Pharmacological Management of Obesity in General Practice: A Systematic Review of Current Approaches

Ann-Charlotte CLAUS, KU Leuven

Elke DOBBELAERE, KU Leuven

Sylvie-Anne DUROO, KU Leuven

Promotor: Prof. Dr. Geert GODERIS, KU Leuven

Co-promotor: Dr. Ine LAURYS

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ABSTRACT

Background: The therapeutic scenery for the treatment of obesity has expanded considerably in recent years since the introduction of glucagon-like peptide-1 (GLP-1) analogues. However, there is a lack of clear guidelines comparing and summarising the efficacy of anti-obesity medication.

Objectives: In this systematic literature review, we provide an overview of the effectiveness of currently available medication in relation to weight loss.

Methods: A systematic and comprehensive literature search was performed by using the following databases: PubMed/MEDLINE, Embase and Cochrane Library. Eligible and relevant articles were identified, screened, and selected up until November 5, 2024. The risk of bias was assessed using the Cochrane RoB 2-tool.

Results: We selected 30 randomised controlled trials (RCTs) after applying the predefined inclusion- and exclusion criteria. All included agents showed a significant weight reduction compared with placebo after at least 40 weeks. Tirzepatide was associated with the highest weight loss of up to 25% followed by semaglutide and liraglutide, with weight reductions of respectively 17.4% and 8%. The combination therapy with exenatide and dapagliflozin and monotherapy with orlistat or naltrexone/bupropion caused a significantly lower weight loss of 5%, 3% and 4%, respectively. Survodutide, a new promising drug, induced a reduction in weight of 14.9%.

Conclusion: According to the available evidence from this systematic review, tirzepatide showed the highest rates of weight loss. Since this is a rapidly evolving topic, further research needs to be done to keep health professionals updated.

ABSTRACT (DUTCH)

Achtergrond: Het therapeutisch landschap voor de behandeling van obesitas is de laatste jaren aanzienlijk uitgebreid sinds de introductie van de glucagon-like peptide-1 (GLP-1) analogen. Er ontbreekt echter een éénduidige richtlijn die de werkzaamheid van anti-obesitas medicatie vergelijkt en samenvat.

Doelstellingen: In dit systematisch literatuuronderzoek geven wij een overzicht van de effectiviteit van de tot op heden beschikbare medicatie met betrekking tot gewichtsverlies.

Methoden: Er werd een systematisch en uitgebreid literatuuronderzoek uitgevoerd met behulp van de volgende databanken: PubMed/MEDLINE, Embase en Cochrane Library. Geschikte artikels werden geïdentificeerd, gescreend en geselecteerd tot en met 5 november 2024. Het risico op bias werd beoordeeld met behulp van de Cochrane RoB 2-tool.

Resultaten: We selecteerden 30 gerandomiseerde klinische studies na toepassen van de vooraf vastgelegde inclusie- en exclusiecriteria. Alle geïncludeerde medicatie toonde na ten minste 40 weken een significante gewichtsreductie in vergelijking met placebo. Tirzepatide ging gepaard met het grootste gewichtsverlies van maximaal 25%, gevolgd door semaglutide en liraglutide, met respectievelijk 17.4% en 8% gewichtsreductie. De combinatietherapie met exenatide en dapagliflozine en de monotherapie met orlistat of naltrexon/bupropion zorgden voor minder gewichtsverlies (respectievelijk 5%, 3% en 4%). Survodutide, een nieuw geneesmiddel, toonde een gewichtsverlies van 14.9%.

Conclusie: Volgens de beschikbare informatie van dit literatuuronderzoek is tirzepatide het meest effectieve product in België. Verder onderzoek dient plaats te vinden om zorgverleners op de hoogte te houden van nieuwe ontwikkelingen in de nabije toekomst.

INTRODUCTION

Obesity is an upcoming global health problem, in both high-income and low- and middle-income countries, according to the World Health Organization (WHO) (WHO, 2025*)*. It is defined as an excessive accumulation of fat that can be detrimental to both physical and mental health. This chronic condition is rooted in a combination of an unbalanced diet, lack of exercise, stress, and genetic predisposition. Consequently, obesity is associated with an increased risk of various other conditions, including cardiovascular disease, diabetes mellitus, chronic kidney disease, chronic respiratory diseases such as sleep apnoea and lower back pain (Dai, 2020).

According to the 'Global Burden of Disease Study', which assessed the effects of multiple diseases on health, including those related to high Body Mass Index (BMI), on a global scale between 1990 and 2017, the number of global deaths and Disability-Adjusted Life Years (DALYs) resulting from high BMI has more than doubled for both females and males (Dai, 2020). This indicates the need for new treatments to address this growing global health issue. Since conservative measures, such as dietary modification, increased exercise and psychological counselling, are often inadequate (Lundgren, 2021), a lot of research is being performed into medicines to treat obesity. New medicines, such as liraglutide (injectable) and semaglutide (oral or injectable) are glucagon-like peptide-1 (GLP-1) agonists that were initially used to treat diabetes, but which have also shown good results in weight loss (Le Roux, 2017; Davies, 2021). Another upcoming medicine is the GLP-1/glucose-dependent insulinotropic polypeptide (GIP) agonist tirzepatide, which has shown even better results (Aronne, 2024). Older medicines, including orlistat and naltrexone/bupropion, have demonstrated less effective weight loss (Gudzune, 2024).

As with most drug treatments for diseases, obesity medicines also cause numerous side effects that need to be investigated. These include nausea, vomiting, diarrhoea, steatorrhoea, gallstones, pancreatitis, and more. In addition to these gastrointestinal effects, cardiovascular adverse effects have also been reported with the use of obesity medicines (EMA, 2025; Khan, 2025). Furthermore, research has indicated that many of these effects may occur after discontinuation of the medicine (Khan, 2025).

Medicine thus has great potential for treating obesity, but guidelines for healthcare practitioners are changing rapidly in response to ongoing research, especially in the non-diabetes group. It is therefore important to periodically review the latest academic conclusions and evidence on this topic.

By 2022, 36% of adults in Belgium aged 18 and older were overweight and 22% were obese (Sciensano, 2024). According to the 2018 Health Survey of Sciensano, the Belgian institute responsible for reporting national health statistics, 49.3% of the Belgian adult population was overweight (BMI ≥25 kg/m^2) and 15.9% was obese (BMI ≥30 kg/m^2). Furthermore, the average BMI of Belgian adults was found to be 25.5 kg/m^2 (Drieskens, 2018).

This paper provides an overview of the current knowledge on medicine-based obesity treatments for people without diabetes in Belgium by performing a systematic review of existing literature. The overarching question we address is: What medicine on today's market is the most effective at treating obesity? Currently, four types of medicine are registered in Belgium for the treatment of obesity: GLP-1 agonists liraglutide and semaglutide; the combined GIP/GLP-1 agonist tirzepatide; orlistat; and naltrexone/bupropion (BCFI, 2025). Other questions we will try to answer are: Is there a clinical indication for the use of combination pharmacological treatment? Which anti-obesity agents are most appropriate for particular patient subgroups, considering their respective side-effect profiles and tolerability? What are the long-term effects of pharmacological interventions on weight loss?

METHODS

Search method

The protocol for this systematic review was written using the PRISMA-P 2015 checklist (see **Appendix I**).

A comprehensive literature search was performed by using the following databases: PubMed/MEDLINE, Embase and the Cochrane Library. No time or language limitations were applied initially. The systematic search strings used for each database are added in **Appendix II**. Each database was randomly assigned to an individual, who then developed the search strategy for their respective database. We checked each other's work to ensure that no errors were overlooked. Furthermore, we enlisted the help of a library assistant (a doctoral student who supervises thesis students) to advise us on refining our search strategy.

The articles were successively screened by title, abstract and full text for relevance and eligibility, considering the following inclusion and exclusion criteria.

Inclusion criteria

- ✓ Age: ≥18 years, with no upper limit
- ✓ BMI: ≥30 kg/m^2 OR ≥27 kg/m^2 with at least one weight-related comorbidity (e.g. hypertension, dyslipidaemia, obstructive sleep apnoea or cardiovascular disease)
- ✓ Intervention: GLP-1 agonists (semaglutide, liraglutide, dulaglutide, exenatide, lixisenatide, efpeglenatide and albiglutide), GLP-1/GIP agonist (tirzepatide, survodutide), orlistat or naltrexone/bupropion
- ✓ Study length: at least 40 weeks
- ✓ Time of publication: 2014-present
- ✓ Study type: randomised controlled trials (RCTs) only
- ✓ Language: English

Exclusion criteria

- × Age: <18 years
- × BMI: <27 kg/m^2 OR <30 kg/m^2 without a weight-related comorbidity
- × Patients of Asian origin
- × Concomitant diabetes mellitus type 1 or 2
- × Obesity secondary to a treatable cause (e.g. hypothyroidism, Cushing's syndrome, use of corticosteroids, anti-androgens, antipsychotics, anti-epileptics, or antidepressants (TCA or SSRI))

Study selection

Articles from several databases were selected using the following steps: identification, screening and inclusion. We used EndNote for data management. To ensure a double check, each of us independently screened two databases. This screening was always carried out in the same systematic manner. To include the most recent literature, we applied a time limitation of 10 years (with eligible publications not dating from before 2014). Only articles written in English were included. After careful screening and consideration, 30 articles were included in this systematic review. **Figure 1** graphically represents this study selection. We used the PRISMA flowchart for systematic reviews to transparently report the selection process of the included studies.

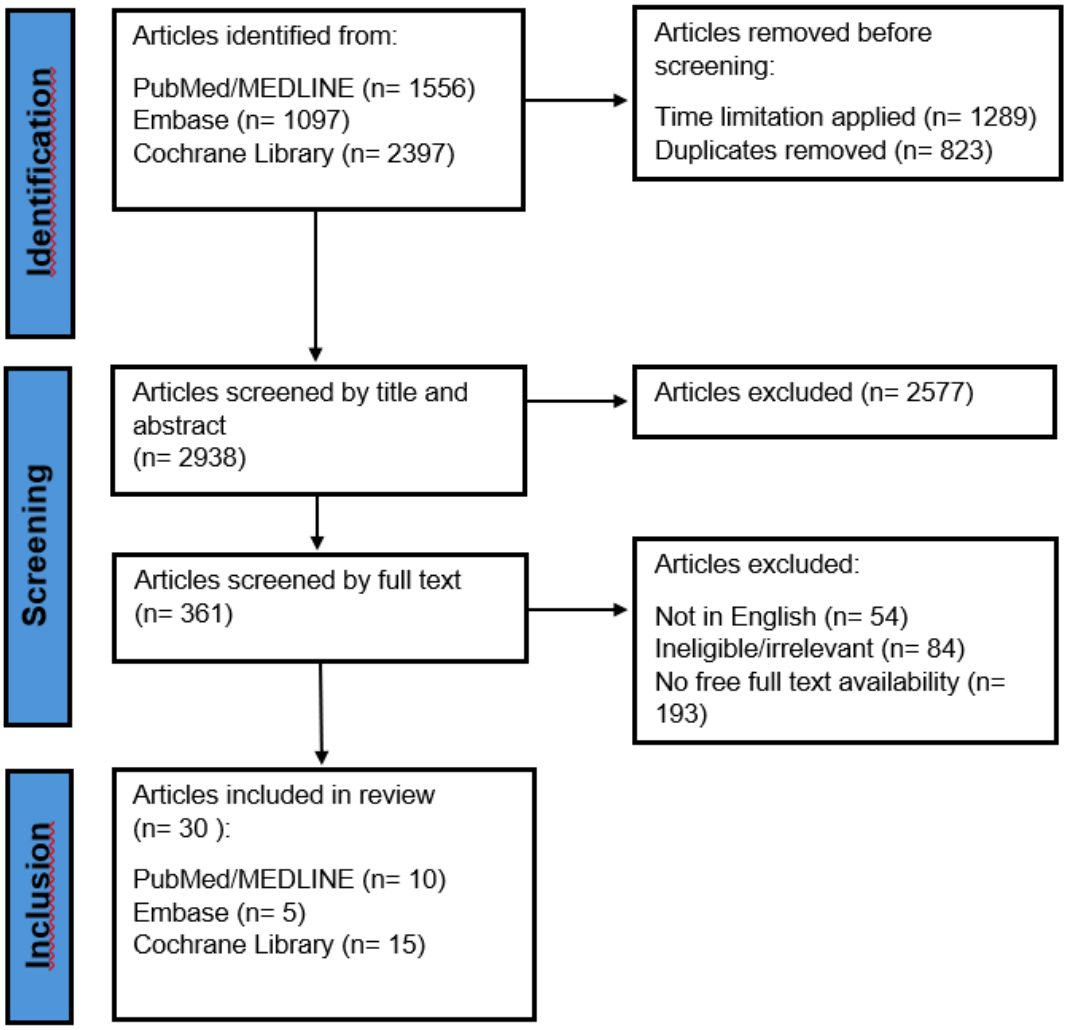


Figure 1 Flow diagram of the articles included in our review

RESULTS

Appendix III provides an overview of the included articles.

