care 45(3): 576-584	- Insufficient follow up *No follow-up after diet is completed*
Jenkins, D.J.A., Wong, J.M.W., Kendall, C.W.C. et al. (2014) Effect of a 6-month vegan low-carbohydrate ('Eco-Atkins') diet on cardiovascular risk factors and body weight in hyperlipidaemic adults: A randomised controlled trial. BMJ Open 4(2): e003505	- Insufficient follow up *Study included a 6 month follow up.*

Study	Reason
Jenkins, David J A, Jones, Peter J H, Abdullah, Mohammad M H et al. (2022) Low-carbohydrate vegan diets in diabetes for weight loss and sustainability: a randomized controlled trial. The American journal of clinical nutrition	- Insufficient follow up
Jenkins, David J A, Wong, Julia M W, Kendall, Cyril W C et al. (2009) The effect of a plant-based low-carbohydrate ("Eco-Atkins") diet on body weight and blood lipid concentrations in hyperlipidemic subjects. Archives of internal medicine 169(11): 1046-54	- Insufficient follow up *Study included a 4 week follow up.*
Jensen, Nicole Jacqueline, Wodschow, Helena Zander, Skytte, Mads Juul et al. (2022) Weight-loss induced by carbohydrate restriction does not negatively affect health-related quality of life and cognition in people with type 2 diabetes: A randomised controlled trial. Clinical nutrition (Edinburgh, Scotland) 41(7): 1605-1612	- Insufficient follow up
Jesudason, David, Nordin, Be Christopher, Keogh, Jennifer et al. (2013) Comparison of 2 weight-loss diets of different protein content on bone health: a randomized trial. The American journal of clinical nutrition 98(5): 1343-52	- Study does not contain a relevant intervention
Jimenez, A.M., Oliva, S.L., Vilar, E.G. et al. (2019) The Mediterranean diet pattern with intermittent semi-fasting may facilitate weight loss: Randomised controlled trial. Mediterranean Journal of Nutrition and Metabolism 12(2): 153-161	- Insufficient follow up *Participants followed 2-4 months from baseline*
Josse, A.R., Atkinson, S.A., Tarnopolsky, M.A. et al. (2011) Increased consumption of dairy foods and protein during diet- and exercise-induced weight loss promotes fat mass loss and lean mass gain in overweight and obese premenopausal women. Journal of Nutrition 141(9): 1626-1634	- Study does not contain a relevant intervention
Josse, Andrea R, Atkinson, Stephanie A, Tarnopolsky, Mark A et al. (2012) Diets higher in dairy foods and dietary protein support bone health during diet- and exercise-induced weight loss in overweight and obese premenopausal	- Insufficient follow up *Followed 4 months from baseline*

Study	Reason
women. The Journal of clinical endocrinology and metabolism 97(1): 251-60	
Juanola-Falgarona, M., Ibarrola-Jurado, N., Salas-Salvado, J. et al. (2013) Design and methods of the GLYNDIET study; assessing the role of glycemic index on weight loss and metabolic risk markers. Nutricion hospitalaria 28(2): 382-390	- Insufficient follow up *Followed 6 months from baseline*
Juanola-Falgarona, M., Salas-Salvado, J., Ibarrola-Jurado, N. et al. (2014) Effect of the glycemic index of the diet on weight loss, modulation of satiety, inflammation, and other metabolic risk factors: A randomized controlled trial. American Journal of Clinical Nutrition 100(1): 27-35	- Insufficient follow up *Followed 6 months from baseline*
Kahathuduwa, C.N., Davis, T., O'Boyle, M. et al. (2018) Effects of 3-week total meal replacement vs. typical food-based diet on human brain functional magnetic resonance imaging food-cue reactivity and functional connectivity in people with obesity. Appetite 120: 431-441	- Incorrect outcomes *Outcomes linked to brain structure and function*
Kahleova, H., Dort, S., Holubkov, R. et al. (2018) A plant-based high-carbohydrate, low-fat diet in overweight individuals in a 16-week randomized clinical trial: The role of carbohydrates. Nutrients 10(9): 1302	- Insufficient follow up *Study only included a 16 week follow up.*
Kahleova, H., Fleeman, R., Hlozkova, A. et al. (2018) A plant-based diet in overweight individuals in a 16-week randomized clinical trial: metabolic benefits of plant protein. Nutrition and Diabetes 8(1): 58	- Insufficient follow up *Study only included a 16 week follow up.*
Kahleova, H., Hlozkova, A., Fleeman, R. et al. (2019) Fat quantity and quality, as part of a low-fat, vegan diet, are associated with changes in body composition, insulin resistance, and insulin secretion. A 16-week randomized controlled trial. Nutrients 11(3): 615	- Insufficient follow up *Study only included a 16 week follow up.*
Kahleova, H., Petersen, K.F., Shulman, G.I. et al. (2020) Effect of a Low-Fat Vegan Diet on Body Weight, Insulin Sensitivity, Postprandial Metabolism, and Intramyocellular and	- Insufficient follow up *Study included a 16 week follow up.*

Study	Reason
Hepatocellular Lipid Levels in Overweight Adults: A Randomized Clinical Trial. JAMA Network Open: 25454	
Kahleova, H, Klementova, M, Herynek, V et al. (2017) The Effect of a Vegetarian vs Conventional Hypocaloric Diabetic Diet on Thigh Adipose Tissue Distribution in Subjects with Type 2 Diabetes: A Randomized Study. Journal of the American College of Nutrition 36(5): 364-369	- Incorrect outcomes - Insufficient follow up *Study included a 6 month follow-up.*
Kahleova, H, Matoulek, M, Malinska, H et al. (2011) Vegetarian diet improves insulin resistance and oxidative stress markers more than conventional diet in subjects with Type 2 diabetes. Diabetic medicine : a journal of the British Diabetic Association 28(5): 549-59	- Insufficient follow up *Study included a 24 week follow up.*
Karimi, Golgis, Azadbakht, Leila, Haghighatdoost, Fahimeh et al. (2016) Low energy density diet, weight loss maintenance, and risk of cardiovascular disease following a recent weight reduction program: A randomized control trial. Journal of research in medical sciences : the official journal of Isfahan University of Medical Sciences 21: 32	- Study does not contain a relevant intervention *Low energy diet without replacement*
Keenan, SJ, Cooke, MB, Hassan, EB et al. (2022) Intermittent fasting and continuous energy restriction result in similar changes in body composition and muscle strength when combined with a 12 week resistance training program. European journal of nutrition	- Insufficient follow up *No follow-up after 12 week diet intervention*
Kempf, K., Rohling, M., Banzer, W. et al. (2021) High-protein, low-glycaemic meal replacement decreases fasting insulin and inflammation markers-a 12-month subanalysis of the acoorh trial. Nutrients 13(5): 1433	- Incorrect outcomes *Analysis linked to fasting insulin outcome*
Kempf, K., Rohling, M., Niedermeier, K. et al. (2018) Individualized meal replacement therapy improves clinically relevant long-term glycemic control in poorly controlled type 2 diabetes patients. Nutrients 10(8): 1022	- Incorrect study design *There was no randomised allocation to the control group*

Study	Reason
Kempf, Kerstin, Rohling, Martin, Banzer, Winfried et al. (2022) High-Protein, Low-Glycaemic Meal Replacement Improves Physical Health-Related Quality of Life in High-Risk Persons for Metabolic Syndrome-A Subanalysis of the Randomised-Controlled ACOORH Trial. Nutrients 14(15)	- Study does not contain a relevant intervention *Study states diet was high-protein, low glycaemic meal replacement but exact composition not provided*
Keogh, Jennifer B, Brinkworth, Grant D, Noakes, Manny et al. (2008) Effects of weight loss from a very-low-carbohydrate diet on endothelial function and markers of cardiovascular disease risk in subjects with abdominal obesity. The American journal of clinical nutrition 87(3): 567-76	- Insufficient follow up *Participants were followed 2 months from baseline*
Keogh, Jennifer B and Clifton, Peter M (2012) Meal replacements for weight loss in type 2 diabetes in a community setting. Journal of nutrition and metabolism 2012: 918571	- Insufficient follow up *No follow-up period after diet phase completed*
Khoo, J., Ling, P.-S., Chen, R.Y.-T. et al. (2014) Comparing the effects of meal replacements with an isocaloric reduced-fat diet on nutrient intake and lower urinary tract symptoms in obese men. Journal of human nutrition and dietetics : the official journal of the British Dietetic Association 27(3): 219-226	- Insufficient follow up *No follow-up after diet phase completed*
Khoo, J., Ling, P.-S., Tan, J. et al. (2014) Comparing the effects of meal replacements with reduced-fat diet on weight, sexual and endothelial function, testosterone and quality of life in obese Asian men. International Journal of Impotence Research 26(2): 61-66	- Study does not contain a relevant intervention
Kikuchi, Takako, Kushiyama, Akifumi, Yanai, Miho et al. (2023) Comparison of Weight Reduction, Change in Parameters and Safety of a Very Low Carbohydrate Diet in Comparison to a Low Carbohydrate Diet in Obese Japanese Subjects with Metabolic Disorders. Nutrients 15(6)	- Insufficient follow up
Kimura, M, Kondo, Y, Aoki, K et al. (2018) A Randomized Controlled Trial of a Mini Low-Carbohydrate Diet and an Energy-Controlled Diet Among Japanese Patients With Type 2	- Study does not contain a relevant intervention *Not a low energy diet*

