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Weight management drugs and adjunct care: a rapid review

Version 1.0

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Details of Evidence Review Report

Title: Weight management drugs and adjunct care: a rapid review

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Other organisational involvement: if applicable specify affiliations of authors above if outside Public Health Wales. Use superscript numbering system to differentiate affiliations.

Commissioning organisation: if applicable insert name of organisation(s).

Date: September 2025

Version: 1.0

Publication/Distribution: To be shared with Ilona Johnson, PHW and published on Public Health Wales website.

Review date: TBC

Protocol details: A protocol is available on request.

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1. Key messages/ Executive summary

This review aimed to investigate the components of adjunct care offered alongside GLP-1 receptor agonist weight management drugs (specifically semaglutide and tirzepatide) for weight loss management. We also aimed to explore whether there was any evidence associated with the effectiveness of adjunct care offered alongside semaglutide and tirzepatide amongst this population. The following key messages can be summarised from the review:

- 17 primary studies (15 randomised controlled trials and two retrospective cohorts utilising real-world data) reporting weight loss outcomes associated with semaglutide or tirzepatide *plus* adjunct care were identified, published between 2021 and 2025.

- No study investigated the impact of adjunct care and as drug dosages and adjunct care interventions were not comparable across studies, it was not possible to determine the impact of adjunct care on the overall findings within each study.

- Lifestyle counselling sessions (covering diet and exercise), reduced-calorie diet, and advice to exercise for a minimum of 150 minutes/week were the most commonly offered types of adjunct care across the trials. In one study, participants were offered meal replacement diets and in another, a personalised diet and exercise programme.

- In almost all studies, the adjunct care interventions were offered during the main trial 'on-treatment' period; in one study, participants were offered adjunct care during the 12 week run-in period as well as during the main trial period.

- In two studies, lifestyle counselling sessions were based on a specific therapeutic approach: *motivational interviewing* and *Intensive Behaviour Therapy*. In most studies, participants were also frequently asked to record their food intake and exercise in a diary format, which was then discussed during counselling sessions.

- Given that trials investigating the effectiveness of semaglutide and tirzepatide for weight management frequently incorporate dietary and exercise interventions, the focus of future research could also include an analysis of the contribution of adjunct care towards the overall effectiveness reported within these trials. This would then enable identification of the most effective type, combinations and duration of adjunct care to offer people taking these drugs for weight loss purposes.

- Furthermore, given all studies included adjunct care for the duration of the drug intervention, this could potentially have significant resource implications, if replicated in NHS Wales. Therefore, more evidence is needed to understand the most effective type and duration of adjunct care so that resources are also used most effectively.

- There was a paucity of evidence on the effectiveness of psychological interventions for weight loss outcomes alongside weight management drugs. Future research may need to explore the most effective psychological interventions that might support individuals to maintain lifestyle changes whilst taking and after stopping weight management drugs, which may in turn help to prevent potential weight cycling.

- It is also important for future research to consider the potential impact of adjunct care offered alongside weight management drugs on longer term behaviour change, and whether this influences weight maintenance and regain after the intervention has ended.

2. Background and purpose

NICE recommendations state that tirzepatide and semaglutide are recommended for specific patients as options to manage overweight and obesity *alongside* adjunct care such as a reduced-calorie diet and physical activity (NICE 2023; NICE 2025). With the introduction of new weight management drugs into the weight management pathway within Wales, there is a need to identify the types of adjunct care that might best be delivered alongside these drugs. This work builds on previous projects undertaken by the Evidence Service investigating the effectiveness, safety and cost effectiveness of weight management drugs (Hookway et al., 2024) and to identify which population groups have been examined within the trial evidence for the different types of drugs currently available for weight management within Wales (Shaw et al., 2025). The systematic reviews and primary studies identified in these previous projects form the basis of this work, along with any relevant studies identified in an updated search that was undertaken.

The aim of this review was to investigate the following question:

What are the components of adjunct care being offered for people taking GLP-1 receptor agonists (specifically semaglutide and tirzepatide) medication for weight management, and which components may be most effective for this population?

3. Methods

This rapid review focused only on semaglutide and tirzepatide medication for weight management. Initially, we had been asked to focus on three weight management drugs; liraglutide, semaglutide and tirzepatide (hence why our searches make reference to liraglutide). However, upon further discussion with stakeholders after searching was completed, the decision was made to focus on semaglutide and tirzepatide only, as these are the most recently approved (at the time of writing) pharmacological interventions for use within Wales as part of the weight management pathway. Therefore studies examining liraglutide were subsequently excluded.

3.1. Eligibility criteria

Table 1 describes the PICO categories used to formulate the research question, and Table 2 specifies the inclusion and exclusion criteria used to screen studies.

Table 1. PICO categories used to formulate the research question

Review questions
What are the components of adjunct care being offered for people taking GLP-1 (specifically, semaglutide, tirzepatide) medication for weight management, and which components may be effective for this population?

Population	Overweight or obese adults aged 18 years + on GLP-1 treatment for weight management. They can have comorbidities, but GLP-1 treatment should be for weight management (i.e. not diabetes).
Intervention	Lifestyle (dietary, exercise), behavioural support (CBT etc) or other adjunctive care interventions used alongside GLP-1 (tirzepatide or semaglutide) pharmacology for weight management
Comparator	GLP-1 treatment for weight management without adjunct care, or placebo + adjunct care or placebo alone
Outcome	Measures of weight change – kg/BMI/clinically meaningful % etc and waist circumference
Research type	Primary studies (Primary studies may also be extracted from systematic reviews)
Other Study Considerations (see eligibility criteria)	

Table 2. Inclusion and exclusion criteria

	Inclusion criteria	Exclusion criteria
Population	Overweight and obese people aged 18+ with or without comorbidities prescribed GLP-1 injectable/ subcutaneous weight loss drugs for weight loss management and weight loss maintenance only (Semaglutide and Tirzepatide only)	Studies looking *only* at GLP-1 drugs other than semaglutide and tirzepatide. For instance, orlistat Studies looking at GLP-1 drugs in oral form Patients prescribed GLP-1 drugs for purposes other than weight loss (e.g. pre-diabetes, diabetes, sleep apnoea) Studies looking at weight loss in patients with hypothalamic obesity Patients prescribed GLP-1 drugs for weight loss *following bariatric surgery* Studies where the outcome is muscle fat.
Intervention	Studies looking at GLP-1 drugs plus adjunct care for weight management (adjunct care may include nutritional/dietary, exercise,	Studies only looking at GLP-1 drugs for weight management with *no* adjunct care

	or behavioural interventions, for instance)	
Comparator	Comparative, primary study* conducted in any country *relevant systematic reviews will be included at title/abstract screening and individual primary studies screened	Protocols, conference proceedings
Other considerations	Studies published in English language	

3.2. Search methods

This review utilised the included studies from a previous agile scoping review undertaken on weight management drugs (Hookway et al., 2025). All primary studies included in this piece of work (or contained within the systematic reviews included) were screened for inclusion in this review.

However, as this is a rapidly moving area of research, we also conducted a top-up search in MEDLINE and epistomonikos in July 2025, to capture studies which may have been published since our last searches were undertaken in November 2024. This search consisted of keywords and subject headings covering our initial drugs of interest (semaglutide, liraglutide, and tirzepatide) or GLP-1s more broadly, combined with keywords and subject headings on overweight, obesity and weight management, and terms around study design to try to limit our results to randomized controlled trials. Searches were limited to studies published from 2024 onwards, as this search was only designed to top-up the results from the previous piece of work. Full search strategies can be found in Appendix 1.

3.3. Study record management

Studies identified during the top-up search were first saved to Endnote and duplicates were removed. The final list of unique studies was then uploaded to Rayyan for screening. Further duplicates were identified and removed using the duplicate tool on Rayyan.

3.4. Selection process

Search results were screened independently in duplicate at title and abstract stage and also at full text stage, using Rayyan. Any disagreements were resolved by a third reviewer.

3.5. Critical appraisal

Critical appraisal was conducted using the CASP checklist for randomised controlled trials and the CASP checklist for cohort studies. Critical appraisal was carried out independently in duplicate and any disagreements were resolved by a third reviewer.

3.6. Data extraction

Data extraction was carried out individually and then consistency checked by a second reviewer. Data extraction and results of critical appraisal are presented in Appendix 2 in Data Extraction Tables 1 (Tirzepatide) and 2 (Semaglutide). Studies are grouped together by trial.

4. Results

4.1. Study Selection

Ten primary studies included in our previous agile scope (or included in a systematic review within our previous agile scope) met the inclusion criteria for, and were subsequently included in this review.

A further 532 records were exported (after deduplication) from Endnote into Rayyan. Of these, 461 did not meet our inclusion criteria and were excluded at title and abstract. Sixty-seven were retrieved for full text screening, and 29 of these were subsequently excluded at full text review. This left us with 38 additional studies from our top-up search, however 33 of these were systematic reviews. Rather than include the systematic reviews themselves, we re-screened the included primary studies for additional studies meeting our inclusion criteria that hadn't already been identified. In total, our combined methods resulted in 17 primary studies which met the inclusion criteria for this review (ten from our original agile scoping review, five from our top-up search and two from relevant systematic reviews identified in our top up search).

4.2. Study characteristics

Study characteristics are presented in Tables 1 and 2 in the Appendix. Six studies looked at weight loss outcomes associated with tirzepatide plus adjunct care, covering five different randomized controlled trials (SURMOUNT; SURMOUNT 3; SURMOUNT 4; SURMOUNT-J; SURMOUNT-CN). Eleven studies looked at weight loss outcomes associated with semaglutide plus adjunct care. Nine studies reported results from seven different randomized controlled trials (STEP 1; STEP 3; STEP 4; STEP 5; STEP 6; STEP 7; STEP 8), and two studies were retrospective 'real-world studies' (Tzoulis et al. 2024; Talay & Vickers, 2024), one of which described weight loss outcomes from the Juniper programme in the UK (Talay & Vickers, 2024).

All studies offered both nutritional and exercise adjunct care. Most randomised controlled trials were conducted in multiple different countries globally. Trial durations ranged from 44 weeks to 193 weeks. Mean body weight at baseline ranged from 84 to 108 kg across the studies. In almost all studies, the adjunct care interventions were offered during the main trial period; in one study, participants were offered adjunct care during the 12-week run-in period as well as during the main trial period (Wadden et al., 2023). No studies continued the adjunct care beyond the trial period.

4.3. Critical appraisal

Summaries from critical appraisal are presented in the data extraction tables within the Appendix. All randomised controlled trials were found to be of high quality, using a double-blind approach,

recruiting participants with similar baseline characteristics, and with reported p-values and confidence intervals. Missing values were explained and dealt with appropriately.

The two real-world studies reporting weight loss outcomes associated with semaglutide were of lower quality. In the retrospective chart review study by Tzoulis et al. (2024), whilst weight was measured objectively, there was limited analysis of potential confounding variables that could have been associated with weight loss, as well as a lack of reporting of statistical significance. In the study reporting findings from the Juniper programme in the UK (Talay & Vickers, 2024), there were numerous flaws. For instance, no information was given on how the cohort was recruited or who they were, and a low number of participants completed the questionnaire, with reasons for non-response not provided nor information on characteristics of participants who dropped out, potentially leading to sample bias. The final sample was not representative of the general population, with participants predominantly white (85%) and female (91%). Self-report bias may have also been introduced into the study as participants were asked to weigh themselves, and this data was used in the analysis. The evidence was not of a high-enough quality to conclude that weight loss was a direct result of the Juniper programme, particularly as confounding factors were not considered and there was no comparison group in this study.

4.4 Results of syntheses

Two categories of adjunct care were found in the literature: nutritional and exercise. For each study included in this review, the same adjunct care was delivered to all participants (i.e. those within the control group and the intervention groups). Therefore, it was not possible to identify the impact adjunct care had on weight loss outcomes.