The data was collected by reviewing and analysing the existing RCTs that were included during the selection process.

Appendix IV provides an overview of the risk of bias assessment.

We used the Cochrane Risk of Bias 2 tool to assess the risk of bias of each individual article of the included studies.

GLP-1 agonists

Liraglutide

Liraglutide is an agonist of the GLP-1 receptor. GLP-1 is a gut hormone that increases the secretion of insulin, suppresses the release of glucagon, and delays gastric emptying. By increasing satiety and reducing the feeling of hunger, it reduces food intake (BCFI). We found ten RCTs examining the efficacy, safety, and long-term outcomes of liraglutide for weight loss in adults with obesity.

The SCALE Obesity and Prediabetes trial (Pi-Sunyer, 2015) was the largest and most influential study that demonstrated liraglutide as an effective and safe therapy for chronic weight management when combined with lifestyle changes. In this 56-week trial, adults with obesity were randomised to receive either liraglutide (3.0 mg daily) or placebo, together with dietary counselling and increased physical activity. On average, those receiving liraglutide lost 8% of their total weight, compared to 2.6% in the placebo group. Moreover, 63% of participants in the liraglutide group achieved a weight loss of ≥5% and 33% a weight loss of ≥10%, compared to 27% and 11%, respectively, in the placebo group.

The effectiveness of liraglutide as an add-on to intensive behavioural therapy (IBT) was further confirmed by studies of *Wadden et al.* in 2019 and 2020. In these studies, adults with obesity received IBT alone, IBT plus liraglutide, or IBT plus liraglutide combined with portion-controlled meal replacements of 12 weeks. After 52 weeks, the mean weight loss was -6.1% for the IBT-only group, -11.5% for the IBT-plus-liraglutide group, and -11.8% for the combination with meal replacements group. Approximately 70% of participants who took liraglutide achieved a weight loss of ≥5% compared to 44% in the IBT-only group, while 46% achieved a weight loss of ≥10% compared to 26% with IBT alone.

Weight regain remains a major clinical challenge in the treatment of obesity. Several studies have investigated the role of liraglutide in maintaining weight loss.

Lundgren et al. 2021 and *Jensen et al. 2022* gave insight into long-term weight regulation. After an 8-week low-calorie diet, which resulted in an average weight loss of 13.1 kg, adults were randomised into four groups: liraglutide, exercise, a combination of both; or placebo for one year. The group receiving the combination of liraglutide and exercise achieved the greatest sustained weight loss (-9.5 kg), compared with the group receiving liraglutide alone (-6.8 kg), exercise alone (-4.1 kg), or placebo (which experienced a weight regain of 6.1 kg). The combination group also achieved the greatest reduction in body fat percentage.

Jensen et al. 2024 examined the sustainability of these results. They conducted a follow-up study one year after stopping liraglutide to examine the post-treatment effects. While those who had used liraglutide alone gained significantly more weight after stopping treatment (6.0 kg more than those who had exercised alone), participants who received combination therapy

continued to show a decrease in body weight (-5.1 kg) and body fat percentage (-2.3 percentage points) compared to baseline. A greater proportion of participants in the combination and exercise-alone groups maintained a weight loss of at least 10% one year after treatment than in the liraglutide-only group.

The overall safety profile of liraglutide was consistent across trials. *Lean et al. 2014* investigated gastrointestinal side effects among adults receiving liraglutide at doses of up to 3.0 mg, placebo, or orlistat. Almost half (48%) of patients treated with liraglutide experienced nausea, with 13% reporting vomiting, primarily during the initial phase of dose escalation. However, these effects were transient and generally mild or moderate. They rarely led to treatment discontinuation (affecting only 4% of participants) and did not impede improvements in quality of life. Notably, participants who experienced these symptoms lost significantly more weight (-9.2 kg) than those who did not (-6.3 kg).

More recent trials have shown that liraglutide has the potential to enhance weight loss following bariatric surgery.

Hany et al. 2024 evaluated the use of liraglutide in patients who had undergone conversional Roux-en-Y gastric bypass (cRYGB) due to insufficient weight loss or regain following sleeve gastrectomy. Liraglutide (up to 3.0 mg/day) or placebo was administered six weeks after surgery and continued for six months. Patients receiving liraglutide achieved significantly greater total and excess weight loss, compared to the placebo group (percent total weight loss (TWL) 18.3% vs 15.6%; percent excess weight loss (EWL) 60.6% vs 50.6%). Furthermore, 15.8% of patients on liraglutide achieved >20% TWL, compared to none in the placebo group. Even after discontinuation at 12 months, the liraglutide group maintained higher weight loss (24.2% vs 22.7%). Furthermore, patients treated with liraglutide showed better resolution of comorbidities such as diabetes, hypertension, dyslipidaemia and sleep apnoea.

Lofton et al. 2024 evaluated the use of liraglutide (3.0 mg) in treating weight regain following Roux-en-Y gastric bypass (RYGB) surgery. Adults who had regained ≥10% of their postsurgical weight were randomised to receive either liraglutide or placebo for 56 weeks, alongside lifestyle counselling. Participants receiving liraglutide lost an average of 8.8% of their body weight, compared to an average loss of 1.1% in the placebo group. Furthermore, 76% of participants achieved weight loss of ≥5% with liraglutide (compared to 17% with placebo), and 21% returned to or below their postsurgical nadir weight; none of the participants in the placebo group achieved this.

Semaglutide

Semaglutide, like liraglutide, is a GLP-1 agonist. Overall, we found fifteen RCTs investigating the efficacy, safety and long-term outcomes of semaglutide for weight loss in adults with obesity. As mentioned above regarding liraglutide, the different studies reveal many similarities in terms of populations, side effects and results.

The STEP (Semaglutide Treatment Effect in People with Obesity) trials investigated the effects of semaglutide on different populations using different methods (Kushner, 2020; Moiz, 2024). These reviews include STEP 1-5, 8 and 10, but not trial 2, which included patients with type 2 diabetes. *Wilding et al. 2021* analysed the STEP 1 trial, which investigated the difference between semaglutide and placebo in addition to a 68-week lifestyle intervention. The estimated mean weight change at week 68 was -14.9% with 2.4 mg of semaglutide compared to -2.4% in the placebo group. An extension study of STEP 1 for up to one year after the withdrawal of semaglutide or placebo showed that patients regained 11.6% of their weight after the withdrawal of semaglutide, with an overall mean weight loss of 5.6%. The placebo group regained 1.9%, resulting in an overall loss of 0.1% over the duration of both studies (Wilding, 2022). *Wadden et al. 2021* examined the STEP 3 trial, which combined semaglutide or

placebo, with intensive behavioural therapy. Both groups began with an 8-week low-calorie diet. At week 68, the estimated mean weight change from baseline was greater in the semaglutide group than in the placebo group; -16.0% versus -5.7% respectively. *Rubino et al. 2021* analysed the STEP 4 trial. In this trial, both groups initially received semaglutide, but after 20 weeks, they were randomised to receive either semaglutide or placebo. In the group that continued to receive semaglutide, the mean change in body weight from week 20 to week 68 was -7.9%, as opposed to a +6.9% increase in the group that switched to placebo. Over the entire trial period, the estimated mean change in body weight from week 0 to week 68 was −17.4% with continued semaglutide versus −5.0% with placebo. *Garvey et al. 2022* explored the two-year effects of semaglutide in the STEP 5 trial. Here, the mean change in body weight from week 0 to week 104 was -15.2% in the semaglutide group versus -2.6% in the placebo group, suggesting a plateau effect. *Wharton et al. 2023 a*lso investigated STEP 5, using questionnaires to assess eating behaviour. The mean weight loss with semaglutide was −14.8%, as not all patients in the STEP 5 trial completed the questionnaires. *Kyrillos et al. 2022* took a closer look at STEP 1-4, achieving the aforementioned results. *Rubino et al. 2022* compared semaglutide with liraglutide in the STEP 8 trial. There was a significant difference in weight loss between semaglutide (-15.8%) and liraglutide (-6.4%) at week 68. The number of adverse effects was similar. The STEP 10 trial included patients with obesity and prediabetes. *McGowan et al. 2024* found similar results to those described in the above articles. The semaglutide group showed a mean weight loss of 13.9% at week 52, compared to a loss of 2.7 % in the placebo group. After 80 weeks (28 weeks off treatment), the semaglutide group had lost 7.8% of their body weight. Other outcomes included reconversion to normoglycaemia and progression to diabetes.

In addition to the STEP trials, there is also the SELECT trial (Semaglutide Effects on Heart Disease and Stroke in Patients with Overweight or Obesity). This trial includes patients with established heart disease who are overweight but do not have diabetes. *Ryan et al. 2024* examined the weight loss effects of this trial in more detail. As the primary focus of the SELECT trial was not weight loss, there are some differences with the STEP trials. These differences include for example the absence of a combined lifestyle intervention and different study populations. Nevertheless, the outcome shows a weight loss of 10.2% in the semaglutide group, compared to -1.5% in the control group, after 208 weeks. Additionally, *Kahn et al. 2024* reports that the mean weight loss was -9.74% (+/-0.09%) at week 65 and remained stable thereafter. Both studies are prespecified analyses of the SELECT trial.

Other authors also examined the impact on mental and physical health via questionnaires, including the IWQOL-Lite-CT Physical Function scores, the SF-36v2 Physical Functioning scores, and EQ-5D-3L. All of them found a positive evolution in the scores (Rubino, 2024; Bjorner, 2023; Rubino, 2021).

O'Neil et al. 2018 investigated the effect of semaglutide versus liraglutide and placebo in a phase two trial. At week 52, semaglutide led to the greatest weight loss at a maximum dose of 0.4mg.