Study	Reason
Diabetes. Journal of clinical medicine research 10(3): 182-188	
Kitabchi, A.E., McDaniel, K.A., Wan, J.Y. et al. (2013) Effects of high-protein versus high-carbohydrate diets on markers of beta- Cell function, oxidative stress, lipid peroxidation, proinflammatory cytokines, and adipokines in obese, premenopausal women without diabetes. Diabetes Care 36(7): 1919-1925	- Insufficient follow up *Followed 3 months from baseline*
Konig, D., Zdzieblik, D., Deibert, P. et al. (2015) Internal fat and cardiometabolic risk factors following a meal-replacement regimen vs. comprehensive lifestyle changes in obese subjects. Nutrients 7(12): 9825-9833	- Study does not contain a relevant intervention *The diet was low energy for 6 weeks but raised above this for the majority of the trial*
Kord Varkaneh, Hamed, Salehi Sahlabadi, Ammar, Gaman, Mihnea-Alexandru et al. (2022) Effects of the 5:2 intermittent fasting diet on non-alcoholic fatty liver disease: A randomized controlled trial. Frontiers in nutrition 9: 948655	- Insufficient follow up
Kord-Varkaneh, Hamed, Salehi-Sahlabadi, Ammar, Tinsley, Grant M et al. (2023) Effects of time-restricted feeding (16/8) combined with a low-sugar diet on the management of non-alcoholic fatty liver disease: A randomized controlled trial. Nutrition (Burbank, Los Angeles County, Calif.) 105: 111847	- Insufficient follow up
Kotarsky, C.J., Johnson, N.R., Mahoney, S.J. et al. (2021) Time-restricted eating and concurrent exercise training reduces fat mass and increases lean mass in overweight and obese adults. Physiological Reports 9(10): e14868	- Insufficient follow up *No follow-up after 8 week diet intervention*
Kunduraci, Y.E. and Ozbek, H. (2020) Does the energy restriction intermittent fasting diet alleviate metabolic syndrome biomarkers? A randomized controlled trial. Nutrients 12(10): 1-13	- Insufficient follow up *No follow-up after 12 week diet intervention*
Kuriyan, R., Lokesh, D.P., D'Souza, N. et al. (2017) Portion controlled ready-to-eat meal replacement is associated with short term weight loss: a randomised controlled trial. Asia	- Insufficient follow up *No follow-up after diet phase completed*

Study	Reason
Pacific journal of clinical nutrition 26(6): 1055-1065	
Lasker, D.A.W.; Evans, E.M.; Layman, D.K. (2008) Moderate carbohydrate, moderate protein weight loss diet reduces cardiovascular disease risk compared to high carbohydrate, low protein diet in obese adults: A randomized clinical trial. Nutrition and Metabolism 5(1): 30	- Insufficient follow up *Followed 4 months from baseline*
Lee, Yu-Mi, Kim, Se-A, Lee, In-Kyu et al. (2016) Effect of a Brown Rice Based Vegan Diet and Conventional Diabetic Diet on Glycemic Control of Patients with Type 2 Diabetes: A 12-Week Randomized Clinical Trial. PLOS ONE 11(6): e0155918	- Insufficient follow up *Study included 12 week follow up.*
Li, C., Sadraie, B., Steckhan, N. et al. (2017) Effects of A One-week Fasting Therapy in Patients with Type-2 Diabetes Mellitus and Metabolic Syndrome - A Randomized Controlled Explorative Study. Experimental and Clinical Endocrinology and Diabetes 125(9): 618-624	- Insufficient follow up *Participants followed 4 months from baseline*
Li, S., Lin, G., Chen, J. et al. (2022) The effect of periodic ketogenic diet on newly diagnosed overweight or obese patients with type 2 diabetes. BMC Endocrine Disorders 22(1): 34	- Insufficient follow up *Followed 3 months from baseline*
Lin, YJ, Wang, YT, Chan, LC et al. (2022) Effect of time-restricted feeding on body composition and cardio-metabolic risk in middle-aged women in Taiwan. Nutrition (Burbank, Los Angeles County, Calif.) 93: 111504	- Insufficient follow up *No follow-up after 8 week diet intervention*
Lindqvist, Catarina, Holmer, Magnus, Hagstrom, Hannes et al. (2023) Macronutrient composition and its effect on body composition changes during weight loss therapy in patients with non-alcoholic fatty liver disease: Secondary analysis of a randomized controlled trial. Nutrition (Burbank, Los Angeles County, Calif.) 110: 111982	- Insufficient follow up
Liu, X., Zhang, G., Ye, X. et al. (2013) Effects of a low-carbohydrate diet on weight loss and cardiometabolic profile in Chinese women: A	- Insufficient follow up *Followed 3 months from baseline*

Study	Reason
randomised controlled feeding trial. British Journal of Nutrition 110(8): 1444-1453	
Llanos, Adana Am, Krok, Jessica L, Peng, Juan et al. (2014) Favorable effects of low-fat and low-carbohydrate dietary patterns on serum leptin, but not adiponectin, among overweight and obese premenopausal women: a randomized trial. SpringerPlus 3: 175	- Incorrect outcomes *Relevant study that did not report any outcomes in this review's protocol*
Lobene, A.J., Panda, S., Mashek, D.G. et al. (2021) Time-restricted eating for 12 weeks does not adversely alter bone turnover in overweight adults. Nutrients 13(4): 1155	- Insufficient follow up *No follow-up after 12 week diet intervention*
Lowe, D.A., Wu, N., Rohdin-Bibby, L. et al. (2020) Effects of Time-Restricted Eating on Weight Loss and Other Metabolic Parameters in Women and Men with Overweight and Obesity: The TREAT Randomized Clinical Trial. JAMA Internal Medicine 180(11): 1491-1499	- Insufficient follow up *No follow-up after 12 week diet intervention*
Lowe, M.R.; Butryn, M.L.; Zhang, F. (2018) Evaluation of meal replacements and a home food environment intervention for long-term weight loss: A randomized controlled trial. American Journal of Clinical Nutrition 107(1): 12-19	- Insufficient follow up *No follow-up after 12 week diet intervention*
Marco-Benedi, V., Perez-Calahorra, S., Bea, A.M. et al. (2020) High-protein energy-restricted diets induce greater improvement in glucose homeostasis but not in adipokines comparing to standard-protein diets in early-onset diabetic adults with overweight or obesity. Clinical Nutrition 39(5): 1354-1363	- Insufficient follow up *Followed 6 months from baseline*
Maroofi, M. and Nasrollahzadeh, J. (2020) Effect of intermittent versus continuous calorie restriction on body weight and cardiometabolic risk markers in subjects with overweight or obesity and mild-to-moderate hypertriglyceridemia: A randomized trial. Lipids in Health and Disease 19(1): 216	- Insufficient follow up *No follow-up after 8 week diet intervention*
Martin, C.K., Rosenbaum, D., Han, H. et al. (2011) Change in food cravings, food preferences, and appetite during a low-	- Study does not contain a relevant intervention

Study	Reason
carbohydrate and low-fat diet. Obesity 19(10): 1963-1970	*Diet includes elements of both very low carbohydrates diet and low carbohydrates diet*
Mateo-Gallego, R., Lamiquiz-Moneo, I., Perez-Calahorra, S. et al. (2018) Different protein composition of low-calorie diet differently impacts adipokine profile irrespective of weight loss in overweight and obese women. Nutrition, Metabolism and Cardiovascular Diseases 28(2): 133-142	- Insufficient follow up *Followed 3 months from baseline*
Mateo-Gallego, R., Marco-Benedi, V., Perez-Calahorra, S. et al. (2017) Energy-restricted, high-protein diets more effectively impact cardiometabolic profile in overweight and obese women than lower-protein diets. Clinical Nutrition 36(2): 371-379	- Insufficient follow up *Followed 3 months from baseline*
McDiarmid, Sarah, Harvie, Michelle, Johnson, Rhona et al. (2021) Intermittent Versus Continuous Low-Energy Diet in Patients With Type 2 Diabetes: Protocol for a Pilot Randomized Controlled Trial. JMIR research protocols 10(3): e21116	- Protocol of an included study
Merra, G., Gratteri, S., De Lorenzo, A. et al. (2017) Effects of very-low-calorie diet on body composition, metabolic state, and genes expression: A randomized double-blind placebo-controlled trial. European Review for Medical and Pharmacological Sciences 21(2): 329-345	- Study does not contain a relevant intervention *This was not a partial or total replacement diet*
Merra, G., Miranda, R., Barrucco, S. et al. (2016) Very-low-calorie ketogenic diet with aminoacid supplement versus very low restricted-calorie diet for preserving muscle mass during weight loss: a pilot double-blind study. European review for medical and pharmacological sciences 20(12): 2613-2621	- Study does not contain a relevant intervention
Michalczyk, Malgorzata Magdalena, Klonek, Grzegorz, Maszczyk, Adam et al. (2020) The Effects of a Low Calorie Ketogenic Diet on Glycaemic Control Variables in Hyperinsulinemic Overweight/Obese Females. Nutrients 12(6)	- Study does not contain a relevant intervention