Table 1 summarises the different types of adjunct care interventions by study. The different types of adjunct care offered to participants are narratively subsequently summarised below the table.

Table 3. Summary of adjunct care interventions by study (blue are the interventions from tirzepatide studies and pink are interventions from semaglutide studies)

Adjunct care intervention	Lifestyle (dietary & exercise) counselling	Reduced-calorie diet	Meal replacement diet	Personalised diet & exercise plan	Minimum of 150 minutes/ week exercise advised
Tirzepatide					
Jastreboff et al. 2025					
Jastreboff et al. 2022					
Wadden et al. 2023					
Aronne et al. 2024					
Kadowaki et al. 2025					
Zhao et al. 2024					
Adjunct care intervention	**Lifestyle (dietary & exercise) counselling**	**Reduced - calorie diet**	**Meal replacement diet**	**Personalised diet & exercise plan**	**Minimum of 150 minutes/week exercise advised**
Semaglutide					
Wilding et al. 2021					
Wilding et al. 2022					
Wadden et al. 2021					
Rubino et al. 2021					
Garvey et al. 2022					
Kadowaki et al. 2022					
Mu et al. 2024					
Gu et al. 2025					
Rubino et al. 2022					
Tzoulis et al. 2024					
Talay & Vickers, 2024					

Nutritional adjunct care

Nutritional adjunct care consisted of four types of interventions: **dietary counselling**, **reduced-calorie diet**, **meal-replacement diets** and **personalised diet plan.** Dietary or nutritional counselling has been defined as 'the overarching method of guiding clients in changing their diet' and includes the setting of goals and action plans for self-management (Barkmeijer et al.,2022). In the studies described in this review, dietary counselling normally came under the broader description of 'lifestyle counselling', where participants were also offered counselling on exercise. Reduced-calorie diets varied but were most often described as a 500 calorie deficit, and meal replacement diets included liquid shakes, solid bars, or pre-prepared meals.

Tirzepatide

Tirzepatide trials offered a range of different dietary counselling and reduced calorie diet nutritional adjunct care. These were generally offered during the 'on-treatment' period, with only one trial offering a reduced calorie diet as part of the lead-in period prior to the drug intervention (Wadden et al.,2023).

Dietary counselling (as part of lifestyle counselling) included provision of advice on healthy food choices throughout the duration of the main trial period (when participants were also taking tirzepatide) (Jastreboff et al., 2025; Jastreboff et al., 2022; Kadowaki et al., 2025; Zhao et al., 2024), as well as encouragement and behaviour modification strategies to help adhere to the dietary recommendations (Aronne et al., 2024; Wadden et al., 2023). In some trials, participants were asked to keep a 3-day food and exercise diary prior to their visits, which was then reviewed at each counselling visit and 'advice to maximize adherence' was provided if necessary (Jastreboff et al., 2025; Jastreboff et a., 2022; Kadowaki et al., 2025; Zhao et al., 2024). Lifestyle counselling was offered at Weeks 0, 4, 8 and 12 during dose escalation and then at Week 24 and every 12 weeks thereafter through 72 weeks (Jastreboff et al., 2025; Jastreboff et a., 2022; Kadowaki et al., 2025; Zhao et al., 2024).

Participants were also advised to undergo varying **reduced-calorie diets.** In the SURMOUNT-4 trial, participants were advised to adhere to a healthy 500 kcal/d deficit diet (Aronne et al., 2024). In the SURMOUNT-1 trial, participants were advised to consume a maximum 30% of energy from fat; approximately 20% of energy from protein; approximately 50% of energy from carbohydrates; an energy deficit of approximately 500 kcal/day compared to the participant's estimated total energy expenditure (Jastreboff et al., 2025; Jastreboff et al., 2022). In the SURMOUNT-J trial, participants were advised to follow a hypercaloric diet with macronutrient composition of approximately 50% to 60% of energy from carbohydrate; approximately 15% to 20% of energy from protein; approximately 20% to 25% of energy from fat, and daily energy intake up to 25 kCal/kg × standard body weight (as determined by BMI = 22 kg/m2) for the participant whose BMI is ≥27 kg/m2 and 20 to 25 kcal/kg × standard body weight for the participant whose BMI is ≥35 kg/m2. In the SURMOUNT-CN trial (China), participants were advised to undertake a hypercaloric diet with the following macronutrient composition: approximately 20%-30% of energy from fat; approximately 15%-20% of energy from protein; approximately 40-55% of energy from carbohydrates, and with an energy deficit of approximately 500 kcal/day compared to the participant's total daily energy or use the equation: (body height (cm) - 105) × 25 kcal/day as calorie restrict diet energy target (Zhao et al., 2024).

In the SURMOUNT-3 Phase 3 trial, participants received a lifestyle management counselling intervention during the 12 week *lead in* period, and then during the 72-week trial period alongside tirzepatide (Wadden et al., 2023). During the lead-in period, participants were advised to reduce their daily caloric energy intake to approximately 1200 kcal/day for women or 1500 kcal/day for men (Wadden et al., 2023). After randomization, participants were advised to maintain their daily energy intake at 500 kcal below their individualised energy requirements for the duration/remainder of the trial period (Wadden et al., 2023).

Semaglutide

The semaglutide trials offered a range of different dietary counselling, meal replacement diets and reduced calorie diet nutritional adjunct care. One real-world study left this adjunct care to the discretion of the participant, all others appeared to be mandatory.

In the semaglutide studies, participants were also offered regular dietary counselling sessions which covered healthy eating education throughout the trial period with a dietitian or similarly qualified professional, (Wadden et al., 2021; Wilding et al., 2021; Wilding et al., 2022; Rubino et al., 2021; Garvey et al., 2022; Kadowaki et al., 2022; Rubino et al., 2022). In one real-world study, these sessions took the form of *motivational interviewing* (Tzoulis et a., 2024). Participants were generally encouraged to record a food diary or use a smartphone application to record their food intake, which was reviewed during counselling visits (Wadden et al., 2021; Wilding et al., 2021; Wilding et al., 2022; Rubino et al., 2021; Kadowaki et al., 2022; Mu et al., 2024; Gu et al., 2025). In the real-world study described by Tzoulis et al., (2024), sessions with a dietician took the form of *motivational interviewing* (Tzoulis et a., 2024).

In one trial (Wadden et al., 2021), participants were offered counselling sessions with *Intensive Behavioural Therapy* (IBT) as described below:

'Each IBT counseling session covered a specific topic, for example, advice on modifying diet or physical activity as well as behavioral strategies to facilitate these changes (eg, monitoring food intake, challenging negative thoughts, obtaining social support). From the randomization visit through week 12, participants received weekly IBT counseling from a dietitian (or a similarly qualified healthcare professional) who discussed participants' progress, reviewed food and activity diaries, addressed any adherence problems, and prepared for transition to the next phase of the diet. Most of the topics were accompanied by a homework assignment, found in the participant hand-outs to be completed before the next visit according to the visit schedule. From weeks 12 to 24, IBT counseling visits decreased to every other-week, and from weeks 24 to 68 were every 4 weeks (for a total of 30 IBT visits over the 68 weeks). The first three IBT visits lasted for 30–45 minutes, while the remaining visits lasted for 20–30 minutes.'

Participants in the same trial were also provided with meal replacement diets: *'the first 8 weeks [of the main trial period and drug intervention] consisted of a 1000–1200 kcal/day low-calorie diet (LCD), provided as meal replacements (e.g. liquid shakes and solid bars) and heat-and-serve, pre-prepared meals. These foods were manufactured by Nutrisystem and supplied to participants free of charge by Novo Nordisk. After 8 weeks on LCD, participants were gradually transferred to a less strict hypo-caloric diet comprised of conventional foods.'*

Following the initial 8 weeks participants were then advised to follow a **reduced-calorie diet**, based on the following algorithm: *'Participants weighing less than 200 lbs (91 kg) were prescribed a diet of 1200 kcal/day; participants weighing between 200 lbs (91 kg) and 300 lbs (136 kg) were prescribed a diet calculated as: Daily caloric target (kcal) = body weight (lb) * 6 (kcal/lb) ; participants weighing more than 300 lbs (136 kg) were prescribed 1800 kcal/day This caloric target was kept for the remainder of the trial. If a participant achieved a BMI ≤22.5 kg/m2, the recommended energy intake was re-calculated with no caloric deficit for the remainder of the trial'* (Wadden et al., 2021).

Other semaglutide trials advised participants to follow a **reduced-calorie diet** of '*500-kcal deficit per day relative to the energy expenditure estimated at the time they underwent randomization*' (Wilding et al., 2021; Wilding et al., 2021; Garvey et al., 2022; Rubino et al., 2021; Kadowaki et al., 2022; Mu et al., 2024; Gu et al., 2025; Rubino et al., 2022).

In the Juniper programme, conducted within in the UK, participants were allocated a multidisciplinary team (MDT), consisting of a doctor, health coach and medical support officer, who provided participants with a **personalised diet**. This could be modified at any stage through consultation with the MDT via the app (Talay & Vickers, 2024).

Exercise adjunct care

Exercise adjunct care took for form of **advice** and **counselling**, and **personalised exercise plan.** The exercise element tended to vary in duration but were most often classed as moderate intensity. However, there was limited information available on the type of exercise suggested and how the duration recommended was split over the course of a week.

Tirzepatide

Exercise adjunct care in the tirzepatide studies consisted mostly of the **advice** to exercise for a minimum 150 minutes weekly for the duration of the trial. (Aronne et al., 2024; Jastreboff et al. 2025; Jastreboff et al., 2022; Wadden et al., 2023; Zhao et al., 2024). For instance, brisk walking (Wadden et al., 2023). In the SURMOUNT-J trial, the JASSO guidelines were used. These indicated the amount of physical activity according to the purpose of weight loss: '*for prevention of weight gain; 150 to 250 minutes (1,200-2,000 kcal) per week; for weight loss moderate-intensity physical activity less than 150 minutes per week to provide only modest weight loss moderate-intensity physical activity between 225 and 420 minutes per week to provide 5 to 7.5 kg weight loss o greater amounts of physical activity to provide more weight loss'* (Kadowaki et al., 2025).

Semaglutide

Participants in the semaglutide trials were also given the **advice** to exercise for 150 minutes a week (Wilding et al., 2021; Wilding et al., 2022; Rubino et al., 2021; Kadowaki et al., 2022; Mu et al., 2024; Gu et al., 2025; Rubino et al., 2022). Examples given were walking and climbing the stairs (Wilding et al., 2021; Kadowaki et al., 2022). In the trial described by Wadden et al. (2021), participants were prescribed with *'a target of 100 minutes physical activity/week. Participants were counselled to be physically active in bouts of >10 minutes in duration with moderate intensity (such as*

brisk walking), and the physical activity was spread equally across 4–5 days each week. The physical activity target progressed gradually by 25 minutes every 4 weeks and up to 200 minutes/week, consistent with targets required for maintenance of lost weight.' As part of the Juniper real-world study, participants were provided with **a personalised exercise plan** by their multidisciplinary team, whereby '*patients were able to modify their diet and exercise plan in consultation with their health coach at any stage of their care journey*' via the app chat or email (Talay & Vickers, 2024).

Some trial participants were also asked to record their exercise in a diary or smartphone app, which was reviewed during **counselling sessions** (as part of lifestyle counselling sessions), and occurred every four weeks during the trial period (Wilding et al., 2021; Rubino et al., 2021; Kadowaki et al., 2022). These sessions took the form of *motivational interviewing* in one real-world study, where they were offered every 12 weeks (Tzoulis et al., 2024).

5. Discussion

5.1. Summary of evidence

This review aimed to investigate the components of adjunct care being offered for people taking semaglutide and tirzepatide weight management medication, and whether there was any evidence in relation to which components may be effective for this population. Whilst we identified 17 primary studies which explored weight loss outcomes associated with semaglutide and tirzepatide drugs plus adjunct care, no studies provided evidence on the effectiveness of adding adjunct care to GLP-1 drugs. This means all participants of the trials and studies included undertook some form of adjunct care, regardless of which arm they were in (i.e. control or intervention arms).