One article (OASIS 1) conducted a clinical trial using oral semaglutide (50mg) instead of the most widely studied subcutaneous form. After 68 weeks, the results of OASIS 1 favoured semaglutide versus placebo, with a weight loss of 15.1% with oral semaglutide versus -2.4% with placebo (Knop, 2023).

The dose of semaglutide used was 2.4 mg weekly, following a sixteen-week dose-escalation period with escalation every four weeks unless otherwise specified. The oral or subcutaneous form of semaglutide have similar effects, according to a systematic review conducted by *Drygalski et al. 2025*. Furthermore, all trials had a similar study design (randomised and double-blind), but differed in duration, with some also being open label (OASIS 1). The number

of adverse events was similar across the articles with most being gastrointestinal, e.g. nausea, vomiting, diarrhoea and constipation. These were generally mild to moderate.

Exenatide + Dapaglifozin

Exenatide is a GLP-1 receptor agonist that induces weight loss by slowing gastric emptying, increasing satiety and reducing appetite. *Lundkvist et al. 2017* investigated the potential synergistic effect of exenatide in combination with a sodium-glucose linked transporter-2 (SGLT-2) inhibitor called dapagliflozin on weight loss. Dapagliflozin promotes weight loss through a different mechanism than exenatide. It increases urinary glucose excretion resulting in urinary caloric loss, but with a compensatory appetite increase leading to a smaller weight loss than GLP-1 receptor agonists. In the clinical study conducted by *Lundkvist et al.* in 2017, participants were randomly assigned to oral dapagliflozin 10 mg once daily plus subcutaneous exenatide 2 mg once weekly or to placebo for 24 weeks. From week 24 to week 52, all participants entered an open-label extension period, during which they all received active treatment with dapagliflozin and exenatide. The main endpoint was change in body weight from baseline to 52 weeks and from 24 to 52 weeks. Among participants on active treatment with dapagliflozin and exenatide throughout the entire study period, this trial showed a weight loss of 4.5 kg at week 24. Which was maintained at week 52 with an additional weight loss of 1.2 kg that did not reach statistical significance. The other study group that switched at week 24 from placebo to active therapy with dapagliflozin and exenatide achieved a reduction in body weight of 4.2 kg from week 24 to week 52. This result is comparable to that of the active treatment regimen during the first 24 weeks. In total, 40% of all participants achieved a reduction of initial body weight of ≥5% at 52 weeks. The most commonly reported side effects of combination therapy with dapagliflozin and exenatide were nausea, decreased appetite, headache, dizziness and pollakiuria.

Unfortunately, exenatide has not been available in Belgium since December 2024.

Tirzepatide

Tirzepatide represents a significant recent breakthrough in the pharmacological management of obesity, owing to its dual mechanism of action (Wadden, 2023). This molecule acts as an agonist at both the GLP-1 and GIP receptors which are involved in metabolic regulation and play an important role in the delay of gastric emptying, enhancing satiety and reducing hunger, with the result that total calorie intake decreases, and weight loss is facilitated. Concurrent activation of both GLP-1 and GIP receptors appeared to act synergistically and to allow a greater weight reduction in mice than that achieved with GLP-1 receptor mono-agonists (Jastreboff, 2022). To date, several clinical studies in humans have been conducted to investigate the effect of once-weekly subcutaneous tirzepatide on weight loss, demonstrating significant and sustained efficacy.

Wadden et al. 2023 examined the effect of tirzepatide (at the maximum tolerated dose of 10 or 15 mg) on weight loss from randomisation to week 72 after an intensive 12-week lifestyle intervention. Results showed a significant average weight loss at week 72 from randomisation of 18.4% in the tirzepatide group compared to a weight regain of 2.5% in the placebo group. In addition, more participants on tirzepatide than placebo achieved reductions in body weight of ≥5%, ≥10%, ≥15% and ≥20%: 87.5% versus 16.5%, 76.7% versus 8.9%, 65.4% versus 4.2% and 44.7% versus 2.2%, respectively. Overall, intensive lifestyle intervention followed by 72 weeks of tirzepatide caused a total weight change of −24.3% compared with −4.5% in the placebo group. Moreover, *Wadden et al. 2023* observed that 94.0% of participants in the tirzepatide group maintained ≥80% of the body weight lost during the 12-week lifestyle intervention period versus 43.8% in the placebo group. Besides the large effect on total weight reduction, a significant decrease in BMI was also observed: tirzepatide: -7.7 kg/m^2 vs. placebo: +1.2 kg/m^2.

Other RCTs have yielded similar significant results. *Aronne et al. 2024* conducted a study with an initial 36-week open-label tirzepatide lead-in period, during which all participants received the maximum tolerated dose of tirzepatide (10 or 15 mg) subcutaneously once weekly, followed by a 52-week double-blind, placebo-controlled period. The mean percent weight change from week 36 to week 88 was –5.5% with tirzepatide in comparison to +14.0% with placebo. Moreover, 89.5% participants receiving tirzepatide at 88 weeks maintained ≥80% of the body weight lost during the 36-week lead-in period versus 16.6% receiving placebo. The overall mean weight reduction from week 0 to 88 was 25.3% for tirzepatide and 9.9% for placebo. This demonstrates that weight is gradually regained after cessation of the anti-obesity agent tirzepatide. The 72-week double-blind, randomised controlled trial of *Jastreboff et al. 2022* assigned participants to tirzepatide 5 mg, 10 mg, 15 mg or placebo to evaluate the effect on weight reduction. Results show a mean percentage weight change after 72 weeks of –15%, -19.5%, -20.9 % with 5 mg, 10mg, 15mg of tirzepatide respectively and –3.1% with placebo. In addition, 85%, 89% and 91% of the participants receiving 5 mg, 10mg and 15 mg tirzepatide had a weight reduction of 5% or more at week 72 compared to 35% with placebo.

The occurence of gastrointestinal adverse events was similar in all the studies and significantly higher in the tirzepatide group than in the placebo group, with mostly nausea, vomiting, diarrhoea and constipation. These side effects were generally mild to moderate and occurred mainly during dose escalation. The occurrence of pancreatitis, cholelithiasis and acute cholecystitis was rare and comparable in participants treated with tirzepatide and placebo (Wadden, 2023; Aronne, 2024; Jastreboff, 2022).

Survodutide

Survodutide is like tirzepatide a new revolutionary drug, currently being investigated as a new medical treatment for obesity and non-alcoholic steatohepatitis. This agent is not yet available, but the results so far are promising. Survodutide is a dual glucagon and GLP-1 receptor agonist with potential to induce greater weight loss than GLP-1 receptor mono-agonists liraglutide or semaglutide. This improved efficacy of survodutide is attributed to the activation of glucagon receptors in the liver, which leads to stimulation of glycogenolysis, gluconeogenesis and lipolysis resulting in an increased energy consumption (Le Roux, 2024).

The double-blind, placebo-controlled phase 2 trial by *Le Roux et al. 2024* investigated the percentage change in body weight from baseline to week 46 after participants were randomly assigned to once weekly subcutaneous survodutide 0.6 mg, 2.4 mg, 3.6 mg or 4.8 mg or placebo for 46 weeks. A mean change in body weight of –6.2%, -12.5%, -13.2% and –14.9% was observed with survodutide 0.6 mg, 2.4 mg, 3.6 mg or 4.8 mg respectively and –2.8% with placebo. Furthermore, a higher percentage of participants receiving survodutide 4.8 mg achieved body weight losses of 5%, 10% and 15% or greater compared to the placebo group: 83% versus 26%, 69% versus 11% and 55% versus 6%, respectively.

Gastrointestinal disorders, such as nausea, vomiting, diarrhoea and constipation, were the most common adverse events and occurred more frequently in the survodutide group than in the placebo group (75% versus 42%). These side effects were mainly mild to moderate, and no treatment-emergent events like pancreatitis or hepatic injury were reported.

Orlistat

Orlistat is one of the first and oldest drugs used to treat obesity. It acts as an inhibitor of gastrointestinal lipases, thereby reducing fat absorption and inducing weight reduction. The loss of weight achieved through lifestyle changes can be slightly enhanced by orlistat, approximately 3% more than with placebo (Gudzune, 2024). However, it is known that weight gradually increases again after treatment is ceased. Currently, its use in clinical practice has declined dramatically due to its limited effect on weight loss, unpleasant side effects e.g. steatorrhoea, flatulence, bloating, dyspepsia and the emergence of GLP-1 receptor agonists.

Compared to orlistat, the GLP-1 receptor agonist liraglutide causes a significantly greater weight reduction. This has been demonstrated in an RCT conducted by *Lean et al. 2014*, which investigated the effects of liraglutide on weight loss and on the incidence and tolerability of nausea and vomiting. In this study, participants were divided into different groups receiving 1.2 mg, 1.8 mg, 2.4 mg, or 3.0 mg of liraglutide subcutaneously once daily, 120 mg of orlistat three times daily, or placebo for 1 year. After 1 year of treatment, the estimated mean weight loss from randomisation with liraglutide 3.0 mg was 9.2 kg for those who had had at least one episode of nausea/vomiting and 6.3 kg for those who had not. With liraglutide 3.0 mg, weight loss in individuals who had episodes of nausea or vomiting was significantly greater than in those who used orlistat or placebo, with a treatment difference of 6.6 kg and 7.8 kg, respectively. Weight loss after one year in individuals taking liraglutide 3.0 mg without episodes of nausea or vomiting was still significant compared to individuals taking orlistat or placebo, with a treatment difference of 2.3 kg and 4.2 kg, respectively.

Naltrexone/Bupropion

This combination drug also belongs to the older generation of anti-obesity medications. Naltrexone is an antagonist of the central and peripheral opioid receptors. Bupropion is a norepinephrine and dopamine reuptake inhibitor. This combination results in an additional weight loss of approximately 4% compared to placebo. It is unclear whether this effect is maintained over time. Therefore, it is recommended to discontinue treatment if no weight loss of at least 5% occurs after 16 weeks and if the weight loss is not maintained after 1 year of use (Gudzune, 2024). Like orlistat, this combination preparation is rarely used in clinical practice today.

After applying our systematic search strategy and study selection, no suitable articles were found on naltrexone/bupropion as a pharmacological treatment for obesity.

DISCUSSION

The aim of this systematic review was to provide an overview of the most recent evidence regarding registered anti-obesity medicines in Belgium. To this end, we examined direct and indirect evidence from 30 randomised controlled trials involving obese patients who were not diabetic. The core findings of this study are the following.

Firstly, tirzepatide demonstrated the most significant overall impact on weight loss, with reductions up to 25% observed after at least one year of treatment. It is also associated with a higher likelihood of achieving a weight reduction of at least 5%, compared to the other included anti-obesity agents and placebo (Wadden, 2023; Aronne, 2024). Semaglutide and liraglutide follow with total weight reductions of up to 17.4% and 8%, respectively, after 68 and 56 weeks of treatment (Rubino, 2021; Pi-Sunyer, 2015). Combination therapy involving exenatide and dapagliflozine resulted in an average weight loss of 4.5 kg over 24 weeks (Lundkvist, 2017). Unfortunately, exenatide is currently unavailable in Belgium. Orlistat and naltrexone/bupropion lead to significantly lower weight loss compared to GLP-1 agonists: 3% and 4% respectively compared to placebo (Gudzune, 2024). Survodutide is a new, promising anti-obesity drug which has been studied for its ability to induce a weight loss of up to 14.9% after 46 weeks of treatment (Le Roux, 2024). However, it is not yet available on the global market as further investigation is ongoing. Other new promising anti-obesity agents are currently under clinical development, such as cagrisema, retatrutide and orforglipron.