Study	Reason
Michalczyk, Malgorzata Magdalena; Maszczyk, Adam; Stastny, Petr (2020) The Effects of Low-Energy Moderate-Carbohydrate (MCD) and Mixed (MixD) Diets on Serum Lipid Profiles and Body Composition in Middle-Aged Men: A Randomized Controlled Parallel-Group Clinical Trial. International journal of environmental research and public health 17(4)	- Study does not contain a relevant intervention *Low energy diet without replacement*
Mijatovic, J, Louie, JCY, Buso, MEC et al. (2020) Effects of a modestly lower carbohydrate diet in gestational diabetes: a randomized controlled trial. The American journal of clinical nutrition 112(2): 284-292	- Incorrect population *People who were pregnant were included*
Mishra, S, Xu, J, Agarwal, U et al. (2013) A multicenter randomized controlled trial of a plant-based nutrition program to reduce body weight and cardiovascular risk in the corporate setting: the GEICO study. European journal of clinical nutrition 67(7): 718-24	- Insufficient follow up *Study included an 18 week follow up period.*
Mitra, S.R. and Tan, P.Y. (2019) Effect of an individualised high-protein, energy-restricted diet on anthropometric and cardio-metabolic parameters in overweight and obese Malaysian adults: A 6-month randomised controlled study. British Journal of Nutrition 121(9): 1002-1017	- Insufficient follow up *Followed 6 months from baseline*
Mollentze, W.F., Joubert, G., Prins, A. et al. (2019) The safety and efficacy of a low-energy diet to induce weight loss, improve metabolic health, and induce diabetes remission in insulin-treated obese men with type 2 diabetes: a pilot RCT. International Journal of Diabetes in Developing Countries 39(4): 618-625	- Study does not contain a relevant intervention *Low energy diet without replacement*
Moore, W.J.; McGrievy, M.E.; Turner-McGrievy, G.M. (2015) Dietary adherence and acceptability of five different diets, including vegan and vegetarian diets, for weight loss: The New DIETs study. Eating Behaviors 19: 33-38	- Insufficient follow up *Study follow up= 6 months*
Moretti, Laura and Canada, Todd (2006) A Randomized Study Comparing the Effects of a Low-Carbohydrate Diet and a Conventional Diet on Lipoprotein Subfractions and C-reactive Protein Levels in Patients With Severe Obesity.	- Insufficient follow up *Followed 6 months from baseline*

Study	Reason
Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition 21(2): 187-188	
Moro, T, Tinsley, G, Pacelli, FQ et al. (2021) Twelve Months of Time-restricted Eating and Resistance Training Improves Inflammatory Markers and Cardiometabolic Risk Factors. Medicine and science in sports and exercise 53(12): 2577-2585	- Incorrect population *Not in people living with overweight or obesity*
Morris, E., Aveyard, P., Dyson, P. et al. (2020) A food-based, low-energy, low-carbohydrate diet for people with type 2 diabetes in primary care: A randomized controlled feasibility trial. Diabetes, Obesity and Metabolism 22(4): 512-520	- Insufficient follow up *Followed 3 months from baseline*
Mraovic, T., Radakovic, S., Medic, D.R. et al. (2018) The effects of different caloric restriction diets on anthropometric and cardiometabolic risk factors in overweight and obese females. Vojnosanitetski Pregled 75(1): 30-38	- Insufficient follow up *Participants followed for 42 weeks from baseline*
Muirhead, R., Kizirian, N., Lal, R. et al. (2021) A pilot randomized controlled trial of a partial meal replacement preconception weight loss program for women with overweight and obesity. Nutrients 13(9): 3200	- Insufficient follow up *No follow-up after diet phase completed*
Neacsu, M., Fyfe, C., Horgan, G. et al. (2014) Appetite control and biomarkers of satiety with Vegetarian (soy) and meat-based high-protein diets for weight loss in obese men: A randomized crossover trial. American Journal of Clinical Nutrition 100(2): 548-558	- Insufficient follow up *Study included a 2 week follow up period.*
Obermayer, Anna, Tripolt, Norbert J, Pferschy, Peter N et al. (2023) Efficacy and Safety of Intermittent Fasting in People With Insulin-Treated Type 2 Diabetes (INTERFAST-2)-A Randomized Controlled Trial. Diabetes care 46(2): 463-468	- Insufficient follow up
Ofir, Noa, Mizrakli, Yuval, Greenshpan, Yariv et al. (2023) Vertebrae but not femur marrow fat transiently decreases in response to body	- Study does not contain a relevant intervention *Calorie restriction did not match the protocol*

Study	Reason
weight loss in an 18-month randomized control trial. Bone 171: 116727	
Overland, J., Toth, K., Gibson, A.A. et al. (2018) The safety and efficacy of weight loss via intermittent fasting or standard daily energy restriction in adults with type 1 diabetes and overweight or obesity: A pilot study. Obesity Medicine 12: 13-17	- Data not reported in an extractable format *Data reported as median and range*
Panizza, C.E., Lim, U., Yonemori, K.M. et al. (2019) Effects of intermittent energy restriction combined with a mediterranean diet on reducing visceral adiposity: A randomized active comparator pilot study. Nutrients 11(6): 1386	- Insufficient follow up *Participants followed 6 months from baseline*
Paoli, A., Cenci, L., Pompei, P. et al. (2021) Effects of two months of very low carbohydrate ketogenic diet on body composition, muscle strength, muscle area, and blood parameters in competitive natural body builders. Nutrients 13(2): 1-14	- Incorrect population *Not only in people living with overweight or obesity*
Parr, E.B., Coffey, V.G., Cato, L.E. et al. (2016) A randomized trial of high-dairy-protein, variable-carbohydrate diets and exercise on body composition in adults with obesity. Obesity 24(5): 1035-1045	- Insufficient follow up *Followed 4 months from baseline*
Parvaresh, A., Razavi, R., Abbasi, B. et al. (2019) Modified alternate-day fasting vs. calorie restriction in the treatment of patients with metabolic syndrome: A randomized clinical trial. Complementary Therapies in Medicine 47: 102187	- Insufficient follow up *No follow-up after 8 week diet intervention*
Pattinson, A.L., Seimon, R.V., Harper, C. et al. (2021) Diet Quality following Total Meal Replacement Compared with Food-Based Weight-Loss Diets in Postmenopausal Women with Obesity: A Secondary Analysis of the TEMPO Diet Trial. Journal of Nutrition 151(11): 3299-3312	- Insufficient follow up *No follow-up after diet phase completed*
Pattinson, AL, Seimon, RV, Harper, C et al. (2021) Diet Quality following Total Meal Replacement Compared with Food-Based Weight-Loss Diets in Postmenopausal Women	- Insufficient follow up *No follow-up after diet phase completed*