Lifestyle counselling sessions, reduced-calorie diet, and advice to exercise for 150 minutes/week were the most commonly offered adjunct care across the trials. In two studies, the counselling sessions were based on a specific psychological therapy: *motivational interviewing* (Tzoulis et al., 2024), and *Intensive Behaviour Therapy* (Wadden et al., 2021). Participants were also frequently asked to record their food intake and exercise in a diary format, which was then discussed during counselling sessions.

Although the adjunct care offered across the included trials were similar, they had subtle differences which makes direct comparison difficult. In addition, the protocols of these trials contained the most useful information relating to the adjunct care components offered. It is therefore uncertain if these were conducted *verbatim* during the trials, or if any deviations occurred.

Most trials included in this review incorporated some form of adjunct care for the duration of the drug intervention. If this is replicated in NHS Wales, it could potentially have major resource implications for weight management services offering weight loss drugs. Therefore, careful consideration and ideally further evidence would first be needed to establish the most effective type and intensity of adjunct care offered, and also what specialist skills would be required for those implementing the adjunct care portion.

5.2. Strengths and limitations

This review has identified the main trials and real world studies investigating weight loss outcomes associated with semaglutide and tirzepatide, and described the adjunct care provided in these studies in detail. However, as participants in all studies were given the same adjunct care, it was not possible to comment on the effectiveness of the adjunct care interventions.

This review has been unable to examine in detail why differences in adjunct care components exist between the trials included. It would be useful to look at the characteristics of participants to see whether the adjunct care component differences are in response to differing characteristics.

5.3. Implications for practice, policy, and future research

This review has provided a descriptive overview of the types of adjunct care that have been used in semaglutide and tirzepatide trials and in two real-life studies. Reduced calorie diets and a minimum of 150 minutes of prescribed exercise were most commonly advised, alongside counselling to support individuals to maintain these lifestyle changes.

Trials investigating the effectiveness of semaglutide and tirzepatide for weight management frequently incorporate dietary and exercise interventions alongside weight management drugs. This could have significant resource implications if replicated in NHS Wales. However, none of the studies in this review provided evidence on the most effective adjunct care intervention. Therefore, we emphasise that further consideration and evidence are needed to understand the most effective type and duration of adjunct care.

In addition, future research may need to include an analysis of the contribution of adjunct care towards the overall effectiveness reported within these trials. This would then enable identification of the most effective type, combinations and duration of adjunct care to offer people taking these drugs for weight loss purposes. Also, given the paucity of evidence on the effectiveness of psychological interventions alongside weight management drugs, future research may need to explore the most effective psychological interventions that might support individuals to maintain lifestyle changes whilst taking and after stopping weight management drugs, which could in turn help to prevent potential weight cycling.

6. Conclusions

This review identified 17 primary studies which reported weight loss outcomes associated with semaglutide or tirzepatide plus adjunct care. No studies provided evidence on the effectiveness of adding adjunct care to a GLP-1 regime. However, this work has usefully collated information focussing on the adjunct care on offer in trials associated with the use of semaglutide and tirzepatide for weight management. Further research is required to identify the most effective adjunct care for people using GLP-1 drugs for weight loss purposes, as this will help inform what adjunct care might look like as part of weight management programmes within Wales.

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8. Additional information

8.1. Funding support

No sources of financial or non-financial support were provided for the review.

8.2. Competing interests

There are no competing interests of review authors.

8.3. Supplementary information/ Appendices

Appendix 1: Medline Search Strategy

	Ovid MEDLINE(R) ALL <1946 to July 22, 2025>	Hits
1	Liraglutide/ or Glucagon-Like Peptide-1 Receptor Agonists/ or Glucagon-Like Peptides/ or Anti-Obesity Agents/ or Tirzepatide/	14850
2	(tirzepatide* or semaglutide* or liraglutide* or "glucagon-like peptide-1 receptor agonist*" or "GLP-1*" or wegovy or saxenda or ozempic or rybelsus or victoza or mounjaro or zepbound).ti,ab.	25429
3	1 or 2	32663
4	(overweight or obese or obesity or "body weight*" or "body mass*").ti,ab.	866209
5	Obesity/ or Overweight/ or Adipose Tissue/ or Body Weight/ or weight loss/ or Obesity, Abdominal/ or Obesity, Morbid/	546609
6	((manage adj3 weight) or (weight adj3 loss) or (weight adj3 reduc*) or (fat adj3 reduc*) or (fat adj3 loss)).ti,ab.	180976
7	4 or 5 or 6 1170435	
8	3 and 7	16357
9	limit 8 to (english language and yr="2024 -Current")	3756
10	("randomi#ed controlled trial*" or "RCT").ti,ab.	318745
11	Randomized Controlled Trial/	642490
12	10 or 11	851992
13	9 and 12	521

Appendix 2: Data Extraction Tables

Table 1: Data Extraction-Tirzepatide

Tirzepatide: SURMOUNT 1- Jastreboff et al. (2025); Jastreboff et al. (2022)			
Reference and trial details	**Adjunct care description**	**Weight loss outcomes**	**Critical appraisal**
Reference: Jastreboff, A., et al. (2025) Tirzepatide for Obesity Treatment and Diabetes Prevention. The New England journal of medicine, 392(10), 958–971. DOI: 10.1056/NEJMoa2410819 **Study aim:** To report the **3-year safety and efficacy outcomes** with tirzepatide, including its effect on achieving and sustaining longer-term weight reduction and preventing type 2 diabetes in participants with prediabetes at baseline. **Study design:** Randomised controlled trial **Countries:** Argentina, Brazil, Mexico, China, Japan, Taiwan, India, Russian Federation, US. **Study duration**: 193 weeks (Participants with obesity and without prediabetes at baseline were offered treatment for 72 weeks, whereas participants with obesity and prediabetes at baseline were offered treatment for 176 weeks.)	**Dietary: Counselling & reduced-calorie diet** At Visit 3 and subsequent visits, study participants will receive diet counselling by a dietician/nutritionist, or equivalent qualified delegate, according to local standard. Dietary counselling will consist of advice on healthy food choices and focus on calorie restriction using a hypocaloric diet with macronutrient composition of: maximum 30% of energy from fat; approximately 20% of energy from protein; approximately 50% of energy from carbohydrates; an energy deficit of approximately 500 kcal/day compared to the participant's estimated total energy expenditure (TEE). To encourage adherence, it is recommended that a 3-day diet and exercise diary be completed prior to each counselling visit. During each visit, the participant's diet is reviewed and advice to maximize adherence is provided if needed. The hypocaloric	At 176 weeks, the mean percent change in body weight among the participants who received tirzepatide was −12.3% with the 5-mg dose, −18.7% with the 10-mg dose, and −19.7% with the 15-mg dose, as compared with −1.3% among those who received placebo (P<0.001 for all comparisons with placebo).	This was a double blind trial, with participants randomised to treatment or placebo groups. Groups had similar baseline characteristics. Any missing values were accounted for and adjusted for in the analyses. P-values and confidence intervals were reported.

Tirzepatide: SURMOUNT 1- Jastreboff et al. (2025); Jastreboff et al. (2022)			
Reference and trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
Population: Tirzepatide 5mg- N=172 (Age= 49.3; Female sex= 160 (64.8%); Body weight= 104.6 kg) Tirzepatide 10mg- N=185 (Age= 47.4; Female sex= 168 (64.1%); Body weight= 108.9 kg) Tirzepatide 15mg- N=184 (Age= 48.4; Female sex= 161 (63.6%); Bodyweight= 108.6kg) Placebo- N=136 (Age= 47.7; Female sex= 170 (63.0%); Bodyweight= 107.3kg) **GLP-1 Intervention:** Participants were randomly assigned in a 1:1:1:1 ratio to receive tirzepatide at a dose of 5 mg, 10 mg, or 15 mg or placebo, administered subcutaneously once weekly for 176 weeks, followed by a 17-week off-treatment period (safety follow-up), for a total trial duration of 193 weeks. **Comparison:** Placebo **Inclusion & exclusion criteria:** In the current analysis, the trial participants had a body-mass index (BMI, the weight in kilograms divided by the square of the height in meters) of at least 30 or at least 27 with at least one obesity-related complication, and all had prediabetes. A key exclusion criterion was diabetes mellitus.	diet is continued after randomization and throughout the treatment period. If a BMI ≤22 kg/m2 is reached, the recommended energy intake should be recalculated with no kcal deficit for the remainder of the trial. Total energy expenditure (TEE) is calculated by multiplying the estimated Basal Metabolic Rate (BMR) (see table below) with a Physical Activity Level value of 1.3 (FAO/WHO/UNU 2004), which reflects an inactive lifestyle. **Exercise: minimum of150 minutes/week advised.** At Visit 3 and all subsequent visits, participants will be advised to increase their physical activity to at least 150 minutes per week. **When was adjunct care delivered?** During main trial period		
Reference: Jastreboff, A. et al. (2022) Tirzepatide Once Weekly for the Treatment of Obesity. The New England journal of medicine, 387(3), 205–216. DOI: 10.1056/NEJMoa2206038	As above	The mean percentage change in weight at week 72 was −15.0% (95% confidence interval [CI],	This was a double blind trial, with participants

Tirzepatide: SURMOUNT 1- Jastreboff et al. (2025); Jastreboff et al. (2022)			
Reference and trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
Study aim: The SURMOUNT-1 trial evaluated the efficacy and safety of tirzepatide in adults with obesity or overweight who did not have diabetes. **Study design:** Randomised controlled trial **Countries:** Argentina, Brazil, Mexico, China, Japan, Taiwan, India, Russian Federation, US. **Study duration:** 72 weeks **Population:** Tirzepatide 5 mg-N = 630 (Age- 45.6; female sex- 426 (67.6%), Body weight- 102.9kg) Tirzepatide 10 mg-N = 636 (Age- 44.7; Female sex- 427 (67.1%); Body weight- 105.8kg) Tirzepatide 15 mg-N = 630 (Age-44.9; Female sex- 425(67.5%); Body weight- 105.6kg) Placebo-N = 643 (Age- 44.4; Female sex- 436 (67.8%); Body weight- 104.8kg) **GLP-1 intervention:** Participants were randomly assigned in a 1:1:1:1 ratio to receive tirzepatide at a dose of 5 mg, 10 mg, or 15 mg or placebo, administered subcutaneously once weekly for 72 weeks as an adjunct to lifestyle intervention. **Comparison:** placebo		–15.9 to –14.2) with 5-mg weekly doses of tirzepatide, –19.5% (95% CI, –20.4 to –18.5) with 10-mg doses, and –20.9% (95% CI, –21.8 to –19.9) with 15-mg doses and –3.1% (95% CI, –4.3 to –1.9) with placebo (P<0.001 for all comparisons with placebo). The percentage of participants who had weight reduction of 5% or more was 85% (95% CI, 82 to 89), 89% (95% CI, 86 to 92), and 91% (95% CI, 88 to 94) with 5 mg, 10 mg, and 15 mg of tirzepatide, respectively, and 35% (95% CI, 30 to 39) with placebo; 50% (95% CI, 46 to 54) and 57% (95% CI, 53 to 61) of participants in the 10-mg and 15-mg groups had a reduction in body weight of 20% or more, as compared with 3% (95% CI, 1 to 5) in the placebo group (P<0.001 for	randomised to treatment or placebo groups. Groups had similar baseline characteristics. Any missing values were accounted for and adjusted for in the analyses. P-values and confidence intervals were reported.