Secondly, the long-term effects are rather limited, considering that a substantial amount of weight is regained after stopping the medication. Two studies showed that patients regained the weight they had lost after stopping semaglutide treatment. After one year, patients had regained two thirds of their lost weight (Wilding, 2022; McGowan, 2024). *Jensen et al. 2024* and *Aronne et al. 2024* demonstrated similar results of weight regain after discontinuation of liraglutide and tirzepatide, respectively. Conversely, several studies have suggested that weight regain can be reduced to 15% within one year through participating in a weight maintenance program offering regular lifestyle counselling (Wadden, 2023; Jensen, 2024). This emphasises the importance of integrating pharmacotherapy and exercise for long-term weight maintenance. Anti-obesity agents decrease appetite, while exercise promotes behavioural and metabolic adaptations that sustain weight loss over time (Lundgren, 2021; Jensen, 2022). Beyond weight reduction, liraglutide has been shown to improve fasting glucose, HbA1c, systolic blood pressure, lipid profile, and quality of life (Pi-Sunyer, 2015). It is important to note that combination therapy with exenatide and dapagliflozin causes an even greater reduction in systolic blood pressure than liraglutide at the higher dose of 3 mg once daily (Lundkvist, 2017). Furthermore, combining exercise with liraglutide treatment results in greater reductions in metabolic syndrome severity, visceral adiposity, and inflammation, potentially reducing the risk of long-term cardiometabolic disease (Sandsdal, 2023). In addition, the use of tirzepatide is also associated with a significant improvement of fasting glucose, HbA1c, systolic and diastolic blood pressure and lipid profile (Wadden, 2023; Aronne, 2024; Jastreboff, 2022).

Thirdly, patients with a history of recurrent pancreatitis and cholecystitis should avoid GLP-1 agonists and orlistat (Wadden, 2023; Gudzune, 2024). Conversely, naltrexone/bupropion should be avoided in patients with a high cardiovascular risk profile, eating disorders, or central nervous system tumours. However, it can be used in patients whose overweight is driven by cravings (Gudzune, 2024). Multiple studies have shown that GLP-1 agonists are generally well tolerated. Nausea mainly occurs in half of participants but is mostly transient and mild in the early phases of treatment (Knop, 2023). Importantly, patients experiencing gastrointestinal side effects exhibited greater weight loss, indicating a potential correlation between gastrointestinal tolerance and treatment efficacy (Lean, 2014). In addition, two studies investigated the role of liraglutide in improving weight loss after bariatric surgery. These studies showed that weight loss with liraglutide was significantly greater than with placebo, even after

treatment was discontinued, resulting in an improved resolution of obesity-related comorbidities. It was also demonstrated that liraglutide can be safely used in this patient group (Hany, 2024; Lofton, 2024).

According to the new 2024 Belgian guidelines, the treatment of obesity should be multimodal and multidisciplinary. It is highly patient-specific, with multiple options possible. The first-line treatment involves changing lifestyle habits, such as eating healthily and exercising regularly. The Flemish government refers patients to various apps to help them eat healthier and exercise more. If these recommendations are insufficient, a dietitian or personal trainer can provide guidance. Only if these interventions are ineffective can a physician suggest medication to treat obesity. The preferred first-line treatments are liraglutide (Saxenda®) and semaglutide (Wegovy®), followed by the combination of naltrexone and bupropion (Mysimba®) and orlistat. This guideline was written before tirzepatide (Mounjaro®) became available on the Belgian market. However, current evidence also suggests tirzepatide as a preferred treatment (Deconinck, 2024). The financial cost should also be considered, as these medicines are not reimbursed by health insurance unless they are prescribed to people with diabetes who are included in a specific care pathway, with the approval of the health insurance's company medical advisor, since 01/02/2026 (RIZIV, 2025). Thus, an important limitation of obesity treatment is the financial cost to patients, which makes it accessible only to the wealthy. This raises the following relevant questions: 'Why are GLP-1 receptor agonists not reimbursed for the treatment of obesity, whereas bariatric surgery is reimbursed under specific conditions despite its substantially higher societal cost?' and 'What factors underlie this discrepancy?'. We therefore consider whether the implementation of a structured primary care pathway for patients with obesity, within which this medication would be reimbursed, may represent a viable solution. Such an approach would require patients to receive comprehensive, multidisciplinary care from healthcare professionals including a general practitioner, dietitian, and psychologist, throughout the patient's weight-loss trajectory.

This study has some limitations. Firstly, it is important to note that only three studies have investigated tirzepatide, compared to fifteen for semaglutide and ten for liraglutide. This is because the literature search was completed in November 2024, and tirzepatide is a more recently approved and marketed drug. This topic is evolving rapidly, with new medicines still coming to the market. Therefore, this systematic review must be considered in this context. Since both new and old medicines were included, the number of trials for different medicines is unequal. For example, the available evidence regarding orlistat and naltrexone/bupropion is much more limited, which could affect the results. Furthermore, there is a lot of heterogeneity among the different studies, which have multiple different protocols and outcomes. This can affect the comparability of the different trials. Nevertheless, strict inclusion and exclusion criteria were used to minimise heterogeneity. Multiple trials implemented behavioural changes alongside medical treatment. As we did not consider the exact measures taken, the results discussed here should be interpreted with caution. Some of the selected studies were prespecified analyses of trial. For example, the SELECT trial's primary outcome was semaglutide's effect on death from cardiovascular causes, non-fatal myocardial infarction, or non-fatal stroke with patients who have pre-existing cardiovascular diseases. Weight loss was a secondary outcome. The results concerning cardiovascular outcomes favour semaglutide above placebo (Lincoff, 2023).

Future research should explore alternative treatment strategies such as intermittent or cyclical use of anti-obesity medications. In addition, real-world studies conducted in primary care settings are needed. Most existing trials include highly selected patient populations and are conducted in specialised centres. Observational studies in routine clinical practice could provide valuable information on long-term adherence, effectiveness, safety and cost-effectiveness of these treatments in more heterogeneous patient populations.

CONCLUSION

This systematic review shows that GLP-1 receptor agonists and dual GLP-1/GIP receptor agonists lead to clinically meaningful weight loss, alongside behavioural changes, in patients with obesity. Tirzepatide is the most promising drug, with a weight loss of up to 25%, followed by the other GLP-1 agonists semaglutide and liraglutide, with weight losses of 17.4% and 8%, respectively. For general practitioners, these medications may represent an important addition to lifestyle interventions, although long-term effectiveness and safety, cost and accessibility remain important considerations. Therefore, further research is needed into the long-term side effects, as well as the sustained effect of weight loss. Finally, we are awaiting the availability of novel pharmacotherapeutic agents, such as survodutide. We expect that a revision of the present evaluation will be necessary within the following years, given the many drugs currently in development.

PERSOONLIJKE REFLECTIES MASTERPROEF

Persoonlijke reflectie – Ann-Charlotte Claus

Verloop van het groepsproces en persoonlijk aandeel

Over het algemeen kan ik positief terugblikken op het groepswerk samen met Elke en Sylvie-Anne. Van bij de start hadden we een gelijkaardige visie over wat voor onderzoek we wouden doen en hoe we de thesis tot een goed einde zouden brengen. Sylvie-Anne kwam met het idee om een thesis te maken over anti-obesitas medicatie en Elke en ik sprongen snel mee op de kar. Er werd al snel beslist om voor een literatuuronderzoek te kiezen, aangezien dit voor ons alle drie de voorkeur had. Na een groepsgesprek met Professor Goderis werd het definitieve onderwerp: de effecten van de beschikbare anti-obesitas medicatie op dat moment.

In onderling overleg werd uiteindelijk beslist om geen systematic review met meta-analyse te schrijven, maar te kiezen voor louter een literatuuronderzoek. We dienden onze thesis dan ook niet in bij PROSPERO.

De start van het onderzoek begon met het opstellen van een zoekstrategie. Hiervoor schakelden we de hulp in van een onderzoeker bij de bib. We stelden elk een zoekstrategie op voor een gekozen databank (PubMed, Cochrane en Embase). De onderzoeker bij de bib gaf meermaals feedback op de opgestelde zoekstring. Deze stap nam meer tijd in dan dat ik oorspronkelijk had gedacht. We moesten regelmatig onze zoekstring bijstellen.

Hierna gingen we aan de slag met het selecteren van geschikte studies volgens onze in- en exclusiecriteria. We gebruikten de app ‘Endnote’ voor het opslaan van de studies en vervolgens het verwijderen van duplicaten. We screenden elk een databank en keken dan het werk van de ander na. Daarna begon de risicobepaling van de bias. Hiervoor gebruikten we de Rob2 tool of bias. Elk screende zijn gevonden artikels op bias.

In tussentijd maakte Sylvie-Anne ook nog een tussentijds rapport op, dat we uploadden op de website van ICHO. Na de check op bias, begon de data extractie uit de gekozen artikels. Hiervoor gebruikten we een evidence tabel. Deze wordt toegevoegd aan de thesis. Ondertussen kregen we ook feedback van onze promotor bij onze tweemaandelijkse videocalls. Op basis van de feedback werd de evidence tabel nog wat uitgebreid.

Dan begon het schrijven van de thesis pas echt. Het werk werd ongeveer gelijk verdeeld tussen het schrijven de intro (door mezelf), de methodensectie door Elke en het verfijnen van de evidence tabel en Rob2 tool door Sylvie-Anne. De resultatensectie werd verdeeld per medicatie en zo had iedereen opnieuw ongeveer een gelijke bijdrage. Dit werd aangepast naar de feedback van de promotor. De discussie en conclusie sectie hebben we samen geschreven op een afgesproken dag. Hierdoor konden we ongeveer dezelfde stijl hanteren. Hierna volgde nog knip en plak werk om de thesis in het juiste formaat te krijgen. Elke en Sylvie-Anne hebben voor dit werk gezorgd.

Dit werk werd voor feedback opnieuw doorgestuurd naar onze promotor en ook co-promotor. Op basis van de feedback van de co-promotor werd de thesis nog verder verfijnd en enkele zaken verwijderd of toegevoegd. Het abstract schrijven was opnieuw een groep sessie om dezelfde schrijfstijl na te streven.

We hadden tweemaandelijkse videocalls met onze promotor waarbij we steeds nieuwe deadlines vooropstelden. We waren alle drie gemotiveerd om de thesis op tijd klaar te krijgen en dit lukte ook net omdat we de vooropgestelde deadlines respecteerden.

Persoonlijke visie op wat het werk nu betekent voor het werkveld

Obesitas is een wereldwijd gezondheidsprobleem dat een specifieke aanpak vraagt. Gezien overgewicht en obesitas voor veel nadelige gezondheidseffecten zorgen, dringt zich de vraag naar doeltreffende behandelingen op. Deze thesis draagt dan ook bij aan het ontstane debat hierover.

Wanneer ik kijk naar de eigen dagelijkse werkdag in een huisartsenpraktijk, merk ik al snel hoe vaak we de problematiek tegen komen. Heel veel problemen zoals hoge bloeddruk, hypercholesterolemie maar ook mentale problemen zijn te herleiden naar de te hoge BMI van een patiënt. Wanneer we in eerste instantie de oorzaak van de problemen kunnen aanpakken, kan dit voordelig zijn voor de polyfarmacie van de latere patiënt.