Study	Reason
with Obesity: A Secondary Analysis of the TEMPO Diet Triall. The Journal of nutrition	
Perissiou, M., Borkoles, E., Kobayashi, K. et al. (2020) The effect of an 8 week prescribed exercise and low-carbohydrate diet on cardiorespiratory fitness, body composition and cardiometabolic risk factors in obese individuals: A randomised controlled trial. Nutrients 12(2): 482	- Insufficient follow up *Followed 2 months from baseline*
Perna, S., Alalwan, T.A., Gozzer, C. et al. (2019) Effectiveness of a hypocaloric and low-carbohydrate diet on visceral adipose tissue and glycemic control in overweight and obese patients with type 2 diabetes. Bahrain Medical Bulletin 41(3): 159-164	- Unable to acquire paper
Phillips, N.E., Mareschal, J., Schwab, N. et al. (2021) The effects of time-restricted eating versus standard dietary advice on weight, metabolic health and the consumption of processed food: A pragmatic randomised controlled trial in community-based adults. Nutrients 13(3): 1042	- Insufficient follow up *Participants followed 6 months from baseline*
Pinto, A.M., Bordoli, C., Buckner, L.P. et al. (2020) Intermittent energy restriction is comparable to continuous energy restriction for cardiometabolic health in adults with central obesity: A randomized controlled trial; the Met-IER study. Clinical Nutrition 39(6): 1753-1763	- Insufficient follow up *Follow-up period unclear but appears less than a year from baseline*
Polito, R., Valenzano, A., Monda, V. et al. (2022) Heart Rate Variability and Sympathetic Activity Is Modulated by Very Low-Calorie Ketogenic Diet. International Journal of Environmental Research and Public Health 19(4): 2253	- Study does not contain a relevant intervention *Very low carbohydrate diet*
Prehn, K., von Schwartzenberg, R.J., Mai, K. et al. (2017) Caloric restriction in older adults-differential effects of weight loss and reduced weight on brain structure and function. Cerebral Cortex 27(3): 1765-1778	- Incorrect outcomes *Outcomes linked to brain structure and function*
Price, S.A., Sumithran, P., Prendergast, L.A. et al. (2020) Time to pregnancy after a	- Incorrect population

Study	Reason
prepregnancy very-low-energy diet program in women with obesity: substudy of a randomized controlled trial. Fertility and Sterility 114(6): 1256-1262	*Study in women who were planning pregnancy during the follow-up of the trial*
Primo, D.; Izaola, O.; de Luis, D. (2020) Effects of a high protein/low carbohydrate low-calorie diet versus a standard low-calorie diet on anthropometric parameters and cardiovascular risk factors, role of polymorphism rs3123554 in the cannabinoid receptor gene type 2 (CB2R). Endocrinologia, Diabetes y Nutricion 67(7): 446-453	- Insufficient follow up *Followed 9 months from baseline*
Pureza, Isabele R O M, Melo, Ingrid S V, Macena, Mateus L et al. (2020) Acute effects of time-restricted feeding in low-income women with obesity placed on hypoenergetic diets: Randomized trial. Nutrition (Burbank, Los Angeles County, Calif.) 77: 110796	- Study does not contain a relevant intervention *No replacement element in the diet*
Ramos, T.L., Eduarda da Silva Fidellis, D., Nicolas dos Santos Ribeiro, J. et al. (2022) "Weight-loss induced by carbohydrate restriction does not negatively affect health-related quality of life and cognition in people with type 2 diabetes: A randomized controlled trial" clinical nutrition 2022. Clinical Nutrition 41(9): 2059-2060	- Unable to acquire paper
Ramos-Lopez, O., Riezu-Boj, J.I., Milagro, F.I. et al. (2018) Differential lipid metabolism outcomes associated with ADRB2 gene polymorphisms in response to two dietary interventions in overweight/obese subjects. Nutrition, Metabolism and Cardiovascular Diseases 28(2): 165-172	- Insufficient follow up *Followed 4 months from baseline*
Ravussin, E., Beyl, R.A., Poggiogalle, E. et al. (2019) Early Time-Restricted Feeding Reduces Appetite and Increases Fat Oxidation But Does Not Affect Energy Expenditure in Humans. Obesity 27(8): 1244-1254	- Incorrect study design *Crossover RCT*
Razmpoosh, E., Zare, S., Fallahzadeh, H. et al. (2020) Effect of a low energy diet, containing a high protein, probiotic condensed yogurt, on biochemical and anthropometric measurements among women with overweight/obesity: A	- Study does not contain a relevant intervention *Low energy diet without replacement*

Study	Reason
randomised controlled trial. Clinical Nutrition ESPEN 35: 194-200	
Rock, Cheryl L, Flatt, Shirley W, Pakiz, Bilge et al. (2014) Weight loss, glycemic control, and cardiovascular disease risk factors in response to differential diet composition in a weight loss program in type 2 diabetes: a randomized controlled trial. Diabetes care 37(6): 1573-80	- Study does not contain a relevant intervention
Rock, Cheryl L, Pakiz, Bilge, Flatt, Shirley W et al. (2007) Randomized trial of a multifaceted commercial weight loss program. Obesity (Silver Spring, Md.) 15(4): 939-49	- Study does not contain a relevant intervention
Rock, CL, Flatt, SW, Sherwood, NE et al. (2010) Effect of a free prepared meal and incentivized weight loss program on weight loss and weight loss maintenance in obese and overweight women: a randomized controlled trial. JAMA 304(16): 1803-10	- Study does not contain a relevant intervention
Rodriguez-Lozada, C., Cuervo, M., Cuevas-Sierra, A. et al. (2019) Changes in anxiety and depression traits induced by energy restriction: Predictive value of the baseline status. Nutrients 11(6): 1206	- Insufficient follow up *Followed 4 months from baseline*
Rolland, C., Hession, M., Murray, S. et al. (2009) Randomized clinical trial of standard dietary treatment versus a low-carbohydrate/high-protein diet or the LighterLife Programme in the management of obesity*. Journal of diabetes 1(3): 207-217	- Insufficient follow up *9 months from baseline rather than a year and the intervention diet lasted 9 months in some cases*
Rolls, B.J., Roe, L.S., James, B.L. et al. (2017) Does the incorporation of portion-control strategies in a behavioral program improve weight loss in a 1-year randomized controlled trial?. International Journal of Obesity 41(3): 434-442	- Study does not contain a relevant intervention
Rosenkilde, M., Rygaard, L., Nordby, P. et al. (2018) Exercise and weight loss effects on cardiovascular risk factors in overweight men. Journal of applied physiology (Bethesda, Md. : 1985) 125(3): 901-908	- Study does not contain a relevant intervention *Very low energy diet without replacement*

Study	Reason
Rostanzo, E, Marchetti, M, Casini, I et al. (2021) Very-Low-Calorie Ketogenic Diet: A Potential Treatment for Binge Eating and Food Addiction Symptoms in Women. A Pilot Study. International journal of environmental research and public health 18(23)	- Incorrect study design *Not a comparative trial*
Ruth, M.R., Port, A.M., Shah, M. et al. (2013) Consuming a hypocaloric high fat low carbohydrate diet for 12 weeks lowers C-reactive protein, and raises serum adiponectin and high density lipoprotein-cholesterol in obese subjects. Metabolism: Clinical and Experimental 62(12): 1779-1787	- Insufficient follow up *Followed 3 months from baseline*
Rynders, C.A., Thomas, E.A., Zaman, A. et al. (2019) Effectiveness of intermittent fasting and time-restricted feeding compared to continuous energy restriction for weight loss. Nutrients 11(10): 2442	- Incorrect study design *Systematic review of intermittent fasting*
Sacks, G, Veerman, JL, Moodie, M et al. (2011) 'Traffic-light' nutrition labelling and 'junk-food' tax: a modelled comparison of cost-effectiveness for obesity prevention. International journal of obesity (2005) 35(7): 1001-9	- Incorrect study design *Not an randomised controlled trial*
Sadeghian, M, Hosseini, SA, Zare Javid, A et al. (2021) Effect of Fasting-Mimicking Diet or Continuous Energy Restriction on Weight Loss, Body Composition, and Appetite-Regulating Hormones Among Metabolically Healthy Women with Obesity: a Randomized Controlled, Parallel Trial. Obesity surgery 31(5): 2030-2039	- Insufficient follow up *No follow-up after 2 month diet intervention*
Sanchez, E., Santos, M.-D., Nunez-Garcia, M. et al. (2022) Randomized clinical trial to evaluate the morphological changes in the adventitial vasa vasorum density and biological markers of endothelial dysfunction in subjects with moderate obesity undergoing a very low-calorie ketogenic diet. Nutrients 14(1): 33	- Insufficient follow up *No follow-up after diet is completed*
Saslow, L.R., Kim, S., Daubenmier, J.J. et al. (2014) A randomized pilot trial of a moderate carbohydrate diet compared to a very low carbohydrate diet in overweight or obese	- Insufficient follow up *No follow-up after diet is completed*