Tirzepatide: SURMOUNT 1- Jastreboff et al. (2025); Jastreboff et al. (2022)			
Reference and trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
Inclusion & exclusion criteria: Adults who were 18 years of age or older, with a body-mass index (BMI, the weight in kilograms divided by the square of the height in meters) of 30 or more, or a BMI of 27 or more and at least one weight-related complication (e.g., hypertension, dyslipidemia, obstructive sleep apnea, or cardiovascular disease), and who reported one or more unsuccessful dietary effort to lose weight were eligible to participate. Key exclusion criteria were diabetes, a change in body weight of more than 5 kg within 90 days before screening, previous or planned surgical treatment for obesity, and treatment with a medication that promotes weight loss within 90 days before screening.		all comparisons with placebo).	

Tirzepatide: SURMOUNT 3-Wadden et al. (2023)			
Reference and Trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
Reference: Wadden, T. et al. (2023) Tirzepatide after intensive lifestyle intervention in adults with overweight or obesity: the SURMOUNT-3 phase 3 trial. Nat Med 29, 2909–2918 DOI: 10.1038/s41591-023-02597-w **Study aim:** To evaluate the efficacy of tirzepatide at 72 weeks post randomization in adults with obesity or overweight (but not diabetes)	**Dietary: Counselling on behaviour modification strategies; reduced-calorie diet** During the intensive lifestyle modification lead-in period, participants will receive instruction from a dietician, or equivalent qualified delegate, to reduce their daily caloric energy intake to approximately 1200 kcal/day for women or 1500 kcal/day for men for 12 weeks. During this lead-in period, up to 2	The coprimary endpoint of additional mean per cent weight change from randomization to week 72 was met with changes of −18.4% (standard error (s.e.) 0.7) with tirzepatide and 2.5% (s.e. 1.0) with placebo (estimated treatment	This was a double blind trial, with participants randomised to treatment or placebo groups. Groups had similar baseline characteristics.

Tirzepatide: SURMOUNT 3-Wadden et al. (2023)			
Reference and Trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
who successfully lost ≥5% of baseline weight during a 12-week lead-in period that provided intensive lifestyle intervention. **Study design:** Randomised-controlled trial **Countries:** USA, Argentina and Brazil. **Study duration:** 12 week lead in period followed by 72 week trial period **Population:** Tirzepatide MTD-N=287 (Age=45.4; **Female** sex= 181 (63.1%) Placebo-N= 292 (Age=45.7 Female sex= 183 (62.7%) **GLP-1 intervention:** Tirzepatide and matched placebo were administered once weekly as a subcutaneous injection using a single-dose pen. The starting dose of tirzepatide was 2.5 mg, increasing by 2.5 mg every 4 weeks until an MTD dose of 10 or 15 mg was reached. **Comparison:** Placebo **Inclusion & exclusion criteria:** Adults with body mass index ≥30 or ≥27 kg/m2 and at least one obesity-related complication (excluding diabetes), who achieved ≥5.0% weight reduction after a 12-week intensive lifestyle intervention, to tirzepatide maximum tolerated dose (10 or 15 mg) or placebo once weekly for 72 weeks (n = 579).	liquid meal replacements per day are permitted, but not required, to achieve the targeted energy deficit. **Exercise: Counselling on behaviour modification strategies; minimum of 150 mins/week advised** In addition to the diet modification, participants will be encouraged to exercise on a regular basis, with a recommendation of at least 150 minutes per week of moderate intensity activity (for example, brisk walking). Participants will be counseled on behavior modification strategies to help implement and adhere to the diet and exercise recommendations. Participants who achieve a ≥5.0% body weight loss at the end of the 12-week lead-in period (Week 0) will proceed to randomization to either tirzepatide or placebo. After randomization, participants will be advised to maintain their daily energy intake at 500 kcal below their individualized energy requirements (Garvey et al. 2016), as calculated by the Food and Agriculture Organization of the United Nations/World Health Organization [WHO]/United Nations University (FAO/WHO/UNU) estimates of human energy	difference −20.8 percentage points (95% confidence interval (CI) −23.2%, −18.5%; *P* < 0.001). The coprimary endpoint of the percentage of participants achieving additional weight reduction ≥5% was met with 87.5% (s.e. 2.2) with tirzepatide and 16.5% (s.e. 3.0) with placebo achieving this threshold (odds ratio 34.6%; 95% CI 19.2%, 62.6%; *P* < 0.001).	Any missing values were accounted for and adjusted for in the analyses. P-values and confidence intervals were reported.

Tirzepatide: SURMOUNT 3-Wadden et al. (2023)			
Reference and Trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
	requirements, using a "sedentary" physical activity level (PAL) of 1.3 (FAO/WHO/UNU 2004). **When was adjunct care delivered?** 12-week lead-in period and during main trial period		

Tirzepatide: SURMOUNT 4-Aronne et al. (2024)			
Reference & trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
Reference: Aronne, L. et al. (2024). Continued Treatment With Tirzepatide for Maintenance of Weight Reduction in Adults With Obesity: The SURMOUNT-4 Randomized Clinical Trial. JAMA, 331(1), 38–48. DOI: 10.1001/jama.2023.24945 **Study aim:** To assess the effect of tirzepatide, with diet and physical activity, on the maintenance of weight reduction. **Study design:** Randomised controlled trial **Countries:** Argentina, Brazil, Taiwan, and the US.	**Dietary: Counselling; reduced calorie diet.** **Exercise: Minimum of 150 minutes/week advised** All participants received lifestyle counselling by a qualified health care professional throughout the study to encourage adherence to a healthy 500 kcal/d deficit diet and at least 150 minutes of physical activity per week. **When was adjunct care delivered?**	Participants (n = 670; mean age, 48 years; 473 [71%] women; mean weight, 107.3 kg) who completed the 36-week lead-in period experienced a mean weight reduction of 20.9%. The mean percent weight change from week 36 to week 88 was −5.5% with tirzepatide vs 14.0% with placebo (difference, −19.4% [95% CI, −21.2% to −17.7%]; P < .001). Overall, 300	This was a double blind trial, with participants randomised to treatment or placebo groups. Groups had similar baseline characteristics. Any missing values were accounted for and adjusted for in the analyses.

Tirzepatide: SURMOUNT 4-Aronne et al. (2024)			
Reference & trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
Study duration: 36-week, lead-in period followed by a 52-week, double-blind, placebo-controlled period. **Population:** Tirzepatide-N=335 (Age=49 years; Female sex= 236 (70.4%); Body weight= 84.6kg) Placebo-N=335 (Age=48 years; Female sex= 237 (70.7%); Body weight= 85.8kg) **Intervention:** Tirzepatide was administered once weekly as a subcutaneous injection. During the 36-week, open-label lead-in period, the starting dose of tirzepatide was 2.5 mg and was increased by 2.5 mg every 4 weeks until a maximum tolerated dose of 10 or 15 mg was achieved. At the end of the lead-in period, participants who attained the maximum tolerated dose of tirzepatide (10 or 15 mg) were randomized in a 1:1 ratio by a computer-generated random sequence using an interactive web-response system to either continue receiving the maximum tolerated dose of tirzepatide or switch to matching placebo for an additional 52 weeks. **Comparison:** Matched placebo **Inclusion & exclusion criteria:** Eligible participants (18 years or older) had a body mass index (BMI) greater than or equal to 30 or greater than or equal to 27 and at least 1 weight-related complication (ie, hypertension, dyslipidemia, obstructive sleep apnea, or cardiovascular disease). Key exclusion criteria included diabetes, prior or planned	During main trial period.	participants (89.5%) receiving tirzepatide at 88 weeks maintained at least 80% of the weight loss during the lead-in period compared with 16.6% receiving placebo (P < .001). The overall mean weight reduction from week 0 to 88 was 25.3% for tirzepatide and 9.9% for placebo.	P-values and confidence intervals were reported.

Tirzepatide: SURMOUNT 4-Aronne et al. (2024)			
Reference & trial details	**Adjunct care description**	**Weight loss outcomes**	**Critical appraisal**
surgical treatment for obesity, and treatment with a medication that promotes weight loss within 3 months prior to enrolment.			

Tirzepatide: SURMOUNT-J - Kadowaki et al. (2025)			
Reference & trial details	**Adjunct care description**	**Weight loss outcomes**	**Critical appraisal**
Reference: Kadowaki, T., et al. (2025). Efficacy and safety of once-weekly tirzepatide in Japanese patients with obesity disease (SURMOUNT-J): a multicentre, randomised, double-blind, placebo-controlled phase 3 trial. The lancet. Diabetes & endocrinology, 13(5), 384–396. https://doi.org/10.1016/S2213-8587(24)00377-2 **Study aim:** This study aimed to gain a better understanding of tirzepatide for treatment of Japanese patients with obesity disease (BMI ≥25 kg/m² with excessive fat accumulation) as defined by the Japanese Society for the Study of Obesity. **Study design:** Randomised-controlled trial **Country:** Japan **Study duration:** 72 weeks	**Dietary: Counselling & reduced-calorie diet** Participants will receive diet counselling by a dietician/nutritionist, or equivalent qualified delegate, according to JASSO guidelines. Dietary counselling will consist of advice on healthy food choices and focus on calorie restriction using a hypocaloric diet with macronutrient composition of-approximately 50% to 60% of energy from carbohydrate; Approximately 15% to 20% of energy from protein. Approximately 20% to 25% of energy from fat, and daily energy intake up to 25 kCal/kg × standard body weight (as determined by BMI = 22 kg/m2) for the participant whose BMI is ≥27 kg/m2 and 20 to 25 kcal/kg × standard body weight for the participant whose BMI is ≥35 kg/m2 . To encourage adherence, it is recommended that a 3-day diet and exercise diary be completed prior to each	Estimated treatment differences relative to placebo in change in bodyweight at week 72 were −16·1% (95% CI −18·7 to −13·5; p<0·0001) and −21·1% (95% CI −23·6 to −18·5; p<0·0001) following tirzepatide 10 mg and 15 mg, respectively. At week 72, a higher proportion of participants achieved at least 5% bodyweight reduction with tirzepatide 10 mg (67 [94%] of 71) and 15 mg (73 [96%] of 76) compared with placebo (15	This was a double blind trial, with participants randomised to treatment or placebo groups. Groups had similar baseline characteristics. Any missing values were accounted for and adjusted for in the analyses. P-values and confidence intervals were reported.

Tirzepatide: SURMOUNT-J - Kadowaki et al. (2025)			
Reference & trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
Population: Tirzepatide 10mg-N= 73 (Age=49.0; Female sex=43 (59%); Body weight= 92.4kg) Tirzepatide 15mg-N=77 (Age=51.1; Female sex= 32(42%); Body weight= 91.7kg) Placebo- N=75 (Age= 52.3; Female sex=30(40%); Body weight=92.0kg) **Intervention:** Participants were randomly assigned 1:1:1 to receive tirzepatide (10 mg or 15 mg) or placebo vehicle (disodium hydrogen phosphate heptahydrate and sodium chloride in water, adjusted to pH 7·0), administered subcutaneously via a single-use pen. **Comparison:** Placebo **Inclusion & exclusion criteria:** Eligible participants were aged 20 years or older with a BMI of 27 kg/m² or greater and less than 35 kg/m² and at least two obesity-related health disorders or with a BMI of 35 kg/m² or greater and at least one obesity-related health disorder at screening. Obesity-related health disorders included impaired glucose tolerance, hyperlipidaemia, or MASLD. Impaired glucose tolerance was defined as having an oral glucose tolerance test (OGTT) 0-h glucose of at least 110 mg/dL or 2-h glucose of at least 140 mg/dL, or both, inclusive of borderline type impaired fasting serum glucose as defined by Japanese clinical practice guidelines for diabetes.13 Hyperlipidaemia was defined as fasting triglycerides of 150 mg/dL or greater. MASLD was defined as having a hepatic fat fraction of 5% or greater as measured by MRI-proton density fat fraction (MRI-PDFF). Key exclusion criteria included all diabetes, as defined by Japanese clinical practice guidelines;13 treatment with dipeptidyl peptidase-4 (DPP-4) inhibitors, oral GLP-1	counseling visit. During each visit, the participant's diet is reviewed and advice to maximize adherence is provided if needed. **Exercise: Minimum of 150 minutes/week advised.** The JASSO guideline indicated the amount of physical activity according to the purpose of weight loss; for prevention of weight gain; 150 to 250 minutes (1,200-2,000 kcal) per week for weight loss; moderate-intensity physical activity less than 150 minutes per week to provide only modest weight loss; moderate-intensity physical activity between 225 and 420 minutes per week to provide 5 to 7.5 kg weight loss o greater amounts of physical activity to provide more weight loss. For example, moderate-intensity physical activities (3-6 METs) are slightly fast walking (4 km/hour) and bicycle commuting (<16 km/hour), etc. **When was adjunct care delivered?** During main trial period.	[20%] of 75; both p<0·0001).	