De laatste maanden krijg ik in de praktijk ook meer de vraag naar opstart van medicatie om te vermageren. Een grote beperkende factor blijft natuurlijk de kostprijs voor de patiënt. De terugbetaling geldt momenteel enkel voor mensen met diabetes. Toch zijn vele mensen gemotiveerd om (alleszins tijdelijk) deze medicatie te bekostigen. Gezien het gebruik meestal tijdelijk is en het gewicht er achteraf vaak opnieuw bijkomt, is regelmatige opvolging en sensibilisering bij deze mensen cruciaal.

Met het schrijven van deze thesis kan ik de beslissing om te kiezen voor een bepaald product beter staven. Gezien het snel evoluerende onderwerp, zal regelmatige bijscholing in verband met dit onderwerp nodig zijn, gezien op 2 jaar tijd al veel veranderde met betrekking tot dit thema. De toekomst zal uitwijzen of deze medicatie nog meer gebruikt zal worden of er net nog nieuwe middelen op de markt zullen komen. Zeker is dat het broodnodig is om hier verder onderzoek naar te doen.

Persoonlijke reflectie – Elke Dobbelaere

Verloop van het groepsproces en persoonlijk aandeel

Het schrijven van een thesis begint met het vinden van een interessant onderwerp. Het idee om iets te doen rond medicatie bij obesitas kwam van Sylvie-Anne, die in de seminariegroep polste of er mensen geïnteresseerd waren in dit onderwerp, en of die er ook een groepsthesis van wilden maken. Ann-Charlotte en ik waren meteen enthousiast en zo was onze thesisgroep geboren.

Na het indienen van een thesisvoorstel met motivatie, werd Professor Geert Goderis aan ons toegewezen als promotor en al snel volgde een eerste kennismaking. Er werd samen beslist dat het zou gaan over een systematic review. Na goed aflijnen van het onderwerp en schrijven van een thesisprotocol (m.b.v. de PRISMA-P checklist), konden we beginnen aan het opstellen van de zoekstrategie. We schakelden de hulp in van een medewerkster van de bib, een doctoraatsstudente die thesisstudenten begeleidt, voor het finetunen van de zoekstrategie. Verschillende meetings, feedback en aanpassingen later konden we met de definitieve zoekstrategie beginnen aan het doorzoeken van de databanken (PubMed, Embase en Cochrane).

We gebruikten EndNote voor het screenen van de artikels, eerst op titel en abstract, nadien op full-text. We screenden elk twee van de drie databanken. Dit had meer voeten in de aarde dan ik oorspronkelijk had gedacht, we zijn hier toch enkele maanden mee bezig geweest. Na het definitief selecteren van de te includeren artikels, stelden we de evidence tabel op en deden we een risk of bias assessment a.d.h.v de Cochrane Risk of Bias tool.

Nadien konden we beginnen aan het schrijven van de thesis. De inleiding en methoden werden onderling verdeeld. Waar bij alle voorgaande stappen het werk ongeveer werd verdeeld per databank, hebben we voor het schrijven van de resultaten het werk verdeeld per medicatiegroep, namelijk liraglutide voor mezelf, semaglutide voor Ann-Charlotte en al de rest voor Sylvie-Anne. Voor het schrijven van het abstract, de discussie en de conclusie zijn we samengekomen.

Het hele proces werd begeleid door onze promotor met 2-maandelijkse online contactmomenten via Teams. Alle beslissingen werden ook steeds gemaakt in samenspraak met hem. Het idee kwam van ons uit om op regelmatige basis ons werk te updaten aan de promotor en zo ook telkens nieuwe deadlines af te spreken, zodat het werk nooit bleef liggen. Ongeveer jaarlijks waren er vanuit de opleiding ook enkele deadlines, zoals het schrijven van tussentijdse voortgangsverslagen en registreren van de contactmomenten met de promotor.

Over het algemeen vind ik dat het groepsproces heel goed is verlopen. We kwamen goed overeen en konden telkens tot een goede en eerlijke verdeling komen van alle taken. Er zijn nooit onderlinge frustraties of strubbelingen geweest, van mijn kant toch niet. We communiceerden vooral online (via chat en meetings), maar hebben ook enkele keren fysiek afgesproken. Iedereen was gemotiveerd om de thesis op tijd af te krijgen, waardoor we altijd goed op schema bleven en nooit in tijdsnood geraakten. Ik ben heel tevreden met hoe alles gelopen is. Ik heb alleen maar voordelen ondervonden van het in groep samenwerken aan de thesis.

Persoonlijke visie op wat het werk nu betekent voor het werkveld

Obesitas is een belangrijk gezondheidsprobleem en gaat gepaard met verschillende comorbiditeiten, zoals hypertensie, hypercholesterolemie, diabetes mellitus en mentale gezondheidsproblemen. Dit draagt bij aan een hogere zorgnood- en consumptie, alsook polyfarmacie. In de huisartsenpraktijk zie ik dagelijks patiënten met overgewicht of obesitas en

hoe dit invloed heeft op vele andere medische klachten. Het aanpakken van de onderliggende oorzaak (het overgewicht zelf) kan dus een belangrijke impact hebben op de algemene gezondheid van de patiënt op lange termijn. Daarom vraagt obesitas een gerichte en wetenschappelijk onderbouwde aanpak.

Het therapeutisch landschap van obesitas is de laatste jaren aanzienlijk veranderd sinds de introductie van GLP-1-analogen en gecombineerde GIP/GLP-1-analogen. Deze producten zorgen voor een significante gewichtsreductie, waardoor de vraag naar deze anti-obesitasmedicatie in de huisartsenpraktijk zichtbaar is toegenomen. Er hangt wel een kostenplaatje aan vast, aangezien deze medicatie in België momenteel enkel terugbetaald is bij bepaalde indicaties, zoals diabetes mellitus type 2. We zien echter dat de meeste patiënten die niet in aanmerking komen voor terugbetaling, er toch voor openstaan om de behandeling tijdelijk zelf te financieren. Overgewicht en obesitas zijn dus een problematiek waar veel patiënten een oplossing voor zoeken.

Gezien deze evoluties is het daarom belangrijk dat er voor huisartsen een duidelijk overzicht is van de beschikbare medicatie, zowel wat betreft werkzaamheid en nevenwerkingenprofiel, als naar langetermijneffecten en terugbetalingsvoorwaarden. In deze thesis maakten we daarom een actueel en kritisch overzicht van de huidige beschikbare anti-obesitasmedicatie in België. Deze thesis kan dus een houvast bieden bij de overweging tot opstart van medicamenteuze therapie.

Het is echter een snel evoluerend domein. Dit merk ik o.a. aan het aantal vertegenwoordigers dat in de praktijk hun anti-obesitas medicatie komt voorstellen. Ook zijn er sinds de start van onze thesis alweer enkele nieuwe producten op de markt gekomen, of staat er nieuwe medicatie in de pipeline. Daarom is het belangrijk om de meest recente evidence te blijven opvolgen en je regelmatig te blijven bijscholen omtrent het onderwerp.

Persoonlijke reflectie – Sylvie-Anne Duroo

Verloop van het groepsproces en persoonlijk aandeel

Om te starten heb ik eerst grondig nagedacht over welk domein binnen de geneeskunde me het meest interesseerde om mijn masterthesis over te schrijven. Ik kwam al snel uit bij 'Endocrinologie'. Vervolgens moest ik een concreet onderwerp kiezen binnen dit breed vakgebied. Deze keuze was niet al te gemakkelijk aangezien ik een boeiend doch ook vernieuwend onderwerp wilde waar nog geen masterproef over geschreven was. Mijn toenmalige praktijkopleider, die nadien ook onze co-promotor is geworden, heeft mee naar ideeën gezocht. Destijds was net het groot tekort aan de GLP-1 analogen 'Ozempic' en 'Rybelsus' ontstaan waardoor enkel diabetici hier nog recht op hadden en de vele patiënten met obesitas zonder medicatie vielen. Altoen waren de huidige beschikbare alternatieven, zoals Mounjaro of Wegovy, in studiefase en dus nog niet op de markt. Naar aanleiding van de te verwachten opmars van deze revolutionaire anti-obesitas medicatie en het feit dat obesitas een wijdverspreide aandoening is, leek het me innovatief, leerrijk en zinvol om als onderwerp 'de medicamenteuze behandeling van obesitas in de huisartsenpraktijk' te kiezen.

Eens deze belangrijke knoop was doorgehakt, maakte ik al snel de beslissing om hier een 'groepsthesis' van te maken. Dit vanuit mijn eigen zelf die liever samenwerkt met anderen dan alleen. Daarnaast leek het me ook interessanter om input te hebben van andere HAIO's om zo een bredere waaier aan ideeën, opinies en visies te hebben. Een ander voordeel van een groepswerk is de lagere workload die je elk individueel hebt, natuurlijk op voorwaarde dat je het werk eerlijk verdeelt. Daarom was het voor mij uiterst belangrijk om de 'juiste' groepsleden te vinden. Gelukkig had ik in mijn eerste jaar een fijne, hechte seminariegroep waarin ik mijn thesisonderwerp kort voorstelde en vroeg of er toevallig HAIO's waren die mee in dit project wilden stappen. Ann-Charlotte en Elke waren geïnteresseerd en na wat extra uitleg over het onderwerp, waren ze overtuigd. Zo was onze thesisgroep van drie geboren.

Eerstvolgend dienden we, in december 2023, ons onderwerp in en contacteerden we professor Goderis zodra hij aan ons was toegewezen als promotor. Dit contactmoment en alle daarop volgenden verliepen online via 'TEAMS meeting'. In samenspraak met hem, beslisten we om als masterproef een systematische review te maken omtrent het gekozen onderwerp. Een literatuuronderzoek was beduidend zinvoller dan een kwalitatieve/kwantitatieve studie gezien de weinig beschikbare data omtrent het voorschrijfgedrag en gebruik van anti-obesitas medicatie in de eerste lijn. Met behulp van professor Goderis concretiseerden we onze onderzoeksvraag en werkten we ons onderwerp gedetailleerder uit om nadien van start te gaan met het opstellen van een correcte zoekstrategie. De door ons gekozen databanken omvatten PubMed, Embase en Cochrane. Initieel verliep dit naar mijn aanvoelen stroef omdat het moeilijk was om de juiste zoektermen en zoekstrategie per databank te vinden opdat we een geschikte zoekopdracht zouden hebben die niet te breed doch ook niet te beperkt was. Gelukkig hebben we hierbij veel hulp gekregen van een doctoraatsstudente, die in de bibliotheek van Gasthuisberg werkte en masterstudenten bij hun thesis begeleidde/hielp. Het werk was eerlijk verdeeld waarbij ieder de zoekstrategie van één databank opstelde en we nadien elkaars zoekstrategie controleerden op eventuele fouten/nalatigheden. Ik heb de zoekstrategie van Cochrane gemaakt. Na de toepassing van de zoekstrategieën voor iedere databank, kon de stapsgewijze artikelselectie van start gaan. Ook hier was er een eerlijke taakverdeling aanwezig waarbij we elk twee van de drie databanken screenden naar geschikte artikels. Het opstellen van de zoekstrategie en de systematische studieselectie heeft ongeveer een half jaar geduurd, van het voorjaar tot het najaar van 2024. Zo waren we al in ons tweede jaar als HAIO beland.