Study	Reason
individuals with type 2 diabetes mellitus or prediabetes. PLoS ONE 9(4): e91027	
Saslow, Laura R, Mason, Ashley E, Kim, Sarah et al. (2017) An Online Intervention Comparing a Very Low-Carbohydrate Ketogenic Diet and Lifestyle Recommendations Versus a Plate Method Diet in Overweight Individuals With Type 2 Diabetes: A Randomized Controlled Trial. Journal of medical Internet research 19(2): e36	- Insufficient follow up *Insufficient follow-up (32 weeks from baseline)*
Sato, Junko, Kanazawa, Akio, Makita, Sumiko et al. (2017) A randomized controlled trial of 130 g/day low-carbohydrate diet in type 2 diabetes with poor glycemic control. Clinical nutrition (Edinburgh, Scotland) 36(4): 992-1000	- Insufficient follow up *Followed 6 months from baseline*
Sattar, Naveed, Welsh, Paul, Leslie, Wilma S et al. (2023) Dietary weight-management for type 2 diabetes remissions in South Asians: the South Asian diabetes remission randomised trial for proof-of-concept and feasibility (STANDby). The Lancet regional health. Southeast Asia 9: 100111	- Insufficient follow up
Schiavo, L., Pierro, R., Asteria, C. et al. (2022) Low-Calorie Ketogenic Diet with Continuous Positive Airway Pressure to Alleviate Severe Obstructive Sleep Apnea Syndrome in Patients with Obesity Scheduled for Bariatric/Metabolic Surgery: a Pilot, Prospective, Randomized Multicenter Comparative Study. Obesity Surgery 32(3): 634-642	- Insufficient follow up *No follow-up after diet is completed*
Schutte, Sophie, Esser, Diederik, Siebelink, Els et al. (2022) Diverging metabolic effects of 2 energy-restricted diets differing in nutrient quality: a 12-week randomized controlled trial in subjects with abdominal obesity. The American journal of clinical nutrition 116(1): 132-150	- Insufficient follow up
Seimon, Radhika V, Gibson, Alice A, Harper, Claudia et al. (2018) Rationale and Protocol for a Randomized Controlled Trial Comparing Fast versus Slow Weight Loss in Postmenopausal Women with Obesity-The TEMPO Diet Trial. Healthcare (Basel, Switzerland) 6(3)	- Protocol of an included study

Study	Reason
Senkus, K.E., Crowe-White, K.M., Bolland, A.C. et al. (2022) Changes in adiponectin:leptin ratio among older adults with obesity following a 12-month exercise and diet intervention. Nutrition and Diabetes 12(1): 30	- Data not reported in an extractable format
Sharma, V., Ricketts, H.C., McCombie, L. et al. (2023) A total diet replacement weight management programme for difficult-to-treat asthma associated with obesity: a randomised controlled feasibility trial. Chest	- Duplicate reference
Sharma, Varun, Ricketts, Helen Clare, McCombie, Louise et al. (2023) A Total Diet Replacement Weight Management Program for Difficult-to-Treat Asthma Associated With Obesity: A Randomized Controlled Feasibility Trial. Chest	- Insufficient follow up *Although authors say longer 1 and 2 year follow up planned, data not reported for these timepoints yet.*
Shemirani, F., Djafarian, K., Fotouhi, A. et al. (2022) Effect of Paleolithic-based low-carbohydrate vs. moderate-carbohydrate diets with portion-control and calorie-counting on CTRP6, asprosin and metabolic markers in adults with metabolic syndrome: A randomized clinical trial. Clinical Nutrition ESPEN	- Insufficient follow up *Followed 10 weeks from baseline*
Shirai, K., Saiki, A., Oikawa, S. et al. (2013) The effects of partial use of formula diet on weight reduction and metabolic variables in obese type 2 diabetic patients - Multicenter trial. Obesity Research and Clinical Practice 7(1): e43-e54	- Insufficient follow up *No follow-up after diet phase completed*
Simon, Stacey L, Blankenship, Jennifer, Manoogian, Emily N C et al. (2022) The impact of a self-selected time restricted eating intervention on eating patterns, sleep, and late-night eating in individuals with obesity. Frontiers in nutrition 9: 1007824	- Insufficient follow up
Smith-Ryan, A.E., Hirsch, K.R., Blue, M.N.M. et al. (2019) High-fat breakfast meal replacement in overweight and obesity: Implications on body composition, metabolic markers, and satiety. Nutrients 11(4): 865	- Incorrect outcomes *No relevant outcomes presented*

Study	Reason
Sofi, F., Dinu, M., Pagliai, G. et al. (2018) Low-calorie vegetarian versus mediterranean diets for reducing body weight and improving cardiovascular risk profile. Circulation 137(11): 1103-1113	- Insufficient follow up *Study included a 3 month follow up for each phase of the trial (cross over trial).*
Steger, F.L., Donnelly, J.E., Hull, H.R. et al. (2021) Intermittent and continuous energy restriction result in similar weight loss, weight loss maintenance, and body composition changes in a 6 month randomized pilot study. Clinical Obesity 11(2): e12430	- Insufficient follow up *Participants followed 24 weeks from baseline*
Steger, Felicia L, Jamshed, Humaira, Bryan, David R et al. (2023) Early time-restricted eating affects weight, metabolic health, mood, and sleep in adherent completers: A secondary analysis. Obesity (Silver Spring, Md.) 31suppl1: 96-107	- Insufficient follow up
Steger, Felicia L, Jamshed, Humaira, Martin, Corby K et al. (2023) Impact of early time-restricted eating on diet quality, meal frequency, appetite, and eating behaviors: A randomized trial. Obesity (Silver Spring, Md.) 31suppl1: 127-138	- Insufficient follow up
Stentz FB, Brewer A, Wan J et al. (2016) Remission of pre-diabetes to normal glucose tolerance in obese adults with high protein versus high carbohydrate diet: randomized control trial. BMJ open diabetes research & care 4(1): e000258	- Insufficient follow up *Followed 6 months from baseline*
Stenvers, Dirk J., Schouten, Lydia J., Jurgens, Jordy et al. (2014) Breakfast replacement with a low-glycaemic response liquid formula in patients with type 2 diabetes: a randomised clinical trial. British Journal of Nutrition 112(4): 504-512	- Study does not contain a relevant intervention *Unclear if diet is low energy*
Struik, N.A., Brinkworth, G.D., Thompson, C.H. et al. (2020) Very Low and Higher Carbohydrate Diets Promote Differential Appetite Responses in Adults with Type 2 Diabetes: A Randomized Trial. Journal of Nutrition 150(4): 800-805	- Insufficient follow up *Insufficient follow-up (16 weeks from baseline)*

Study	Reason
Sulaj, A., Kopf, S., von Rauchhaupt, E. et al. (2021) A six-month periodic fasting reduces microalbuminuria and improves metabolic control in patients with type 2 diabetes and diabetic nephropathy: A randomized controlled study. medRxiv	- Insufficient follow up *Participants followed 9 months from baseline*
Sun, J, Wang, Y, Chen, X et al. (2008) An integrated intervention program to control diabetes in overweight Chinese women and men with type 2 diabetes. Asia Pacific journal of clinical nutrition 17(3): 514-524	- Study does not contain a relevant intervention *Not an intervention linked to a diet specified in this review*
Sundfor, T.M.; Tonstad, S.; Svendsen, M. (2019) Effects of intermittent versus continuous energy restriction for weight loss on diet quality and eating behavior. A randomized trial. European Journal of Clinical Nutrition 73(7): 1006-1014	- Insufficient follow up *Participants followed 3 months from baseline*
Sutton, E.F., Beyl, R., Early, K.S. et al. (2018) Early Time-Restricted Feeding Improves Insulin Sensitivity, Blood Pressure, and Oxidative Stress Even without Weight Loss in Men with Prediabetes. Cell Metabolism 27(6): 1212	- Incorrect study design *Crossover trial without sufficient follow-up after each diet period*
Tang, F. and Lin, X. (2020) Effects of Fasting-Mimicking Diet and Specific Meal Replacement Foods on Blood Glucose Control in Patients with Type 2 Diabetes: A Randomized Controlled Trial. Oxidative Medicine and Cellular Longevity 2020: 6615295	- Insufficient follow up *No follow-up after diet phase completed*
Tay, J., Brinkworth, G.D., Noakes, M. et al. (2008) Metabolic Effects of Weight Loss on a Very-Low-Carbohydrate Diet Compared With an Isocaloric High-Carbohydrate Diet in Abdominally Obese Subjects. Journal of the American College of Cardiology 51(1): 59-67	- Insufficient follow up *Followed 6 months from baseline*
Tay, J., Luscombe-Marsh, N.D., Thompson, C.H. et al. (2014) A very low-carbohydrate, low-saturated fat diet for type 2 diabetes management: A randomized trial. Diabetes Care 37(11): 2909-2918	- Insufficient follow up