Tirzepatide: SURMOUNT-J - Kadowaki et al. (2025)			
Reference & trial details	**Adjunct care description**	**Weight loss outcomes**	**Critical appraisal**
receptor agonists, or any injectable type 2 diabetes therapy within 3 months before screening; and liver disease other than MASLD.			

Tirzepatide: SURMOUNT-CN -Zhao et al. (2024)			
Reference & trial details	**Adjunct care description**	**Weight loss outcomes**	**Critical appraisal**
Reference: Zhao, L., et al. (2024). Tirzepatide for Weight Reduction in Chinese Adults With Obesity: The SURMOUNT-CN Randomized Clinical Trial. JAMA, 332(7), 551–560. https://doi.org/10.1001/jama.2024.9217 **Study aim:** To assess the efficacy and safety of treatment with tirzepatide for weight reduction in Chinese adults with obesity or overweight and weight-related comorbidities. **Study design:** Randomised controlled trial **Country:** China **Study duration:** 52 weeks **Population:** Tirzepatide 10mg-N= 70 (Age=34.7; Female sex=35 (50%); Body weight= 92.2kg)	**Dietary: Counselling; reduced-calorie diet** At Visit 2 and subsequent visits study participants will receive diet counselling by a dietician/nutritionist, or equivalent qualified delegate, according to local standard. Dietary counselling will consist of advice on healthy food choices and focus on calorie restriction using a hypocaloric diet with macronutrient composition of: approximately 20%-30% of energy from fat x approximately 15%-20% of energy from protein; approximately 40-55% of energy from carbohydrates, and with an energy deficit of approximately 500 kcal/day compared to the participant's total daily energy or use the equation: (body height (cm) - 105); 25 kcal/day as calorie restrict diet energy target (Committee of China expert consensus of medical nutrition therapy to	Of 210 randomized participants (103 [49.0%] female; mean [SD] age, 36.1 [9.1] years; body weight, 91.8 [16.0] kg; BMI, 32.3 [3.8]), 201 (95.7%) completed the trial. The mean change in body weight at week 52 was −13.6% (95% CI, −15.8% to −11.4%) with tirzepatide 10 mg, −17.5% (95% CI, −19.7% to −15.3%) with tirzepatide 15 mg, and −2.3% with placebo (difference between 10 mg and placebo, −11.3% [95% CI, −14.3% to −8.3%; P < .001];	This was a double blind trial, with participants randomised to treatment or placebo groups. Groups had similar baseline characteristics. Any missing values were accounted for and adjusted for in the analyses. P-values and confidence intervals were reported.

Tirzepatide: SURMOUNT-CN -Zhao et al. (2024)			
Reference & trial details	**Adjunct care description**	**Weight loss outcomes**	**Critical appraisal**
Tirzepatide 15mg- N=71 (Age=35.8; Female sex= 35(49.3%); Body weight= 91.3kg) Placebo-N= 69 (Age= 37.8; Female sex=33(47.8%); Body weight=92.0kg) **Intervention:** Participants received self-administered subcutaneous injections of tirzepatide 10 mg, tirzepatide 15 mg, or placebo once a week, plus a lifestyle intervention, for 52 weeks, followed by a 4-week safety follow-up period without treatment. **Comparison:** Placebo **Inclusion & exclusion criteria:** Key inclusion criteria were adults (aged 18 years or older) with a BMI greater than or equal to 28, or greater than or equal to 24 with at least 1 weight-related comorbidity (eg, hypertension, dyslipidemia, cardiovascular disease), and who reported at least 1 unsuccessful dietary effort to lose weight. Key exclusion criteria included diabetes, a self-reported change in body weight of 5 kg or more within 3 months before screening, a previous or planned surgical treatment for obesity, and treatment with medications or alternative remedies intended for weight reduction within 3 months before randomization.	patients who are overweight or obese, 2016; Ge et al. 2018) To encourage adherence, it is recommended that a 3-day food and exercise diary be completed prior to each counselling visit. During each visit, the participant's diet is reviewed and advice to maximize adherence is provided if needed. The hypocaloric diet is continued after randomization and throughout the treatment period. If a %0,0 kg/m2 is reached the recommended energy intake should be recalculated with no kcal deficit for the remainder of the trial. Also, it is recommended total daily energy is at least 1000 kcal for women and at least 1200 kcal for men. **Exercise: Minimum of 150 minutes/week advised.** At Visit 2 and all subsequent visits, participants will be advised to increase their physical activity to at least 150 minutes per week. **When was adjunct care delivered?** During main trial period	difference between 15 mg and placebo, −15.1% [95% CI, −18.2% to −12.1%; P < .001]). The percentage of participants achieving body weight reductions of 5% or greater was 87.7% with tirzepatide 10 mg, 85.8% with tirzepatide 15 mg, and 29.3% with placebo (P < .001 for comparisons with placebo).	

Table 2: Data Extraction-Semaglutide

Semaglutide: STEP 1-Wilding et al. (2021); STEP 1 extension -Wilding et al. (2022)			
Reference & trial details	**Adjunct care description**	**Weight loss outcomes**	**Critical appraisal**
Reference: Wilding, J., et al. (2021) Once-Weekly Semaglutide in Adults with Overweight or Obesity. The New England journal of medicine, 384(11), 989–1002. DOI: 10.1056/NEJMoa2032183 **Study aim:** To evaluate the efficacy and safety of semaglutide as compared with placebo as an adjunct to lifestyle intervention for reducing body weight and meeting other related end points in adults with overweight or obesity and without diabetes. **Study design:** Randomised controlled trial **Country:** 16 countries in Asia, Europe, North America, and South America. **Study duration:** 68 weeks **Population:** Semaglutide group: N=1212 (Female sex: 955 (73.1%); Age: 46; Weight: 105.4 kg) Placebo group: N=577 (Female sex= Female: 498 (76.0%); Age: 47; Weight: 105.2 kg) **Intervention:** Semaglutide at a dose of 2.4 mg administered subcutaneously once a week for 68 weeks or matching placebo, in addition to lifestyle intervention; this 68-week period was followed by a 7-week period without receipt of semaglutide or placebo or lifestyle intervention.	**Dietary & exercise: Counselling; reduced calorie diet; minimum of 150 minutes/week advised** All participants received individual counselling sessions every 4 weeks to help them adhere to a reduced-calorie diet (500-kcal deficit per day relative to the energy expenditure estimated at the time they underwent randomization) and increased physical activity (with 150 minutes per week of physical activity, such as walking, encouraged). Both diet and activity were recorded daily in a diary or by use of a smartphone application or other tools and were reviewed during counselling sessions. **When was adjunct care delivered?** During main trial period.	The mean change in body weight from baseline to week 68 was −14.9% in the semaglutide group as compared with −2.4% with placebo, for an estimated treatment difference of −12.4 percentage points (95% confidence interval [CI], −13.4 to −11.5; P<0.001). More participants in the semaglutide group than in the placebo group achieved weight reductions of 5% or more (1047 participants [86.4%] vs. 182 [31.5%]), 10% or more (838 [69.1%] vs. 69 [12.0%]), and 15% or more (612 [50.5%] vs. 28 [4.9%]) at week 68 (P<0.001 for all three comparisons of odds). The change in body weight from baseline to week 68 was −15.3 kg in the semaglutide group as compared with −2.6 kg in the placebo group (estimated treatment	This was a double blind trial, with participants randomised to treatment or placebo groups. Groups had similar baseline characteristics. Any missing values were accounted for and adjusted for in the analyses. P-values and confidence intervals were reported.

Semaglutide: STEP 1-Wilding et al. (2021); STEP 1 extension -Wilding et al. (2022)			
Reference & trial details	**Adjunct care description**	**Weight loss outcomes**	**Critical appraisal**
Semaglutide, administered with a prefilled pen injector, was initiated at a dose of 0.25 mg once weekly for the first 4 weeks, with the dose increased every 4 weeks to reach the maintenance dose of 2.4 mg weekly by week 16 (lower maintenance doses were permitted if participants had unacceptable side effects with the 2.4-mg dose). **Comparison:** Matched placebo **Main inclusion & exclusion criteria:** We enrolled adults (18 years of age or older) with one or more self-reported unsuccessful dietary efforts to lose weight and either a BMI of 30 or greater or a BMI of 27 or greater with one or more treated or untreated weight-related coexisting conditions (i.e., hypertension, dyslipidemia, obstructive sleep apnea, or cardiovascular disease). A subgroup of participants with a BMI of 40 or less underwent dual-energy x-ray absorptiometry (DXA) to assess body composition. All participants provided written informed consent. Key exclusion criteria were diabetes, a glycated hemoglobin level of 48 mmol per mole (6.5%) or greater, a history of chronic pancreatitis, acute pancreatitis within 180 days before enrollment, previous surgical obesity treatment, and use of antiobesity medication within 90 days before enrollment.		difference, −12.7 kg; 95% CI, −13.7 to −11.7).	
Reference: Wilding, J., et al. (2022) Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension. Diabetes, obesity & metabolism, 24(8), 1553–1564. DOI: 10.1111/dom.14725 **Study aim:** To explore changes in body weight and cardiometabolic risk factors after treatment withdrawal in the STEP 1 trial extension.	**Dietary & exercise: Counselling; reduced calorie diet; minimum of 150 minutes/week advised** The lifestyle intervention consisted of counselling every 4 weeks on diet (500 kcal deficit per day relative to total estimated energy expenditure at randomization) and physical activity (150 minutes per week).	From week 0 to week 68, mean weight loss was 17.3% (SD: 9.3%) with semaglutide and 2.0% (SD: 6.1%) with placebo. Following treatment withdrawal, semaglutide and placebo participants regained 11.6 (SD: 7.7) and 1.9 (SD: 4.8)	This was a double blind trial, with participants randomised to treatment or placebo groups. Groups had similar baseline characteristics.