Vervolgens hebben we samen de geïncludeerde artikels op bias beoordeeld a.d.h.v. cochrane RoB 2 tool en een evidence tabel gemaakt die ook een samenvatting van de resultaten is. Bij deze stap heb ik een grotere bijdrage geleverd die nadien gecompenseerd werd door Ann-

Charlotte en Elke die een groter deel van de inleiding en methoden geschreven hebben. Aan dit schrijven zijn we in de lente van 2025 begonnen. De introductie en methoden waren klaar in de zomermaanden en nadien hebben we ieder een even groot deel van de resultaten geschreven. Zo heeft Elke het deel 'Liraglutide' gemaakt, Ann-Charlotte het deel 'Semaglutide' en ik de overige delen gezien al deze afzonderlijk een kleinere hoeveelheid aan literatuur omvatten. In december 2025, zijn we fysiek samen gekomen om de discussie en conclusie gezamenlijk te schrijven en éénzelfde schrijfstijl in de rest van de reeds geschreven delen toe te passen opdat de thesis één mooi geheel zou zijn. Tegen begin februari 2026 was een eerste geschreven versie van onze masterproef af waarop we feedback kregen van professor Goderis en tevens van onze co-promotor. In de laatste twee maanden van het schrijfproces, namelijk maart en april 2026, hebben we de feedback verwerkt en nodige aanpassingen doorgevoerd. Daarnaast hebben we alles meermaals nagelezen op resterende fouten en hebben we het abstract geschreven. We waren mooi op tijd klaar voor de deadline van indiening die viel op 1 mei 2026.

Doorheen het hele proces hebben we verschillende online contactmomenten met professor Goderis gehad. Deze dienden als deadlines voor ons. Daarbij hebben we tevens meerdere overlegmomenten gehad onder ons drie ter bespreking van de volgende taken, taakverdeling, etc. Meestal gingen deze contacten online door, we hebben echter ook een 3-tal keren afgesproken bij iemand thuis. Ik ben erg tevreden van het groepsverloop en onze samenwerking. Elk van ons drie vond het belangrijk om de vooropgestelde deadlines te halen en we werkten dan ook op een goed tempo samen waarbij finaal iedereen evenveel heeft bijgedragen aan deze thesis. Hierdoor heb ik het schrijven van deze masterproef als aangenaam en leerrijk ervaren.

Persoonlijke visie op wat het werk nu betekent voor het werkveld

Zoals reeds hierboven vermeld, heb ik voor dit onderwerp gekozen omdat obesitas een zeer vaak voorkomende aandoening is en huisartsen hier dagdagelijks mee geconfronteerd worden in de praktijk. Door de ontwikkeling en commercialisering van de GLP-1 analogen en GIP/GLP-1 analogen die allen een significant gewichtsverlies bewerkstelligen, is de vraag van patiënten naar anti-obesitas medicatie nog nooit zo hoog geweest. Daarom is het uiterst belangrijk om als huisarts op de hoogte te zijn van alle mogelijke medicamenteuze therapieën die op heden op de markt beschikbaar zijn voor de behandeling van 'obesitas' evenals van hun bijbehorende bijwerkingen, korte- en lange termijneffecten, prijs, etc. Het is echter niet gemakkelijk om up-to-date te blijven gezien de snel ontwikkelende farmaceutische en medische industrie. Met deze thesis wilden we een duidelijke weergave maken van alle beschikbare medicatie die in België kan gebruikt worden bij de indicatie 'obesitas'; inclusief het te verwachten gewichtsverlies en bijwerkingenprofiel. Zo hebben we eruit geleerd dat Semaglutide en Tirzepatide aan de maximale dosis voor de grootste gewichtsreductie zorgen met een aanvaardbaar profiel van gastro-intestinale bijwerkingen. Deze paper kan dan ook als een handvat gebruikt worden bij de (vraag naar) opstart van medicatie. Zelf vind ik het (ethisch) belangrijk om deze geneesmiddelen enkel voor te schrijven aan patiënten die voldoen aan de nodige medische voorwaarden vooropgesteld door de Hoge Gezondheidsraad en die hun levensstijl reeds hebben aangepast. Het is belangrijk om te beseffen dat deze levensstijlaanpassingen de belangrijkste hoeksteen in de behandeling van obesitas blijven gezien na het staken van de medicatie het gewicht terug toeneemt.

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APPENDIX

I. Overview of the systematic review protocol (using PRISMA-P)

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page number
ADMINISTRATIVE INFORMATION			
Title:			1
Identification	1a	Identify the report as a protocol of a systematic review	
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number1	NA
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	
Support:			
Sources	5a	Indicate sources of financial or other support for the review	NA
Sponsor	5b	Provide name for the review funder and/or sponsor	NA
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	NA
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
METHODS			

Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	6
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	30-31
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	7
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	7
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	7
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	NA
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	5
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	8
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	7
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	NA
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	NA
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	NA
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	NA
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	NA

***It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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II. Search strings

Our PubMed/MEDLINE search string was composed of the following terms:

"Obesity"[Mesh:NoExp] OR "Obesity, Abdominal"[Mesh] OR "Obesity, Metabolically Benign"[Mesh] OR "Obesity, Morbid"[Mesh] OR "Obes*"[tiab] AND "Glucagon-Like Peptide 1"[Mesh] OR "Glucagon Like Peptide 1 agonist"[tiab:~2] OR "Glucagon Like Peptide 1 agonists"[tiab:~2] OR "Glucagon Like Peptide 1 mimetic"[tiab:~2] OR "Glucagon Like Peptide 1 mimetics"[tiab:~2] OR "Glucagon Like Peptide 1 analogue"[tiab:~2] OR "Glucagon Like Peptide 1 analogues"[tiab:~2] OR "Glucagon Like Peptide 1 analog"[tiab:~2] OR "Glucagon Like Peptide 1 analogs"[tiab:~2] OR "Glucagon Like Peptide 1 stimulating"[tiab:~2] OR "Glucagon Like Peptide 1 stimulant"[tiab:~2] OR "Glucagon Like Peptide 1 stimulants"[tiab:~2] OR "Glucagon Like Peptide 1 stimulator"[tiab:~2] OR "Glucagon Like Peptide 1 stimulators"[tiab:~2] OR "GLP 1 agonist"[tiab:~2] OR "GLP 1 agonists"[tiab:~2] OR "GLP 1 mimetic"[tiab:~2] OR "GLP 1 mimetics"[tiab:~2] OR "GLP 1 analogue"[tiab:~2] OR "GLP 1 analogues"[tiab:~2] OR "GLP 1 analog"[tiab:~2] OR "GLP 1 analogs"[tiab:~2] OR "GLP 1 stimulating"[tiab:~2] OR "GLP 1 stimulant"[tiab:~2] OR "GLP 1 stimulants"[tiab:~2] OR "GLP 1 stimulator"[tiab:~2] OR "GLP 1 stimulators"[tiab:~2] OR "GLP1 agonist"[tiab:~2] OR "GLP1 agonists"[tiab:~2] OR "GLP1 mimetic"[tiab:~2] OR "GLP1 mimetics"[tiab:~2] OR "GLP1 analogue"[tiab:~2] OR "GLP1 analogues"[tiab:~2] OR "GLP1 analog"[tiab:~2] OR "GLP1 analogs"[tiab:~2] OR "GLP1 stimulating"[tiab:~2] OR "GLP1 stimulant"[tiab:~2] OR "GLP1 stimulants"[tiab:~2] OR "GLP1 stimulator"[tiab:~2] OR "GLP1 stimulators"[tiab:~2] OR "GLPI agonist"[tiab:~2] OR "GLPI agonists"[tiab:~2] OR "GLPI mimetic"[tiab:~2] OR "GLPI mimetics"[tiab:~2] OR "GLPI analogue"[tiab:~2] OR "GLPI analogues"[tiab:~2] OR "GLPI analog"[tiab:~2] OR "GLPI analogs"[tiab:~2] OR "GLPI stimulating"[tiab:~2] OR "GLPI stimulant"[tiab:~2] OR "GLPI stimulants"[tiab:~2] OR "GLPI stimulator"[tiab:~2] OR "GLPI stimulators"[tiab:~2] OR "GLP I agonist"[tiab:~2] OR "GLP I agonists"[tiab:~2] OR "GLP I mimetic"[tiab:~2] OR "GLP I mimetics"[tiab:~2] OR "GLP I analogue"[tiab:~2] OR "GLP I analogues"[tiab:~2] OR "GLP I analog"[tiab:~2] OR "GLP I analogs"[tiab:~2] OR "GLP I stimulating"[tiab:~2] OR "GLP I stimulant"[tiab:~2] OR "GLP I stimulants"[tiab:~2] OR "GLP I stimulator"[tiab:~2] OR "GLP I stimulators"[tiab:~2] OR "Glucagon-Like Peptide-1 Receptor Agonists"[Mesh] OR ("Glucagon-Like Peptide-1 Receptor"[Mesh] AND "1993:2023"[mhda]) OR "Incretin Mimetic"[tiab:~2] OR "Incretin Mimetics"[tiab:~2] OR "Liraglutide"[Mesh] OR "Liraglutid*"[tiab] OR "Saxenda"[tiab] OR "Victoza"[tiab] OR "Exenatide"[Mesh] OR "Exenatid*"[tiab] OR "Ozempic"[tiab] OR "Rybelsus"[tiab] OR "Wegovy"[tiab] OR "Trulicity"[tiab] OR "Bydureon"[tiab] OR "Orlistat"[Mesh] OR "Orlistat"[tiab] OR "Xenical"[tiab] OR "Mysimba"[tiab] OR "dulaglutide" [Supplementary Concept] OR "dulaglutid*"[tiab] OR "semaglutide" [Supplementary Concept] OR "semaglutid*"[tiab] OR "tirzepatide" [Supplementary Concept] OR "tirzepatid*"[tiab] OR "efpeglenatide" [Supplementary Concept] OR "efpeglenatid*"[tiab] OR "rGLP-1 protein" [Supplementary Concept] OR "rGLP-1 protein"[tiab:~0] OR "rGLP-1 proteins"[tiab:~0] OR "bupropion hydrochloride, naltrexone hydrochoride drug combination" [Supplementary Concept] OR "bupropion hydrochloride, naltrexone hydrochoride drug combination"[tiab:~0] OR "lixisenatide" [Supplementary Concept] OR "lixisenatid*"[tiab] AND "Randomized Controlled Trial" [Publication Type] OR "Randomized Controlled Trials as Topic"[Mesh] OR "Randomized Controlled Trials as Topic"[tiab] OR ("random*"[tiab] AND ("trial*"[tiab] OR "stud*"[tiab])) NOT ("conference abstract"[tiab] OR "conference review"[tiab] OR "editorial"[tiab] OR "letter"[tiab] OR "note"[tiab])

1556 results were found on 05/11/2024.