Study	Reason
Tay, J., Thompson, C.H., Luscombe-Marsh, N.D. et al. (2020) Nutritional adequacy of very low- and high-carbohydrate, low saturated fat diets in adults with type 2 diabetes: A secondary analysis of a 2-year randomised controlled trial. Diabetes Research and Clinical Practice 170: 108501	- Incorrect outcomes *No relevant outcomes for this review*
Tay, J., Thompson, C.H., Luscombe-Marsh, N.D. et al. (2015) Long-Term effects of a very low carbohydrate compared with a high carbohydrate diet on renal function in individuals with type 2 diabetes: A randomized trial. Medicine (United States) 94(47): e2181	- Secondary publication of an included study that does not provide any additional relevant information
Tay, J., Zajac, I.T., Thompson, C.H. et al. (2016) A randomised-controlled trial of the effects of very low-carbohydrate and high-carbohydrate diets on cognitive performance in patients with type 2 diabetes. British Journal of Nutrition 116(10): 1745-1753	- Secondary publication of an included study that does not provide any additional relevant information
Teng NI, Shahar S, Manaf ZA et al. (2011) Efficacy of fasting calorie restriction on quality of life among aging men. Physiology & behavior 104(5): 1059-1064	- Insufficient follow up *Participants followed 3 months from baseline*
Teng, NI, Shahar, S, Rajab, NF et al. (2013) Improvement of metabolic parameters in healthy older adult men following a fasting calorie restriction intervention. Aging male 16(4): 177-183	- Insufficient follow up *Participants followed 3 months from baseline*
Teong, X.T., Hutchison, A.T., Liu, B. et al. (2021) Eight weeks of intermittent fasting versus calorie restriction does not alter eating behaviors, mood, sleep quality, quality of life and cognitive performance in women with overweight. Nutrition Research 92: 32-39	- Insufficient follow up *Participants followed 2 months from baseline*
Thomsen, M.N., Skytte, M.J., Samkani, A. et al. (2022) Dietary carbohydrate restriction augments weight loss-induced improvements in glycaemic control and liver fat in individuals with type 2 diabetes: a randomised controlled trial. Diabetologia 65(3): 506-517	- Study does not contain a relevant intervention *Low carbohydrate diet*

Study	Reason
Thomsen, Mads N, Skytte, Mads J, Samkani, Amirsalar et al. (2022) Weight loss improves beta-cell function independently of dietary carbohydrate restriction in people with type 2 diabetes: A 6-week randomized controlled trial. Frontiers in nutrition 9: 933118	- Insufficient follow up
Todd, Sandra (2015) Weight loss intervention trial comparing intermittent low carbohydrates versus continuous Mediterranean diet.	- Insufficient follow up *Participants followed 3 months from baseline*
Trepanowski, J.F., Kroeger, C.M., Barnosky, A. et al. (2018) Effects of alternate-day fasting or daily calorie restriction on body composition, fat distribution, and circulating adipokines: Secondary analysis of a randomized controlled trial. Clinical Nutrition 37(6): 1871-1878	- Secondary publication of an included study that does not provide any additional relevant information *Secondary publication of Trepanowski 2017.*
Trico, Domenico, Moriconi, Diego, Berta, Rossana et al. (2021) Effects of Low-Carbohydrate versus Mediterranean Diets on Weight Loss, Glucose Metabolism, Insulin Kinetics and beta-Cell Function in Morbidly Obese Individuals. Nutrients 13(4)	- Insufficient follow up *Followed 1 month from baseline*
Turner-McGrievy, G.M.; Barnard, N.D.; Scialli, A.R. (2007) A two-year randomized weight loss trial comparing a vegan diet to a more moderate low-fat diet. Obesity 15(9): 2276-2281	- Study does not contain a relevant intervention *Plant based diet was not accompanied with a calorie deficit. They study noted that there was no restriction on energy uptake and participants were encouraged to eat to satiety.*
Turner-McGrievy, G.M., Davidson, C.R., Wingard, E.E. et al. (2014) Low glycemic index vegan or low-calorie weight loss diets for women with polycystic ovary syndrome: A randomized controlled feasibility study. Nutrition Research 34(6): 552-558	- Insufficient follow up *Study included a 6 month follow up.*
Turner-McGrievy, G.M., Davidson, C.R., Wingard, E.E. et al. (2015) Comparative effectiveness of plant-based diets for weight loss: A randomized controlled trial of five different diets. Nutrition 31(2): 350-358	- Insufficient follow up *Study only included a 6 month follow up. Additionally, energy restriction was not required in the study.*
Turner-McGrievy, G.M., Wirth, M.D., Shivappa, N. et al. (2015) Randomization to plant-based dietary approaches leads to larger short-term	- Insufficient follow up *Study included a 6 month follow up.*

Study	Reason
improvements in Dietary Inflammatory Index scores and macronutrient intake compared with diets that contain meat. Nutrition Research 35(2): 97-106	
Turner-McGrievy, Gabrielle M, Wilcox, Sara, Frongillo, Edward A et al. (2023) Effect of a Plant-Based vs Omnivorous Soul Food Diet on Weight and Lipid Levels Among African American Adults: A Randomized Clinical Trial. JAMA network open 6(1): e2250626	- Comparator in study does not match that specified in protocol
Umphonsathien, M., Rattanasian, P., Lokattachariya, S. et al. (2022) Effects of intermittent very-low calorie diet on glycemic control and cardiovascular risk factors in obese patients with type 2 diabetes mellitus: A randomized controlled trial. Journal of Diabetes Investigation 13(1): 156-166	- Insufficient follow up *Participants followed 20 weeks from baseline*
Varady, K.A., Bhutani, S., Klempel, M.C. et al. (2011) Comparison of effects of diet versus exercise weight loss regimens on LDL and HDL particle size in obese adults. Lipids in Health and Disease 10: 119	- Insufficient follow up *Participants followed 3 months from baseline*
Varady, K.A., Bhutani, S., Klempel, M.C. et al. (2013) Alternate day fasting for weight loss in normal weight and overweight subjects: A randomized controlled trial. Nutrition Journal 12(1): 146	- Insufficient follow up *Participants followed 3 months from baseline*
Varady, K.A., Dam, V.T., Klempel, M.C. et al. (2015) Effects of weight loss via high fat vs. low fat alternate day fasting diets on free fatty acid profiles. Scientific reports 5: 7561	- Insufficient follow up *Participants followed 10 weeks from baseline*
Veleba, Jiri, Matoulek, Martin, Hill, Martin et al. (2016) "A Vegetarian vs. Conventional Hypocaloric Diet: The Effect on Physical Fitness in Response to Aerobic Exercise in Patients with Type 2 Diabetes." A Parallel Randomized Study. Nutrients 8(11)	- Study does not contain a relevant intervention *Low energy diet without replacement*
Vergara, M., Hauser, M.E., Aronica, L. et al. (2021) Associations of changes in blood lipid concentrations with changes in dietary cholesterol intake in the context of a healthy	- Incorrect comparison

Study	Reason
low-carbohydrate weight loss diet: A secondary analysis of the dietfits trial. Nutrients 13(6): 1935	
Veum, V.L., Laupsa-Borge, J., Eng, O. et al. (2017) Visceral adiposity and metabolic syndrome after very high-fat and low-fat isocaloric diets: A randomized controlled trial. American Journal of Clinical Nutrition 105(1): 85-99	- Insufficient follow up *Followed 3 months from baseline*
Volek, Jeff S, Phinney, Stephen D, Forsythe, Cassandra E et al. (2009) Carbohydrate restriction has a more favorable impact on the metabolic syndrome than a low fat diet. Lipids 44(4): 297-309	- Insufficient follow up *Followed 3 months from baseline*
Vranceanu, M, Pickering, C, Filip, L et al. (2020) A comparison of a ketogenic diet with a LowGI/nutrigenetic diet over 6 months for weight loss and 18-month follow-up. BMC nutrition 6: 53	- Incorrect study design *Not a randomised trial*
Wang, L.-L., Wang, Q., Hong, Y. et al. (2018) The effect of low-carbohydrate diet on glycemic control in patients with type 2 diabetes mellitus. Nutrients 10(6): 661	- Insufficient follow up *Followed 3 months from baseline*
Watson, N., Dyer, K., Buckley, J. et al. (2016) Effects of low-fat diets differing in protein and carbohydrate content on cardiometabolic risk factors during weight loss and weight maintenance in obese adults with type 2 diabetes. Nutrients 8(5): 289	- Insufficient follow up *Followed 6 months from baseline*
Watson, N.A., Dyer, K.A., Buckley, J.D. et al. (2018) Comparison of two low-fat diets, differing in protein and carbohydrate, on psychological wellbeing in adults with obesity and type 2 diabetes: A randomised clinical trial. Nutrition Journal 17(1): 62	- Insufficient follow up *Followed 6 months from baseline*
Watson, Nerylee A, Dyer, Kathryn A, Buckley, Jonathan D et al. (2018) Reductions in food cravings are similar with low-fat weight loss diets differing in protein and carbohydrate in overweight and obese adults with type 2 diabetes: A randomized clinical trial. Nutrition research (New York, N.Y.) 57: 56-66	- Insufficient follow up *Followed 6 months from baseline*