Semaglutide: STEP 1-Wilding et al. (2021); STEP 1 extension -Wilding et al. (2022)			
Reference & trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
Study design: Randomised controlled trial **Countries:** The extension was offered in five selected countries (Canada, Germany, Japan, the UK and the United States) that were representative of the global trial population and aimed to include approximately 300 participants. **Study duration:** 68 weeks treatment period, followed by 52 week off-treatment follow-up period. **Population:** Extension analyses set included 327 participants: Semaglutide group: (Female sex: 152 (66.7); age-48; weight-105.6kg) Placebo group: (Female sex= 67 (67.7%); age= 50; weight= 105.4 kg) **Intervention:** Once weekly semaglutide 2.4 mg (n = 1306), plus lifestyle intervention. **Comparison:** Placebo plus lifestyle intervention **Main inclusion & exclusion criteria:** To be eligible for the extension, participants were required to have completed treatment with semaglutide 2.4 mg or placebo at week 68 and to provide informed consent for the extension. Exclusion criteria included pregnancy or intention of becoming pregnant during the extension and any factor that could have jeopardized compliance (as judged by the investigator).	**When was adjunct care delivered?** During main trial period.	percentage points of lost weight, respectively, by week 120, resulting in net losses of 5.6% (SD: 8.9%) and 0.1% (SD: 5.8%), respectively, from week 0 to week 120.	Any missing values were accounted for and adjusted for in the analyses. P-values and confidence intervals were reported. No power calculations were performed to determine the sample size. All extension phase analyses were exploratory and performed in the extension analysis set (ExAS), which included all participants eligible for the extension who attended at least one visit on week 75, 80, 104 or 120]

Semaglutide: STEP 3 -Wadden et al. (2021)			
Reference & trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
Reference: Wadden, T., et al. (2021) Effect of Subcutaneous Semaglutide vs Placebo as an Adjunct to Intensive Behavioral Therapy on Body Weight in Adults With Overweight or Obesity: The STEP 3 Randomized Clinical Trial. JAMA, 325(14), 1403–1413. DOI: 10.1001/jama.2021.1831 **Study aim:** To compare the effects of once-weekly subcutaneous semaglutide, 2.4 mg vs placebo for weight management as an adjunct to intensive behavioral therapy with initial low-calorie diet in adults with overweight or obesity. **Study design:** Randomised controlled trial **Country:** US **Study duration:** 68 weeks **Population:** Semaglutide group: n=407(Female sex: 315 (77.4%); Age: 46; Weight: 106.9 kg) Placebo group: n=204 (Female sex: 180 (88.2%); Age: 46; Weight: 103.7 kg) **Intervention:** Once weekly subcutaneous semaglutide, 2.4 mg, or visually identical placebo for 68 weeks. **Comparison:** matched placebo **Inclusion & exclusion criteria:** Eligible participants were aged 18 years or older, reported 1 or more unsuccessful dietary efforts to lose weight,	**Dietary: First eight weeks-meal replacement diet; after eight weeks-reduced calorie diet; counselling sessions underpinned by Intensive Behavioural Therapy.** Dietary intervention started after randomization. The first 8 weeks consisted of a 1000–1200 kcal/day low-calorie diet (LCD), provided as meal replacements (e.g. liquid shakes and solid bars) and heat-and-serve, pre-prepared meals. These foods were manufactured by Nutrisystem and supplied to participants free of charge by Novo Nordisk. After 8 weeks on LCD, participants were gradually transferred to a less strict hypo-caloric diet comprised of conventional foods. From week 8 to the end of treatment, the daily caloric target was calculated based on body weight at randomization (Visit 2) according to the algorithm below: • Participants weighing less than 200 lbs (91 kg) were prescribed a diet of 1200 kcal/day • Participants weighing between 200 lbs (91 kg) and 300 lbs (136 kg) were prescribed a diet calculated as: Daily caloric target (kcal) = body weight (lb) * 6 (kcal/lb) • Participants weighing more than 300 lbs (136 kg) were prescribed 1800 kcal/day This caloric target was kept for the remainder of the trial. If a participant achieved a BMI ≤22.5 kg/m2, the recommended energy intake was re-calculated with no caloric deficit for the remainder of the trial.	At week 68, the estimated mean body weight change from baseline was –16.0% for semaglutide vs –5.7% for placebo (difference, –10.3 percentage points [95% CI, –12.0 to –8.6]; P < .001). More participants treated with semaglutide vs placebo lost at least 5% of baseline body weight (86.6% vs 47.6%, respectively; P < .001). A higher proportion of participants in the semaglutide vs placebo group achieved weight losses of at least 10% or 15% (75.3% vs 27.0% and 55.8% vs 13.2%, respectively; P < .001).	This was a double blind trial, with participants randomised to treatment or placebo groups. Groups had similar baseline characteristics. Any missing values were accounted for and adjusted for in the analyses. P-values and confidence intervals were reported.

Semaglutide: STEP 3 -Wadden et al. (2021)			
Reference & trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
and had either body mass index (BMI) of 27 or higher with at least 1 weight related comorbidity (cardiovascular disease, dyslipidemia, hypertension, or obstructive sleep apnea) or BMI of 30 or higher. Participants were excluded if they had diabetes, glycated hemoglobin levels of 6.5% or more (≥48 mmol/mol), self-reported body weight change greater than 5 kg within 90 days before screening, or prior or planned obesity treatment with surgery or a weight loss device.	**Exercise: 100-200 mins/week advised**. Physical activity was initiated from randomization and was prescribed with a target of 100 minutes physical activity/week. Participants were counselled to be physically active in bouts of >10 minutes in duration with moderate intensity (such as brisk walking), and the physical activity was spread equally across 4–5 days each week. The physical activity target progressed gradually by 25 minutes every 4 weeks and up to 200 minutes/week, consistent with targets required for maintenance of lost weight. **Psychological: Intensive Behavioural Therapy** Each IBT ccounselling session covered a specific topic, for example, advice on modifying diet or physical activity as well as behavioral strategies to facilitate these changes (e.g. monitoring food intake, challenging negative thoughts, obtaining social support). From the randomization visit through week 12, participants received weekly IBT counseling from a dietitian (or a similarly qualified healthcare professional) who discussed participants' progress, reviewed food and activity diaries, addressed any adherence problems, and prepared for transition to the next phase of the diet. Most of the topics were accompanied by a homework assignment, found in the participant hand-outs to be completed before the next visit according to the		

Semaglutide: STEP 3 -Wadden et al. (2021)			
Reference & trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
	visit schedule. From weeks 12 to 24, IBT counseling visits decreased to every other-week, and from weeks 24 to 68 were every 4 weeks (for a total of 30 IBT visits over the 68 weeks). The first three IBT visits lasted for 30–45 minutes, while the remaining visits lasted for 20–30 minutes. Participants received and used an activity tracker and were instructed to record their food intake in order to facilitate behavior change. The activity tracker, food diary/app and content of the participant hand-out from an IBT guide were used for counseling purposes by the dietitian or a similarly qualified healthcare professional at all visits. Data from the activity tracker collected in this trial were used for exploratory purposes. Participants were allowed to keep the activity tracker after approval by the independent ethics committee/institutional review board. Participants could use a food diary of their choice (e.g. paper/app/other tool) for dietary recording, provided it could be reviewed during the counseling sessions. All participants were instructed on how to capture food intake and were encouraged to keep the diary on a daily basis.		

Semaglutide: STEP 4 -Rubino et al. (2021)			
Reference & trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
Reference: Rubino, D., et al. (2021) Effect of Continued Weekly Subcutaneous Semaglutide vs Placebo on Weight Loss Maintenance in Adults With Overweight or Obesity: The STEP 4 Randomized Clinical Trial. JAMA, 325(14), 1414–1425. DOI: 10.1001/jama.2021.3224 **Study aim:** To compare continued once-weekly treatment with subcutaneous semaglutide, 2.4mg, with switch to placebo for weight maintenance (both with lifestyle intervention) in adults with overweight or obesity after a 20-week run-in with subcutaneous semaglutide titrated to 2.4mg weekly. **Study design:** Randomised controlled trial **Country:** Ukraine, Portugal, Spain, Sweden, Switzerland, US, Israel, Denmark, South Africa, Netherlands **Study duration:** Weeks 0-20: run-in period where all participants were given semaglutide dose escalated. Weeks 20-68: participants randomised to either continue semaglutide or switch to placebo **Population:** Semaglutide arm: N=535 (Female sex: 429 (80.2%); Age: 47; Weight= 96.5 kg) Placebo arm: N=268 (Female sex: 205 (76.5%); Age: 46; Weight: 95.4 kg)	**Dietary & exercise: Dietary counselling; reduced-calorie diet; minimum of 150 min/week advised** All participants received a lifestyle intervention from week 0 to week 68, including monthly counselling by qualified health care professionals, in person or by telephone. Participants were prescribed a reduced-calorie diet (500-kcal/d deficit relative to estimated energy expenditure calculated at week 0) and increased physical activity (150 min/wk), recorded daily by participants (using paper diaries, apps, or other tools) and reviewed during counselling visits. **When was adjunct care delivered?** During main trial period	With continued semaglutide, mean body weight change from week 20 to week 68 was −7.9% vs +6.9% with the switch to placebo (difference, −14.8 [95% CI, −16.0 to −13.5] percentage points; P < .001).	This was a double blind trial, with participants randomised to treatment or placebo groups. Groups had similar baseline characteristics. Any missing values were accounted for and adjusted for in the analyses. P-values and confidence intervals were reported.

Semaglutide: STEP 4 -Rubino et al. (2021)			
Reference & trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
Intervention: All participants initially received open-label once-weekly subcutaneous semaglutide, 0.25mg, increased every 4 weeks to the maintenance dose of 2.4mg once weekly by week 16, and continued to week 20 (run-in period). Participants receiving semaglutide, 2.4 mg, at week 20 were randomized in a 2:1 ratio using a blocking schema (block size of 6) in a double-blind manner, via an interactive web-based response system, to continue this treatment or switch to matching placebo for 48 weeks (weeks 20-68; randomized period), with a 7-week follow-up. Participants unable to tolerate semaglutide, 2.4mg/wk, during the randomized period were permitted to receive 1.7mg/wk at the treating investigator's discretion and were recommended to make at least 1 attempt to re-escalate. **Comparison:** Matched placebo given between weeks 20-68. **Inclusion & exclusion criteria:** Adults (≥18 years old) with at least 1 self-reported unsuccessful dietary effort to lose weight and with a body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) of 30 or higher or a BMI of 27 or higher with at least 1 treated or untreated weight-related comorbidity (hypertension, dyslipidemia, obstructive sleep apnea, cardiovascular disease; type 2 diabetes was excluded) were enrolled. Key exclusion criteria were a hemoglobin A1c of 6.5% (48 mmol/mol) or greater and a self-reported change in body weight of more than 5 kg within 90 days of screening.			

Semaglutide: STEP 5 -Garvey et al. (2022)			
Reference & trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
Reference: Garvey, W., et al. (2022) Two-year effects of semaglutide in adults with overweight or obesity: the STEP 5 trial. Nature medicine, 28(10), 2083–2091. DOI: 10.1038/s41591-022-02026-4 **Study aim:** To assess the efficacy and safety of once-weekly subcutaneous semaglutide 2.4 mg versus placebo (both plus behavioral intervention) for long-term treatment of adults with obesity, or overweight with at least one weight-related comorbidity, without diabetes. **Study design:** Randomised controlled trial **Country:** Canada, Italy, Hungary, Spain and the United States **Study duration:** 104 weeks **Population:** Semaglutide group: N=148 (Female sex: 123 (80.9%); Age: 47.3; Weight: 105.6 kg) Placebo group: N=134 (Female sex: 113 (74.3%); Age: 47.4; Weight: 106.5 kg) **Intervention:** Participants received subcutaneous semaglutide 2.4 mg or placebo once weekly for 104 weeks, in addition to standard behavioral intervention, followed by 7 weeks without treatment. Semaglutide was initiated at 0.25 mg per week for the first 4 weeks, escalating in a fixed-dose regimen every 4 weeks to reach the	**Dietary & exercise: Dietary counselling; reduced calorie diet; minimum of 150 minutes/week advised** All subjects in both treatment arms will receive counselling with regards to diet (500 kcal deficit per day relative to the estimated total energy expenditure (TEE) calculated once at randomisation) and physical activity (150 min of physical activity per week is encouraged e.g. walking or, use the stairs). Counselling should be done by a dietician or a similar qualified healthcare professional every 4th week via visits/phone contacts. **When was adjunct care delivered?** During main trial period	The mean change in body weight from baseline to week 104 was −15.2% in the semaglutide group (n = 152) versus −2.6% with placebo (n = 152), for an estimated treatment difference of −12.6 %-points (95% confidence interval, −15.3 to −9.8; P < 0.0001). More participants in the semaglutide group than in the placebo group achieved weight loss ≥5% from baseline at week 104 (77.1% versus 34.4%; P < 0.0001).	This was a double blind trial, with participants randomised to treatment or placebo groups. Groups had similar baseline characteristics. Any missing values were accounted for and adjusted for in the analyses. P-values and confidence intervals were reported.