Our Embase search string was composed of the following terms:

'obesity'/de OR 'abdominal obesity'/exp OR 'morbid obesity'/exp OR 'metabolically benign obesity'/exp OR 'obes*':ti,ab,kw AND 'glucagon like peptide 1 receptor agonist'/de OR (('glucagon like peptide 1' OR 'GLP1' OR 'GLP 1' OR 'GLPI' OR 'GLP I') NEAR/3 ('agonist*' OR 'mimetic*' OR 'analog*' OR 'stimula*')):ti,ab,kw OR (('incretin') NEAR/3 ('mimetic*')):ti,ab,kw OR 'liraglutide'/exp OR 'liraglutid*':ti,ab,kw OR 'saxenda':ti,ab,kw OR 'victoza':ti,ab,kw OR 'semaglutide'/exp OR 'semaglutid*':ti,ab,kw OR 'ozempic':ti,ab,kw OR 'rybelsus':ti,ab,kw OR 'wegovy':ti,ab,kw OR 'dulaglutide'/exp OR 'dulaglutide':ti,ab,kw OR 'trulicity':ti,ab,kw OR 'orlistat':ti,ab,kw OR 'orlistat'/exp OR 'xenical':ti,ab,kw OR 'efpeglenatide'/exp OR 'efpeglenatide':ti,ab,kw OR 'mysimba':ti,ab,kw OR 'exendin 4'/exp OR 'exendin 4':ti,ab,kw OR 'exenatide':ti,ab,kw OR 'bydureon':ti,ab,kw OR 'tirzepatide'/exp OR 'tirzepatid*':ti,ab,kw OR 'lixisenatide'/exp OR 'lixisenatid*':ti,ab,kw OR 'albiglutide'/exp OR 'albiglutide':ti,ab,kw AND 'randomized controlled trial'/exp OR 'clinical trial':ti,ab,kw OR [controlled clinical trial]/lim OR [randomized controlled trial]/lim NOT ('conference abstract'/it OR 'conference review'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it)

1097 results were found on 05/11/2024.

Our Cochrane Library search string was composed of the following terms (by utilising the search manager):

#1: [mh ^"Obesity"] OR [mh "Obesity, Abdominal”] OR [mh "Obesity, Metabolically Benign”] OR [mh “Obesity, Morbid”]

#2: (Obes*):ti,ab,kw

#3: #1 OR #2: 59576 results were found on 05/11/2024.

#4: [mh “Glucagon-Like Peptide 1”] OR [mh “Glucagon-Like Peptide-1 Receptor Agonists”] OR [mh "Glucagon-Like Peptide-1 Receptor"] OR [mh "Liraglutide"] OR [mh "Exenatide"] OR [mh "Orlistat"]

#5:(((“Glucagon Like Peptide 1” OR “GLP1” OR “GLP 1” OR “GLPI” OR “GLP I”) NEAR/3 (agonist* OR mimetic* OR analog* OR stimula*)) OR (“Incretin” NEAR/3 Mimetic*) OR liraglutid* OR semaglutid* OR “Saxenda” OR “Victoza” OR tirzepatid* OR lixisenatid* OR efpeglenatid* OR “rGLP-1 protein” OR Exenatid* OR “Ozempic” OR “Rybelsus” OR “Trulicity” OR “wegovy” OR dulaglutid* OR “Bydureon” OR “Orlistat” OR “Mysimba” OR “Xenical” OR “bupropion hydrochloride, naltrexone hydrochoride drug combination”):ti,ab,kw

#6: #4 OR #5: 7460 results were found on 05/11/2024.

#7: #3 AND #6: 2397 results were found on 05/11/2024.

III. Overview of the included articles (evidence table)

	Reviewer	Author, date and country	Study type	Risks of bias	Patient characteristics	Intervention/Index test/Exposure	Comparator	Study length (duration of intervention/follow-up period	Primary outcome	Secondary outcome (most relevant)	Key results: RR, AR, NNT Sens/Spec, LR+/LR- HR, OR Other
1.	SD	Jensen, S.; 2024; Denmark	RCT	Low	*Adults (age 18-65 years) with obesity (BMI 32 - 43 kg/m^2) without diabetes * Male/female ratio: 71/124 (=36.4%/63.6%) * Race of participants: not specified	Liraglutide 3.0 mg/day SC in combination with exercise (n= 49) OR Liraglutide 3.0 mg/day SC alone (n= 49) OR exercise alone (n=48)	Placebo (n= 49)	* Week 0-52: weight maintenance phase (= treatment phase) *Week 52-104: one-year post-treatment phase	*Change in body weight (kg) from randomisation to one year after termination of the weight maintenance intervention (week 0-104)	*Change in body-fat percentage from week 0-104	*Change in body weight (kg): Placebo: 0-104 wk: 7.6 (3.5; 11.7) Exercise: 0-104 wk: 5.4 (2.0; 8.9) Liraglutide: 0-104 wk: 8.7 (5.3; 12.0) Liraglutide + exercise: 0-104 wk: 3.5 (0.0; 7.1) *Change in body-fat percentage: Placebo: 0-104 wk: 0.1 (-1.6; 1.8) Exercise: 0-104 wk: -0.2 (-1.7; 1.2) Liraglutide: 0-104 wk: 1.2 (-0.2; 2.6) Liraglutide + exercise: 0-104 wk: -1.2 (-2.6; 0.3)
2.	SD	Jensen, S.; 2022; Denmark	RCT	High	*Adults (age 18-65 years) with obesity (BMI 32 - 43 kg/m^2) without diabetes * Male/female ratio: 50/80 (=38.5%/61.5%) * Race of participants: not specified	Liraglutide 3.0 mg/day SC in combination with exercise (n= 29) OR Liraglutide 3.0 mg/day SC alone (n=36) OR exercise alone (n=26)	Placebo (n=39)	*Week 0-52: weight maintenance phase (= treatment phase)	*Change in body weight (kg) from week 0-52	*Changes in appetite, eating and sedentary behaviour, and non-exercise physical activity during one-year weight loss maintenance	*Change in body weight (kg): Placebo: 0-52 wk: 6.1 Exercise: 0-52 wk: 0.7 Liraglutide: 0-52 wk: -1.9 Liraglutide + exercise: 0-52 wk: -6.0 * Postprandial overall appetite suppression score was maintained with liraglutide contrasting a reduction in the placebo group (−0.3% vs. −14.0%; P = 0.02) * Placebo group did not show changes in any of the physical activity parameters; however, daily sedentary time was increased by 31 min (P = 0.03) * Liking for high-fat sweet foods was decreased by 16.1% in the liraglutide

											group (P = 0.04). A decrease in implicit wanting for high-fat sweet foods was observed during the initial weight loss, and this was maintained in the liraglutide group but increased in the placebo group (28%; P = 0.01). The liraglutide group also showed decreased explicit liking and implicit wanting for high-fat savoury foods (P < 0.001 for both). Sedentary time and physical activity measures did not change in the liraglutide group.
3.	SD	Kushner, R.; 2020; USA	RCT	High	STEP 1, 3, 4, 5: *Adults (age ≥ 18 years) with obesity (BMI ≥ 30 kg/m^2) or with overweight (BMI ≥ 27 kg/m^2) and at least one weight-related co-morbidity (treated or untreated): dyslipidaemia, obstructive sleep apnoea, hypertension or CVD. But no diabetes. * Male/female ratio: STEP 1: 25.9%/71.1% STEP 3: 19%/81% STEP 4: 20.5%/79.5% STEP 5: 22.4%/77.6% * Race of participants: white (77.2 %), black/Afro-American, Asian, American Indian (22.8%)	STEP 1,4, 5 (n= 1306, n= 535, n= 152): Semaglutide2.4 mg/week SC STEP 3: Semaglutide 2.4 mg/ week SC in combination with IBT and a restrictive diet (n= 407)	Placebo in STEP 1, 3, 4 ,5 (n=655, n= 204, n= 268, n= 152)	*STEP 1 and 3: 68 weeks (week 0-68) weight maintenance phase (= treatment phase) *STEP 4: 48 weeks weight maintenance phase (week 20-68) *STEP 5: 104 weeks (week 0-104) weight maintenance phase (= treatment phase)	*STEP 1,3,4, 5: Percentage change in body weight from baseline at randomization (note that this was from week 20 in STEP 4) to end of treatment (EOT) *STEP 1, 3: Proportion of participants with ≥ 5% WL from baseline to EOT	* STEP 1, 3: Proportion of participants achieving a body weight reduction ≥ 10% or ≥ 15% from baseline to EOT	The results were not yet available at the time of publication of this article
4.	SD	Lean, M.; 2014; UK	RCT	Low	*Adults (age 18-65 years) with obesity (BMI 30 - 40 kg/m^2) and fasting plasma glucose of <7 mmol /L (or	Liraglutide 1.2, 1.8, 2.4 or 3.0 mg/day SC (n= 95,	Placebo (n= 98) or Orlistat120 mg 3x/d (n= 95)	*104 weeks treatment phase	*Side effects e.g. nausea and vomiting	*Weight loss (kg) *Quality of life scores	*In year 1, more participants reported ⩾1 episode of nausea/vomiting on treatment with liraglutide 1.2–3.0 mg (17–38%) than with placebo or orlistat (both 4%, P⩽0.001).

					<126 mg/ dL) at the start of the run-in period. *Male/female ratio: 144/456 (=24%/76%) *Race of participants: not specified	n=90, n=93, n=93)					* Participants on liraglutide 3.0 mg, 48% reported nausea and 13% vomiting. *1-year weight loss on treatment with liraglutide 3.0 mg from randomization was 9.2 kg for participants reporting nausea/vomiting episodes, versus 6.3 kg for those with none (a treatment difference of 2.9 kg (95% confidence interval 0.5–5.3); P=0.02). Both weight losses were significantly greater than the respective weight losses for participants on placebo (a treatment difference of 4.2 kg (2.1–6.4); P=0.0001) and orlistat (a treatment difference of 2.3 kg (0.14–4.4); P=0.04). * QOL scores: no statistically significant differences were observed between individuals on liraglutide 3.0 mg who reported at least one episode of nausea/vomiting over 20 weeks and those who did not
5.	SD	Lundgren, J.; 2021; Denmark	RCT	Low	*Adults (age 18-65 years) with obesity (BMI 32 - 43 kg/m^2) without diabetes *Male/female ratio: 71/124 (=36%/64%) * Race of participants: not specified	Liraglutide 3.0 mg/day SC in combination with exercise (n= 49) OR Liraglutide 3.0 mg/day SC alone (n= 49) OR exercise alone (n= 48)	Placebo (n= 49)	*Week 0-52: weight maintenance phase (= treatment phase)	*Change in body weight (kg)	* Change in body-fat percentage	*Change in body weight (kg), at 52 weeks, in comparison to placebo: Exercise: −4.1 kg (95% confidence interval [CI], −7.8 to −0.4; P=0.03) Liraglutide: −6.8 kg (95% CI, −10.4 to −3.1; P<0.001) Liraglutide + exercise: −9.5 kg (95% CI, −13.1 to −5.9; P<0.001) *Change in body-fat percentage (%) at 52 weeks, in comparison to placebo: Exercise: −2.2 percentage points (95% CI, −3.8 to −0.7; P=0.004) Liraglutide: −2.0 percentage points (95% CI, −3.5 to−0.6) Liraglutide + exercise: −3.9 percentage points (95% CI, −5.4 to −2.5)