Study	Reason
Weber, Philip, Thomsen, Mads N, Skytte, Mads Juul et al. (2022) Effects of Carbohydrate Restriction on Body Weight and Glycemic Control in Individuals with Type 2 Diabetes: A Randomized Controlled Trial of Efficacy in Real-Life Settings. Nutrients 14(24)	- Insufficient follow up
Westman, E.C., Yancy Jr., W.S., Mavropoulos, J.C. et al. (2008) The effect of a low-carbohydrate, ketogenic diet versus a low-glycemic index diet on glycemic control in type 2 diabetes mellitus. Nutrition and Metabolism 5(1): 36	- Insufficient follow up *Followed 6 months from baseline*
Westman, E.C., Yancy Jr., W.S., Olsen, M.K. et al. (2006) Effect of a low-carbohydrate, ketogenic diet program compared to a low-fat diet on fasting lipoprotein subclasses. International Journal of Cardiology 110(2): 212-216	- Insufficient follow up *Followed 6 months from baseline*
Williamson, Donald A, Anton, Stephen D, Han, Hongmei et al. (2010) Early behavioral adherence predicts short and long-term weight loss in the POUNDS LOST study. Journal of behavioral medicine 33(4): 305-14	- Incorrect outcomes
Wright, N., Wilson, L., Smith, M. et al. (2017) The BROAD study: A randomised controlled trial using a whole food plant-based diet in the community for obesity, ischaemic heart disease or diabetes. Nutrition and Diabetes 7(3): e256	- Insufficient follow up *Study only included a 6 month follow up. Additionally, study did not include calorie restriction in the control arm.*
Wycherley, T.P., Brinkworth, G.D., Keogh, J.B. et al. (2010) Long-term effects of weight loss with a very low carbohydrate and low fat diet on vascular function in overweight and obese patients: Original Article. Journal of Internal Medicine 267(5): 452-461	- Insufficient follow up
Wycherley, T.P., Buckley, J.D., Noakes, M. et al. (2014) Long-term effects of a very low-carbohydrate weight loss diet on exercise capacity and tolerance in overweight and obese adults. Journal of the American College of Nutrition 33(4): 267-273	- Insufficient follow up *No follow-up after diet is completed*

Study	Reason
Wycherley, T.P., Buckley, J.D., Noakes, M. et al. (2013) Comparison of the effects of weight loss from a high-protein versus standard-protein energy-restricted diet on strength and aerobic capacity in overweight and obese men. European Journal of Nutrition 52(1): 317-325	- Insufficient follow up *Followed 3 months from baseline*
Wycherley, T.P., Noakes, M., Clifton, P.M. et al. (2010) A high-protein diet with resistance exercise training improves weight loss and body composition in overweight and obese patients with type 2 diabetes. Diabetes Care 33(5): 969-976	- Insufficient follow up *Followed 4 months from baseline*
Wycherley, T.P., Thompson, C.H., Buckley, J.D. et al. (2016) Long-term effects of weight loss with a very-low carbohydrate, low saturated fat diet on flow mediated dilatation in patients with type 2 diabetes: A randomised controlled trial. Atherosclerosis 252: 28-31	- Insufficient follow up
Yamada, Y, Uchida, J, Izumi, H et al. (2014) A non-calorie-restricted low-carbohydrate diet is effective as an alternative therapy for patients with type 2 diabetes. Internal medicine (Tokyo, Japan) 53(1): 13-9	- Insufficient follow up *Followed 6 months from baseline*
Yancy, W.S., Almirall, D., Maciejewski, M.L. et al. (2009) Effects of two weight-loss diets on health-related quality of life. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation 18(3): 281-289	- Insufficient follow up
Zaghloul, H, Chagoury, O, Elhadad, S et al. (2020) Clinical and metabolic characteristics of the Diabetes Intervention Accentuating Diet and Enhancing Metabolism (DIADEM-I) randomised clinical trial cohort. BMJ open 10(12): e041386	- Incorrect study design *Trial protocol*
Zainordin, N.A., Warman, N.A.E., Mohamad, A.F. et al. (2021) Safety and efficacy of very low carbohydrate diet in patients with diabetic kidney disease-A randomized controlled trial. PLoS ONE 16(10october): e0258507	- Insufficient follow up

Study	Reason
Zhang, Li-Min, Liu, Zhan, Wang, Jia-Qi et al. (2022) Randomized controlled trial for time-restricted eating in overweight and obese young adults. iScience 25(9): 104870	- Insufficient follow up
Zinn, C., McPhee, J., Harris, N. et al. (2017) A 12-week low-carbohydrate, high-fat diet improves metabolic health outcomes over a control diet in a randomised controlled trial with overweight defence force personnel. Applied physiology, nutrition, and metabolism = Physiologie appliquee, nutrition et metabolisme 42(11): 1158-1164	- Insufficient follow up *Followed 3 months from baseline*

Economic studies

Study	Reason
Nuijten M, Dainelli L, Rasouli B, Araujo Torres K, Perugini M, Marczewska A. A Meal Replacement Program for the Treatment of Obesity: A Cost-Effectiveness Analysis from the Swiss Payer's Perspective. Diabetes Metab Syndr Obes. 2021 Jul 8;14:3147-3160. doi: 10.2147/DMSO.S284855. PMID: 34267531; PMCID: PMC8275158.	- Not a UK study
Lewis, L., Taylor, M., Broom, J. and Johnston, K.L. (2014), Cost-effectiveness of LighterLife for obesity. Clinical Obesity, 4: 180-188. https://doi.org/10.1111/cob.12060	- Major limitations: insufficient follow up time; not all CVD events were reported; no PSA performed
Fuller NR, Colagiuri S, Schofield D, Olson AD, Shrestha R, Holzapfel C, Wolfenstetter SB, Holle R, Ahern AL, Hauner H, Jebb SA, Caterson ID. A within-trial cost-effectiveness analysis of primary care referral to a commercial provider for weight loss treatment, relative to standard care--an international randomised controlled trial. Int J Obes (Lond). 2013 Jun;37(6):828-34. doi:	- Major limitations: insufficient follow up time; lack of clarity over cost of complications

Study	Reason
10.1038/ijo.2012.139. Epub 2012 Aug 28. PMID: 22929209; PMCID: PMC3679478.	

Appendix K - Research recommendations

Research recommendation 1

What is the effectiveness and cost-effectiveness of low-energy diets in people living with overweight and obesity with different durations of type 2 diabetes?

Why this is important

The UK has one of the highest rates of obesity in Europe and compares poorly to other high-income countries. Data has also shown that in 2019, 68% of men and 60% of women in England were living with overweight or obesity. Overweight and obesity can affect a person's health in a number of ways, including increasing the risk of developing type 2 diabetes. Data has also shown that 4.3 million people are now living with a diagnosis of diabetes in the UK and more than 2.4 million people are at high risk of developing type2 diabetes.

Studies have shown that it is possible for people with type 2 diabetes, to put their diabetes into remission. This means that your blood sugar levels are below the diabetes range, without people needing to take any diabetes medication. Evidence has suggested that weight loss can help to put diabetes into remission. The Diabetes Remission Clinical Trial (DiRECT) assessed the effective management, delivered in the primary care setting, could produce sustained remission of type 2 diabetes in people living with overweight and obesity. This trial specifically included people with a diabetes duration of 6 years and weight loss was induced with a total diet replacement phase using low-energy formula diet.

In the current review, other studies were also identified which explored the effectiveness of low energy diets in people living with overweight and obesity, with type 2 diabetes. However, the diabetes duration in these trials varied. Based on this evidence, the committee recommended low-energy diets to be considered in people with type 2 diabetes but did not put a limit on diabetes duration. The committee noted that in the general population, duration of diabetes varies, and therefore further research is required to explore the effectiveness of low-energy diets in people with different diabetes duration.

Rationale for research recommendation

Importance to 'patients' or the population	Evidence has been identified on the effectiveness of low-energy diets, but evidence did not explore the effectiveness of low-energy diets in people with different diabetes duration.
Relevance to NICE guidance	Low-energy diets have been considered in people living with overweight and obesity with type 2 diabetes. However, the recommendations do not limit the use of these diabetes to people with a particular diabetes duration. Further research can help identify if low-energy diets are effective in people with short and long term diabetes duration, which can help refine the recommendations in the future.
Relevance to the NHS	The UK has one of the highest rates of obesity in Europe and compares poorly to other high-income countries and data has shown that 4.3 million people are now living with a diagnosis of diabetes in the UK. Further research is needed to draft stronger recommendations for people living with overweight and obesity with type 2 diabetes.
National priorities	High
Current evidence base	Minimal long-term data
Equality considerations	People of Asian, Chinese, Black African/ Caribbean family backgrounds have a higher risk of developing diabetes than people from White family backgrounds. Type 2 diabetes is also more likely to develop at lower BMI thresholds than people from white family backgrounds. People from these family backgrounds are frequently underrepresented in clinical trials and therefore it is important to promote further research in this population.