Semaglutide: STEP 5 -Garvey et al. (2022)			
Reference & trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
maintenance dose of 2.4 mg by week 16 (lower maintenance doses were permitted if participants were unable to tolerate 2.4 mg). **Comparison:** placebo **Inclusion & exclusion criteria**: Participants were eligible to be included in the trial only if all of the following criteria applied: Informed consent obtained before any trial-related activities. Trial-related activities were any procedures that were carried out as part of the trial, including activities to determine suitability for the trial; Male or female, aged ≥18 years at the time of signing informed consent; BMI ≥ 30.0 kg m–2 or ≥27.0 kg m–2 with the presence of at least one of the following weight-related comorbidities (treated or untreated): hypertension, dyslipidemia, obstructive sleep apnea or cardiovascular disease; History of at least one self-reported unsuccessful dietary effort to lose body weight. Participants were excluded from the trial if any of the following criteria applied: Glycemia-related; HbA1c ≥ 48 mmol mol–1 (6.5%) as measured by the central laboratory at screening; History of type 1 or type 2 diabetes; Treatment with glucose-lowering agent(s) within 90 days before screening. Obesity-related; A self-reported change in body weight >5 kg (11 lbs) within 90 days before screening irrespective of medical records; Treatment with any medication for the indication of obesity within the past 90 days before screening; Previous or planned (during the trial period) obesity treatment with surgery or a weight loss device. However, the following were allowed: (1) liposuction and/or abdominoplasty, if performed >1 year before screening; (2) lap banding, if the band had been removed >1 year before screening; (3) intragastric balloon, if the balloon had been removed >1 year before screening; or (4) duodenal-jejunal bypass sleeve, if the sleeve had been removed >1 year before screening;			

Semaglutide: STEP 5 -Garvey et al. (2022)			
Reference & trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
Uncontrolled thyroid disease, defined as thyroid-stimulating hormone >6.0 mIU l–1 or <0.4 mIU l–1 as measured by the central laboratory at screening. Mental health; History of major depressive disorder within 2 years before screening; Diagnosis of other severe psychiatric disorder (for example, schizophrenia, bipolar disorder); A Patient Health Questionnaire-9 score of ≥15 at screening; A lifetime history of a suicidal attempt; Suicidal behavior within 30 days before screening; Suicidal ideation corresponding to type 4 or 5 on the Columbia-Suicide Severity Rating Scale within the past 30 days before screening.			

Semaglutide: STEP 6 -Kadowaki et al. (2022)			
Reference & trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
Reference: Kadowaki, T., et al. (2022). Semaglutide once a week in adults with overweight or obesity, with or without type 2 diabetes in an east Asian population (STEP 6): a randomised, double-blind, double-dummy, placebo-controlled, phase 3a trial. The lancet. Diabetes & endocrinology, 10(3), 193–206. https://doi.org/10.1016/S2213-8587(22)00008-0 **Study aim:** to assess the effect of semaglutide versus placebo for weight management in adults from east Asia with obesity, with or without type 2 diabetes.	**Dietary: Dietary counselling; reduced-calorie diet** Participants were counselled every fourth week via visits or telephone contact by a dietician or similar qualified health-care professional with regard to diet and exercise. Instructions on how to measure food intake and physical exercise were provided and participants were encouraged to record these measurements daily using paper, an app, or similar tool.	From baseline to week 68, greater reductions in bodyweight were observed in the semaglutide 2·4 mg and 1·7 mg groups than the placebo group. The percentage change from baseline to week 68 was –13·2% (SEM 0·5) in the semaglutide 2·4 mg group, –9·6% (0·8) in the semaglutide 1·7 mg group,	This was a double blind trial, with participants randomised to treatment or placebo groups. Groups had similar baseline characteristics. Any missing values were accounted for and

Semaglutide: STEP 6 -Kadowaki et al. (2022)			
Reference & trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
Study design: Randomised controlled trial **Country:** Japan & South Korea **Study duration:** 68 weeks **Population:** Semaglutide 2.4mg group: N=199 (Female sex: 85 (43%); Age: 52; Weight: 86.9 kg) Semaglutide 1.7mg group: N=101 (Female sex: 37 (37%); Age: 51; Weight: 86.1 kg) Placebo group: N=101 (Female sex: 26 (26%); Age: 50; Weight: 90.2 kg) **Intervention:** Participants received subcutaneous semaglutide 2·4 mg, semaglutide 1·7 mg, or placebo once a week for 68 weeks, followed by a 7 week follow-up period without treatment. Semaglutide was initiated at 0·25 mg and escalated in a fixed-dose regimen (0·5 mg, 1·0 mg, 1·7 mg, 2·4 mg) every 4 weeks until the target dose was achieved (week 12 for semaglutide 1·7 mg and week 16 for semaglutide 2·4 mg). **Comparison:** Placebo **Inclusion & exclusion criteria:** Eligible participants were adults (aged ≥18 years in South Korea; ≥20 years in Japan), with at least one self-reported unsuccessful dietary attempt to lose bodyweight. Other key eligibility criteria were a BMI of at least 27·0 kg/m² with two or more treated or untreated weight-related comorbidities, or a BMI of at least 35·0 kg/m² with one or more treated or untreated weight-related comorbidity according to the JASSO guidelines.2 At least one	The dietary intervention included a 500 kcal deficit per day relative to the estimated total daily energy expenditure, calculated at the time of randomisation by multiplying the estimated basal metabolic rate by a physical activity level of 1·3. **Exercise: minimum of 150 mins/week advised** Participants were advised to do 150 min of physical activity per week (eg, walking or climbing the stairs). **When was adjunct care delivered?** During main trial period.	and –2·1% (0·8) in the placebo group. The estimated treatment difference for semaglutide 2·4 mg versus placebo was –11·1 percentage points (95% CI –12·9 to –9·2) and –7·5 percentage points (–9·6 to –5·4) for semaglutide 1·7 mg versus placebo (both p<0·0001). A higher proportion of participants achieved a reduction in bodyweight of 5% or more from baseline at week 68 in the semaglutide 2·4 mg group (160 [83%] of 193 participants with an assessment at the visit) and semaglutide 1·7 mg group (71 [72%] of 98 assessed participants) than the placebo group (21 [21%] of 100 assessed participants). The likelihood of achieving a reduction in bodyweight of 5% or more from baseline was higher with semaglutide 2·4 mg than placebo (odds ratio [OR]	adjusted for in the analyses. P-values and confidence intervals were reported.

Semaglutide: STEP 6 -Kadowaki et al. (2022)			
Reference & trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
comorbidity had to be hypertension or dyslipidaemia, or, in Japan only, type 2 diabetes. A subset consisting of a maximum of 100 randomised Japanese participants were to have type 2 diabetes as a comorbidity at screening, representing a clinically relevant population for pharmacotherapy evaluation; participants in this subset were eligible if they had a type 2 diabetes diagnosis 180 days or more before screening, had a HbA1c 7·0–10·0% (53–86 mmol/mol) at screening, and were receiving treatment with either diet and exercise alone or stable treatment with up to three oral glucose-lowering drugs (metformin, sulfonylureas, SGLT-2 inhibitors, or thiazolidinediones). A subset consisting of a maximum of 180 Japanese participants (with and without type 2 diabetes) had abdominal visceral fat area assessed by CT scan at selected sites where CT scanning was available. Participants were not eligible if they had self-reported changes in bodyweight of 5 kg or more 90 days before screening and had previous or planned (ie, set to occur during the trial period) obesity treatment with surgery or any medication for the indication of obesity.		21·7 [95% CI 11·3–41·9]; p<0·0001) and higher with semaglutide 1·7 mg than placebo (OR 11·1 [5·5–22·2]; both p<0·0001; treatment policy estimand; table 2). Additionally, a higher proportion of participants achieved a reduction in bodyweight of at least 10, 15, and 20% after 68 weeks of treatment in the semaglutide 2·4 mg and 1·7 mg groups than did those in the placebo group (≥20% reduction weight loss threshold was not part of the statistical testing hierarchy). Results were similar for the on-treatment observation period and for the trial product estimand. CI –11·0 to –7·6) and for semaglutide 1·7 mg versus placebo was –5·9 cm (–7·8 to –3·9; both p<0·0001; table 2).	

Semaglutide: STEP 7 -Mu et al. (2024); Gu et al. (2025)			
Reference & trial details	**Adjunct care description**	**Weight loss outcomes**	**Critical appraisal**
Reference: Mu, Y., et al. (2024). Efficacy and safety of once weekly semaglutide 2·4 mg for weight management in a predominantly east Asian population with overweight or obesity (STEP 7): a double-blind, multicentre, randomised controlled trial. The lancet. Diabetes & endocrinology, 12(3), 184–195. https://doi.org/10.1016/S2213-8587(23)00388-1 **Study aim:** To compare the efficacy and safety of semaglutide 2.4mg versus placebo as an adjunct to a reduced-calorie diet and increased physical activity in a predominantly east Asian population with obesity or with overweight and weight-related comorbidities. **Study design:** RCT **Country:** Multiregional; China, Hong Kong, Brazil & South Korea. **Study duration:** Dec 8, 2020 – Aug 23, 2022. 44 weeks on treatment. **Population:** 448 participants (249 assigned to intervention group, 126 to placebo group). **GLP-1 intervention:** Semaglutide 2.4 mg injection (dose escalation from 0.25 with increases every 4 weeks to 0.5, 1.0, 1.7 and 2.4mg reached at week 16) **Comparison:** Placebo injection **Inclusion & exclusion criteria:** Participants with or without type 2 diabetes were included. Eligible participants were 18+ with a history of at least one self-reported unsuccessful dietary effort to lose bodyweight. Patients	**Dietary: Dietary counselling; reduced calorie diet** To be eligible for the study participants had to have been either treated with diet and exercise alone or received stable treatment for at least 60 days before the day of screening with up to three oral anti-diabetes drugs. **Exercise :150 mins/week advised** All participants received a lifestyle intervention that involved counselling on diet (500 kcal deficit per day related to total energy expenditure) and physical activity (150 min of physical activity per week). Participants were instructed to record their food intake daily. **When was adjunct care delivered?** Counselling delivered every 4th week via clinic visits or telephone during main trial period .	Using the treatment policy estimand, the mean percentage change in bodyweight at week 44 was –12·1% (SE 0·5) with semaglutide 2·4 mg versus –3·6% (0·7) with placebo (coprimary endpoint ETD –8·5 percentage points, 95% CI –10·2 to –6·8; p<0·0001) From baseline to week 44, bodyweight was reduced in about 95% of participants on semaglutide 2·4 mg and in about 75% of participants on placebo. The proportion of participants with a weight loss of at least 5% of bodyweight was higher in the semaglutide 2·4 mg group than in the placebo group (coprimary endpoint: 203 [85%] of 238 participants in the semaglutide 2·4 mg group *vs* 36 [31%] of 116 participants in the placebo group.	Random assignment Participant/Investigator blinding Intention to treat analysis Balanced baseline characteristics between groups Subgroup analyses undertaken Range of outcomes studied, P values and CI's reported

Semaglutide: STEP 7 -Mu et al. (2024); Gu et al. (2025)			
Reference & trial details	**Adjunct care description**	**Weight loss outcomes**	**Critical appraisal**
without T2D had to have a BMI of at least 30kg/m^2, or a BMI of 27kg/m^2 with at least one weight related comorbidity. Participants with T2D had to have been diagnosed at least 180 days prior, have a BMI of at least 27kg/m^2 and HbA of 7.0-10.0% (53-86 mmol/mol). Participants were excluded if they had self-reported changes in bodyweight of more than 5kg within 90 days before screening. A HbA of 6.5% or higher were excluded, as were those with uncontrolled T2D or potentially unstable diabetic retinopathy or maculopathy.			
Reference: Gu, W., et al. (2025). Efficacy and safety of once weekly semaglutide 2.4 mg for weight management in participants from China: A prespecified analysis of the STEP 7 randomized clinical trial. Diabetes, obesity & metabolism, 27(5), 2540–2551. https://doi.org/10.1111/dom.16253 **Study aim:** Prespecified analysis compare the efficacy and safety of semaglutide 2.4mg versus placebo as an adjunct to a reduced-calorie diet and increased physical activity in Chinese participants enrolled in STEP 7. **Study design:** Sub analysis of a RCT **Country:** China & Hong Kong **Study duration:** As above **Population:** 300 participants from China/Hong Kong (subset of Mu, et al. study above). 195 in Intervention group, 105 in placebo group. **GLP-1 intervention:** As above **Comparison:** As above	As above	The mean body weight change at Week 44 was _11.8% with semaglutide 2.4 mg versus _3.5% with placebo (estimated treatment difference [ETD] –8.3 percentage points; 95% CI –10.2, -6.4; p< 0.0001), for the treatment policy estimand. During the in-trial observation period, a greater proportion of participants receiving semaglutide 2.4 mg versus placebo had a body weight loss of ≥5% (85.4% vs. 26.8%); the odds of achieving this threshold also favoured semaglutide 2.4 mg (odds ratio [OR] 16.1; 95% CI 8.4,	Random assignment Participant/Investigator blinding Intention to treat analysis Balanced baseline characteristics between groups Subgroup analyses undertaken Range of outcomes studied, P values and CI's reported

Semaglutide: STEP 7 -Mu et al. (2024); Gu et al. (2025)			
Reference & trial details	**Adjunct care description**	**Weight loss outcomes**	**Critical appraisal**
Inclusion & exclusion criteria: As above		30.9; p < 0.0001) for the treatment policy estimand.	