Modified PICO table

Population	People living with overweight or obesity with different durations of type 2 diabetes: • 6 years • 10 years • greater than 10 years Subgroups: • People from minority ethnic groups (black African/Caribbean, South Asian, Chinese, any other Asian background,

	Arab, other ethnic groups, Multiple/ mixed ethnic groups)
Intervention	Low energy (total replacement) diets including low energy liquid diets (defined as diet containing 800-1200 calories per day)
Comparator	Usual care defined use of conventional/ balanced diet with calorie deficit (restriction in total energy intake) Usual care defined as behavioural weight management advice or general health promotion advice no intervention
Outcome	• Measures of weight change (including change in weight, BMI or waist-to-height ratio) • Health related quality of life • Adverse events • Change in HbA1c • T2DM remission
Study design	RCT
Timeframe	Long term
Additional information	Subgroup analysis by ethnicity, if possible

Research recommendation 2

What is the effectiveness and cost-effectiveness of low-energy and very-low-energy diets in achieving and maintaining weight loss in adults who are required to lose weight before receiving treatment for other health conditions because they are living with overweight or obesity?

Why this is important

The 2014 NICE guideline on obesity identification, assessment and management (CG189) recommended very-low-calorie-diets (referred to as very-low-energy diets in current review) to be considered in people who are living with obesity and who have a clinically assessed need to rapidly lose weight (for example, people who need joint replacement surgery or who are seeking fertility services). No evidence on the effectiveness of very-low-energy diets in people who have a clinically assessed need to rapidly lose weight was identified. The committee noted that requiring people to lose weight before receiving other treatment may not only delay people from receiving treatment that can improve their quality of life but can also be stigmatising to people living with overweight and obesity. Therefore, further research is required before low-energy or very-low-energy diets are recommended in these groups.

Rationale for research recommendation

Importance to ‘patients’ or the population	People are often urged to lose weight before receiving other treatments for conditions such as kidney transplant, hip or join replacement and fertility treatment. If robust evidence is identified on the effectiveness of low-energy and very-low energy diets in achieving weight loss outcomes and improvement in treatment outcomes, people who may currently find it difficult to lose weight before receiving other treatments may be able to gain access to low and very-low energy diets.
Relevance to NICE guidance	2014 guidance state that very-low-energy diets should be considered in people who are living with overweight and obesity who have a clinically assessed need to rapidly lose weight. This can include people who need joint replacement surgery or those who are seeking fertility services. No evidence was identified in the current update to support this recommendation as it is unclear if surgical outcomes, for example success rate of joint replacement surgery is better after weight loss after using low or very-low diets. The committee did highlight that surgical feasibility and safety may be improved after weight loss but further evidence is required to see if surgical outcomes, and success rates are improved after

	weight loss following low and very-low energy diets.
Relevance to the NHS	People may be denied access to other treatments due to their degree of overweight or obesity. New evidence can help identify if weight loss is required before receiving other treatment, and if weight loss improves surgical outcomes.
National priorities	High
Current evidence base	Minimal long-term data
Equality considerations	People of Asian, Chinese, Black African/ Caribbean family backgrounds have a higher risk of developing diabetes than people from White family backgrounds. Type 2 diabetes is also more likely to develop at lower BMI thresholds than people from white family backgrounds. People from these family backgrounds are frequently underrepresented in clinical trials and therefore it is important to promote further research in this population.

Modified PICO table

Population	People who are required to lose weight before they receive treatment for other health conditions because they are living with overweight/obesity. For example: • renal transplant • fertility treatment • hip/ joint replacement. Subgroups: • People from minority ethnic groups (black African/Caribbean, South Asian, Chinese, any other Asian background, Arab, other ethnic groups, Multiple/ mixed ethnic groups)
Intervention	• Low energy (total replacement) diets including low energy liquid diets (defined as diet containing 800-1200 calories per day) • Very-low-energy (total replacement) diets (defined as diets containing less than 800 calories per day)
Comparator	• Usual care defined use of conventional/ balanced diet with calorie deficit (restriction in total energy intake) • Usual care defined as behavioural weight management advice or general health promotion advice. • No intervention

Outcome	• Measures of weight change (including change in weight, BMI or waist-to-height ratio)
	• Health related quality of life
	    • Intervention outcomes such as:
	        ○ success rate of intervention received after diet intervention.
	        ○ Improvement in condition (e.g., improvement in fertility outcomes)
	    • Health related quality of life
	    • Adverse events (complications of surgery)

Study design	RCT
Timeframe	Long term
Additional information	Subgroup analysis by ethnicity, if possible

Research recommendation 3

What are the adverse events associated with different dietary approaches to losing weight in people living with overweight and obesity?

Why this is important

Limited evidence was identified on the adverse events associated with different dietary approaches. While new recommendations do promote adverse events to be discussed with people before starting low and very-energy diets, further evidence is required to identify the key adverse events associated with these diets, along with other dietary approaches.

Rationale for research recommendation

Importance to 'patients' or the population	While different dietary approaches can help in weight loss, there are adverse events associated with their use. For example, restrictive diets such as low and very-low energy diets can cause constipation and hair loss, but further evidence is required to understand these risks further.
Relevance to NICE guidance	New recommendations do promote adverse events to be discussed with people before starting low and very-energy diets, however, further evidence is required to identify the key adverse events associated with these diets, along with other dietary approaches.
Relevance to the NHS	People and healthcare professionals should be aware of the adverse events associated with different dietary approaches. Further research is required to strengthen the recommendations.
National priorities	High
Current evidence base	Minimal long-term data
Equality considerations	None

Modified PICO table

Population	People living with overweight or obesity.
Intervention	**Energy restricted diets** • Low energy (total replacement) diets including low energy liquid diets (defined as diet containing 800-1200 calories per day) • Very-low-energy (total replacement) diets (defined as diets containing less than 800 calories per day) **Macronutrient diets:** • Low carbohydrate diet (defined as under 130g of carbohydrates)

	• Very low carbohydrate (defined as under 50g of carbohydrates)
	Other diets:
	• Intermittent energy restriction (patient led fasting)
	  ○ Time restricted eating:
	  ○ Intermittent fasting (e.g., 16/8 intermittent fasting)
	  ○ Alternate day fasting
	  ○ Fasting for two days (e.g. 5:2 diet)

Comparator	• Usual care defined use of conventional/ balanced diet with calorie deficit (restriction in total energy intake) • Usual care defined as behavioural weight management advice or general health promotion advice. • No intervention
Outcome	Adverse events: • Serious adverse events • Development of eating disorders or disordered eating • Hypoglycaemia • Constipation • Gallbladder problems • Hair loss (transient alopecia) • Hypotension • Psychological impact e.g., Depression and anxiety, internalised weight stigma.
Study design	RCT
Timeframe	Long term
Additional information	None

Research recommendation 4

What is the effectiveness and cost-effectiveness of intermittent fasting in achieving and maintaining weight loss in adults living with overweight or obesity?

Why this is important

In the current update, evidence was identified on intermittent energy restriction, which demonstrated some evidence of effectiveness however, this evidence was of low to very low quality. Due to these limitations, the committee could not draft specific recommendations on the use of these diets but noted that in practice intermittent energy restriction is now being used more commonly in practice, and therefore there is scope for further research.

Rationale for research recommendation

Importance to 'patients' or the population	There are a number of different dietary approaches that can be used by people in order to lose weight. Intermittent energy restriction is now being used more commonly in practice.
Relevance to NICE guidance	Currently, NICE guidance does not include any recommendations on the use of intermittent energy restriction diets. Further research is required to understand the effectiveness of these diets.
Relevance to the NHS	Intermittent energy restriction is now being used more commonly in practice. Further research is required to provide robust recommendations on the use of these diets.
National priorities	High
Current evidence base	Minimal long-term data
Equality considerations	People of Asian, Chinese, Black African/ Caribbean family backgrounds have a higher risk of developing diabetes than people from White family backgrounds. Type 2 diabetes is also more likely to develop at lower BMI thresholds than people from white family backgrounds. People from these family backgrounds are frequently underrepresented in clinical trials and therefore it is important to promote further research in this population.

Modified PICO table

Population	People living with overweight or obesity.
Intervention	• Intermittent energy restriction (patient led fasting) ○ Time restricted eating: ○ Intermittent fasting (e.g., 16/8 intermittent fasting) ○ Alternate day fasting

	○ Fasting for two days (e.g. 5:2 diet)
Comparator	• Usual care defined use of conventional/ balanced diet with calorie deficit (restriction in total energy intake) • Usual care defined as behavioural weight management advice or general health promotion advice. • No intervention
Outcome	• Measures of weight change (including change in weight, BMI or waist-to-height ratio) • Health related quality of life • Adverse events • Change in HbA1c
Study design	RCT
Timeframe	Long term
Additional information	None