Semaglutide: STEP 8 -Rubino et al. (2022)			
Reference & trial details	**Adjunct care description**	**Weight loss outcomes**	**Critical appraisal**
Reference: Rubino, D. et al. (2022) Effect of Weekly Subcutaneous Semaglutide vs Daily Liraglutide on Body Weight in Adults With Overweight or Obesity Without Diabetes: The STEP 8 Randomized Clinical Trial. JAMA, 327(2), 138–150. DOI: 10.1001/jama.2021.23619 **Study aim:** To compare the efficacy and adverse event profiles of once-weekly subcutaneous semaglutide, 2.4 mg, vs once-daily subcutaneous liraglutide, 3.0 mg (both with diet and physical activity), in people with overweight or obesity. **Study design:** Randomised controlled trial **Country:** US **Study duration:** 68 weeks **Population:** Semaglutide group: N=126 (Female sex: 102 (81.0%); Age: 48; Weight: 102.5 kg)	**Dietary & exercise: Dietary counselling; reduced calorie diet; minimum of 150/mins/week advised** All participants received counselling (from qualified health care professionals, every 4-6 weeks, via in-person visits or telephone) to adhere to diet (500-kcal/d deficit relative to baseline estimated energy expenditure) and physical activity recommendations (≥150 minutes/week) **When was adjunct care delivered?** During main trial period.	The mean weight change from baseline was –15.8% with semaglutide vs –6.4% with liraglutide (difference, –9.4 percentage points [95% CI, –12.0 to –6.8]; P < .001); weight change with pooled placebo was –1.9%. Participants had significantly greater odds of achieving 10% or more, 15% or more, and 20% or more weight loss with semaglutide vs liraglutide (70.9% of participants vs 25.6% [odds ratio, 6.3 {95% CI, 3.5 to 11.2}], 55.6% vs 12.0% [odds ratio, 7.9 {95% CI, 4.1 to 15.4}], and 38.5% vs 6.0% [odds ratio, 8.2	This was a double blind trial, with participants randomised to treatment or placebo groups. Any missing values were accounted for and adjusted for in the analyses. P-values and confidence intervals were reported. * Demographics and baseline characteristics were similar between active treatment groups, whereas the placebo group had a slightly greater baseline body

Semaglutide: STEP 8 -Rubino et al. (2022)			
Reference & trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
Liraglutide group: N=127 (Female sex: 97 (76.4%); Age: 49; Weight: 103.7 kg) Placebo group: N=85 (Female sex: 66 (77.6%); Age: 51; Weight: 108.8 kg) **GLP-1 intervention:** Once-weekly subcutaneous semaglutide, 2.4mg, or once-daily subcutaneous liraglutide, 3.0 mg **Comparison:** Matched placebo **Inclusion & exclusion criteria:** Adults (≥18 years old) with 1 or more self-reported unsuccessful dietary weight loss efforts and a body mass index (BMI, calculated as weight in kilograms divided by height in meters squared) of 30 or greater or 27 or greater with 1 or more weight-related comorbidities (hypertension, dyslipidemia, obstructive sleep apnea, or cardiovascular disease) were eligible (eAppendix 1 in Supplement 3). Key exclusion criteria included diabetes, hemoglobin A1c (HbA1c) level of 6.5% (48 mmol/mol) or greater, and self-reported body weight changes of more than 5 kg 90 days or less before screening.		{95% CI, 3.5 to 19.1}], respectively; all P < .001)	weight, greater proportions of participants in higher BMI groups, and a greater proportion of participants with 5 or more comorbidities (Table 1).

Semaglutide: Real-World Study -Tzoulis et al. (2024)			
Reference & trial details	**Adjunct care description**	**Weight loss outcomes**	**Critical appraisal**
Reference: Tzoulis, P., Batavanis, M., & Baldeweg, S. (2024). A Real-World Study of the Effectiveness and Safety of Semaglutide for Weight Loss. Cureus, 16(5), e59558. https://doi.org/10.7759/cureus.59558 **Study aim:** This study evaluated the effectiveness and adverse events of semaglutide for weight management in a real-life setting, excluding patients with diabetes mellitus. **Study design:** Real world retrospective chart review **Country:** Greece **Study duration:** November 2021 – November 2022 **Population:** Forty individuals (28 females and 12 males) treated with semaglutide for weight management in an endocrine clinic in Athens, Greece. **Intervention:** Semaglutide use: commenced at a dose of 0.25mg once weekly for the first four weeks, then increased to 0.5mg and after eight weeks to 1mg. **Comparison:** N/A **Inclusion & exclusion criteria:** Adults had to meet the following criteria: • BMI greater than 27kg/m^2 combined with at least one weight related complication	**Dietary & exercise: Counselling sessions (motivational interviewing principles)** All individuals received counselling sessions about nutrition and regular exercise at the time of semaglutide initiation and every 12 weeks thereafter by an endocrinologist, following the principles of motivational interviewing. It was left to the discretion of each individual whether they sought regular dietician input, participated in a structured physical activity program, or received behavioral/psychological therapy. **When was adjunct care delivered?** Initiation onto semaglutide, and every 12 weeks thereafter whilst taking semaglutide	After three months of semaglutide administration, the median (IQR) weight loss was 7 (5.3) kg, equivalent to 6.6% (5.5%) percentage weight loss. Out of 40 patients, 28 (70%) and eight (20%) patients achieved greater than 5% (5.6 kg) and 10% (11.2 kg) weight loss, respectively. Among 25 individuals who completed 6 months of semaglutide treatment, those on a 1mg dose (N=16) experienced a median weight loss of 13.6% (14.9kg) compared to 12.8% (14kg) for those on a 2mg dose (n=9).	Weight was measured objectively. * Very limited analyses of potential confounding variables – mostly just exploring effect in different groups * Lack of reporting of statistical significance

Semaglutide: Real-World Study -Tzoulis et al. (2024)			
Reference & trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
• Being on semaglutide for weight management • Minimum of 3 months duration of semaglutide therapy with data recorded at the end of this period. Adults were excluded if they were diagnosed with diabetes mellitus. Individuals who had undergone bariatric surgery or had taken other AOMs in the past were not excluded, but the concomitant administration of other AOMs during the study period was an exclusion criterion.			

Semaglutide: Juniper -Talay & Vickers (2024)			
Reference & trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
Reference: Talay, L., & Vickers, M. (2024). Effectiveness and care continuity in an app-based, glucagon-like peptide-1 receptor agonist-supported weight-loss service for women with overweight and obesity in the UK: A real-world retrospective cohort analysis. Diabetes, obesity & metabolism, 26(7), 2984–2987. https://doi.org/10.1111/dom.15607	**Dietary & exercise: Counselling and personalised diet** All Juniper UK patients were allocated a coordinated multidisciplinary care team (MDT) consisting of a prescribing doctor, a health coach and a medical support officer. MDTs guided patients through personalized diet and exercise pro-grammes and semaglutide therapy, communicating via the Juniper	In the final analysis cohort, follow-up questionnaires were completed at an average of 153.84 (±6.66) days after programme initiation. The mean weight loss at this point was 10.73%. Regarding milestones, 82.36% of the	No information given on how cohort was recruited or who they were. Only 22.7% of participants completed questionnaire (1882/8276); reasons for

Semaglutide: Juniper -Talay & Vickers (2024)			
Reference & trial details	Adjunct care description	Weight loss outcomes	Critical appraisal
Study aim: The study aimed to analyse several care continuity markers in the Juniper UK weight-loss programme, along with the programme's effectiveness. **Study design:** Retrospective cohort analysis. **Country:** UK **Study duration:** The study analysed a retrospective cohort of 8276 UK-based patients who commenced Juniper weight-management treatment between 28 April 2022 and 1 April 2023. To be included in the final analysis, patients were required to complete the first follow-up questionnaire between 140 and 170 days after programme initiation and to have received a minimum of six semaglutide orders by the completion of this questionnaire. The follow-up questionnaire contains 15 standard questions pertaining to patient experience, side effects and weight and often includes additional questions if MDTs seek further information. Patients measure weight with a standardized set of Juniper scales and report weight data themselves. **Population:** 1882 patients were included in the final analysis. Mean age= 45.2; female sex=1716 (91.2%); mean baseline weight=95.3kg. **Intervention:** Juniper- a digital weight loss service. **Comparison:** N/A	in-app chat feature or email. Patients were able to modify their diet and exercise plan in consultation with their health coach at any stage of their care journey. MDTs are required to check in with patients once a month and use their professional discretion to determine the frequency of additional communication. **When was adjunct care delivered?** Ongoing whilst signed up to the programme.	programme's adherers lost ≥5% of their baseline weight, 52.07% lost ≥10%, and 23.22% lost at least 15%. The median BMI loss was 3.18 kg/m. Pearson test revealed that weight loss was not significantly associated with monthly message volume [r (1880) = 0.04, p > .1], and a Spearman test found that the relationship between weight loss and maximum period without MDT contact was not statistically significant [r (1872) = 0.03, p > .1].	non-completion were not provided. We don't have information on characteristics of participants who dropped out so there could have been sample bias. Final sample does not seem representative of the general population- patients were pre-dominantly White (85%) and female (91%). Although this study is only looking at female users of the Juniper Unable to tell if patients always took drug as it was self-administered. We also don't know if patients followed the dietary and exercise plan. Potential self-report bias as participants were given the same set of scales but

Semaglutide: Juniper -Talay & Vickers (2024)			
Reference & trial details	**Adjunct care description**	**Weight loss outcomes**	**Critical appraisal**
Inclusion & exclusion criteria: To be included in the final analysis, patients were required to complete the first follow-up questionnaire between 140 and 170 days after programme initiation and to have received a minimum of six semaglutide orders by the completion of the questionnaire Exclusion criteria included weight loss or gain of>30% from baseline and doses >1 mg of weekly semaglutide (Ozempic).			were asked to weigh themselves. We can't say for sure if weight loss is directly a result of the Juniper programme. It may be a result of the weight loss drug only; it may be a result of weight plus adjunct care. It could also have been from something external. Maybe patients also followed their own diet. There is no comparison group.

ISBN: 978-1-83766-755-0

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