6.	SD	Wadden, T.; 2023; USA	RCT	Low	*Adults (age ≥ 18 years) with obesity (BMI ≥ 30 kg/m^2) or with overweight (BMI ≥ 27 kg/m^2) and at least one weight-related co-morbidity (treated or untreated): dyslipidaemia, obstructive sleep apnoea, hypertension or CVD. But no diabetes. And a history of at least one unsuccessful dietary effort to lose body weight. *Male/female ratio: 37.1%/62.9% * Race of participants: white (86%)	Tirzepatide 10 or 15 mg/week SC (n= 287)	Placebo (n= 292)	72 weeks of treatment phase (week 0-72)	*Mean percentage reduction in body weight from randomization to week 72 *Participants achieving ≥5% body weight reduction (in %)	/	* The mean change at week 72 was −18.4% with Tirzepatide and 2.5% with placebo. Tirzepatide was superior to placebo, with an estimated treatment difference relative to placebo of −20.8 percentage points (95% CI −23.2, −18.5; P < 0.001) * 87.5% (251) of participants in the Tirzepatide group lost an additional ≥5% of body weight from randomization to week 72 compared with 16.5% (48) in the placebo group (odds ratio (OR) 34.6 (95% CI 19.2, 62.6); P < 0.001)
7.	SD	Wadden, T.; 2019; USA	RCT	High	*Adults with age ≥ 21 years and ≤ 70 years and with obesity: BMI ≥ 30 and ≤ 55 kg/m² *Male/female ratio: 31/119(=20.7%/79.3%) * Race of participants: white (54%); black (44%); other (2%)	Liraglutide 3.0 mg/day SC in combination with IBT (n= 50) OR Liraglutide 3.0 mg/day SC in combination with IBT and a 1,000- to 1,200-kcal/d meal-replacement diet for 12 weeks (n= 50)	IBT alone (n= 50)	52 weeks of treatment phase (week 0-52)	* Mean percentage reduction in baseline body weight at week 52	*Participants achieving ≥5% body weight reduction (in %)	* At week 52, the IBT-alone, IBT-liraglutide, and Multicomponent groups achieved mean reductions in baseline weight of 6.1 ± 1.3%, 11.5 ± 1.3%, and 11.8 ± 1.3%, respectively. Both liraglutide treated groups lost significantly more weight than IBT-alone. The IBT-liraglutide and Multicomponent interventions did not differ significantly at week 52 but did differ at week 24, when losses were 10.1 ± 0.6% and 12.2 ± 0.6%, respectively. * At week 52, 44% of IBT-alone participants lost ≥ 5% of baseline weight, 26% lost ≥ 10%, and 12% lost ≥ 15%. (The categories are overlapping, such that the 44% who lost ≥ 5% includes those who lost ≥ 10% and ≥ 15%.) Among participants in each of the liraglutide-treated groups, 70% or more lost ≥ 5% of baseline weight, 46% or more

											lost ≥ 10%, and ≥ 28% lost ≥ 15% of baseline weight. The IBT-liraglutide and Multicomponent groups did not differ significantly on any of the categorical losses at week 52 or at week 24.
8.	SD	Aronne, L.; 2024; USA	RCT	Low	*Adults (age ≥ 18 years) with obesity (BMI ≥ 30 kg/m^2) or with overweight (BMI ≥ 27 kg/m^2) and at least one weight-related co-morbidity (treated or untreated): dyslipidaemia, obstructive sleep apnoea, hypertension or CVD. But no diabetes. And a history of at least one unsuccessful dietary effort to lose body weight. *Male/female ratio: 197/473 (=29.4%/70.6%) * Race of participants: white (80.1%); black (11.2%); Asian (7.2%), other (1.5%)	Tirzepatide 10 or 15 mg/week SC (n= 335)	Placebo (n= 335)	88 weeks of treatment phase (week 0-36: all participants received once-weekly subcutaneous maximum tolerated dose (10 or 15 mg) of tirzepatide. Week 36-88: randomization (1:1) to continue receiving tirzepatide or switch to placebo	*Mean percent change in weight from week 36 (randomization) to week 88	*Proportion of participants at week 88 who maintained at least 80% of the weight loss during the lead-in period (in %)	*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 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)
9.	SD	Garvey, W.; 2022; USA	RCT	Low	*Adults (age ≥ 18 years) with obesity (BMI ≥ 30 kg/m^2) or with overweight (BMI ≥ 27 kg/m^2) and at least one weight-related co-morbidity (treated or untreated): dyslipidaemia, obstructive sleep apnoea, hypertension or CVD. But no diabetes. And a history of at least one unsuccessful dietary effort to lose body weight. *Male/female ratio: 22.4%/77.6%	Semaglutide 2.4 mg/week SC (n= 152)	Placebo (n= 152)	* 104 weeks (week 0-104) weight maintenance phase (= treatment phase)	*Percentage change in body weight from baseline to week 104 *Participants achieving ≥5% body weight reduction (in %) at week 104	/	*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)

					* Race of participants: white (93.1 %), black/Afro-American, Asian, American Indian (6.9%)						
10.	SD	Jastreboff, A.; 2022; USA	RCT	Low	*Adults (age ≥ 18 years) with obesity (BMI ≥ 30 kg/m^2) or with overweight (BMI ≥ 27 kg/m^2) and at least one weight-related co-morbidity (treated or untreated): dyslipidaemia, obstructive sleep apnoea, hypertension or CVD. But no diabetes. And a history of at least one unsuccessful dietary effort to lose body weight. *Male/female ratio: 825/1714 (32.5%/67.5%) * Race of participants: white (70.6 %), black/Afro-American, Asian, American Indian (29.4%)	Tirzepatide 5 (n= 630),10 (n= 636) or 15 mg (n= 630) /week SC	Placebo (n= 643)	72 weeks of treatment phase (week 0-72)	*Percentage change in body weight from baseline to week 72 *Participants achieving ≥5% body weight reduction (in %) at week 72	/	* Mean percentage change in weight at week 72 was −15.0% (95% confidence interval [CI], −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) * 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
11.	SD	Kyrillos, J.; 2022; USA	RCT	Low	STEP 1, 3, 4: Adults (age ≥ 18 years) with obesity (BMI ≥ 30 kg/m^2) or with overweight (BMI ≥ 27 kg/m^2) and at least one weight-related co-morbidity (treated or untreated): dyslipidaemia, obstructive sleep apnoea, hypertension or CVD. But no diabetes. And a history of at least one unsuccessful dietary effort to lose body weight.	STEP 1 and 4 (n= 1306, n= 535): Semaglutide 2.4 mg/week SC STEP 3: Semaglutide 2.4 mg/ week SC in combination with IBT and a	Placebo in STEP 1, 3, 4 (n=655, n= 204, n= 268)	*STEP 1 and 3: 68 weeks (week 0-68) weight maintenance phase (= treatment phase) *STEP 4: 48 weeks weight maintenance phase (week 20-68)	*STEP 1,3, 4: Percentage change in body weight from baseline at randomization (note that this was from week 20 in STEP 4) to end of treatment (EOT) *STEP 1, 3: Proportion of participants	* STEP 1, 3: Proportion of participants achieving a body weight reduction ≥ 10% or ≥ 15% from baseline to EOT	* Mean percentage change in body weight from baseline to EOT (Semaglutide vs placebo): STEP 1: -14.9 % vs. -2.4% STEP 3: -16 % vs. -5.7% STEP 4: - 7.9% vs. +6.9% --> (P < .001 for all) * Proportion of participants with ≥ 5% WL from baseline to EOT (Semaglutide vs placebo): STEP 1: 86.4 % vs. 31.5 % STEP 3: 86.6 % vs. 47.6 % --> (P < .001 for all)

					* Male/female ratio: STEP 1: 25.9%/71.1% STEP 3: 19%/81% STEP 4: 20.5%/79.5% * Race of participants: white (77.2 %), black/Afro-American, Asian, American Indian (22.8%)	restrictive diet (n= 407)			with ≥ 5% WL from baseline to EOT		* Proportion of participants with ≥ 10% WL from baseline to EOT (Semaglutide vs placebo): STEP 1: 69.1 % vs. 12% STEP 3: 75.3 % vs. 27 % --> (P < .001 for all) * Proportion of participants with ≥ 15% WL from baseline to EOT (Semaglutide vs placebo): STEP 1: 50.5 % vs. 4.9 % STEP 3: 55.8 % vs. 13.2 % --> (P < .001 for all)
12.	SD	Pi-Sunyer, X.; 2015; UK	RCT	Low	*Adults (age ≥ 18 years) with obesity (BMI ≥ 30 kg/m^2) or with overweight (BMI ≥ 27 kg/m^2) and at least one weight-related co-morbidity (treated or untreated): dyslipidaemia, hypertension. But no diabetes. And a history of at least one unsuccessful dietary effort to lose body weight. *Male/female ratio: 803/2928 (21.5%/78.5%) * Race of participants: white (84.9 %), black/Afro-American, Asian, American Indian (15.1%)	Liraglutide 3.0 mg/day SC (n = 2487)	Placebo (n= 1244)	56 weeks treatment phase (week 0-56), 14 weeks follow-up phase (week 57-70)	*Percentage change in body weight from baseline to week 56 *Participants achieving ≥5% body weight reduction (in %) at week 56 *Participants achieving ≥10% body weight reduction (in %) at week 56	*Change in BMI from baseline * Change in waist circumference from baseline * Health-related quality of life	*Liraglutide group with a mean reduction in body weight of 8.4±7.3 kg vs. the placebo group with a mean of 2.8±6.5 kg (a difference of −5.6 kg; 95% confidence interval, −6.0 to −5.1; P<0.001 *63.2% of the patients in the Liraglutide group vs. 27.1% in the placebo group lost at least 5% of their body weight (P<0.001), and 33.1% and 10.6%, respectively, lost more than 10% of their body weight (P<0.001)
13.	SD	Rubino, D.; 2021; USA	RCT	Low	*Adults (age ≥ 18 years) with obesity (BMI ≥ 30 kg/m^2) or with overweight (BMI ≥ 27 kg/m^2) and at least one weight-related co-morbidity (treated or untreated): dyslipidaemia, obstructive sleep apnoea, hypertension or	Semaglutide 2.4 mg/week SC (n= 535)	Placebo (n= 268)	68 weeks of treatment phase (week 0-20: all participants received once-weekly subcutaneous semaglutide;	* Percent change in body weight from week 20 to week 68	*Physical functioning (SF-36 physical functioning score) *Change in BMI from	*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) * SF-36 physical functioning score in continued Semaglutide group: 1.0 (0.6

					CVD. But no diabetes. And a history of at least one unsuccessful dietary effort to lose body weight. *Male/female ratio: 169/634 (21%/79%) * Race of participants: white (83.6 %), black/Afro-American, Asian, American Indian (16.4%)			week 20-68: randomization (1:1) to continue receiving semaglutide or switch to placebo)		week 20 to week 68 * Change in waist circumference from week 20 to week 68	to 1.4) vs. in switch to placebo group: −1.5 (−2.2 to −0.7) --> (P < .001) * Waist circumference in continued Semaglutide group (difference, −9.7 cm [95% CI, −10.9 to −8.5 cm]; P < .001) and BMI (difference, −4.7 [95% CI, −5.2 to −4.3])
14.	SD	Ryan, D.; 2024; USA	RCT	Low	*Adults with age ≥ 45 years with BMI ≥ 27 kg/m^2 and who have established cardiovascular (CV) disease as evidenced by at least one of the following: prior myocardial infarction; prior stroke (ischemic or haemorrhagic stroke); or symptomatic peripheral arterial disease (PAD) *Male/female ratio: 72.3%/27.7% * Participants from 41 different countries	Semaglutide 2.4 mg/week SC (n= 8821)	Placebo (n= 8783)	208 weeks of treatment phase (week 0-208)	*Percentage change in mean body weight from baseline through week 208	*Change in BMI from week 0 to week 104 * Change in waist circumference from week 0 to week 104	* Change in body weight at week 208 in Semaglutide group −10.2% vs placebo group −1.5% ; treatment difference −8.7%; 95% CI −9.42 to −7.88; P < 0.0001)
15.	SD	Wharton, S.; 2023; USA	RCT	High	*Adults (age ≥ 18 years) with obesity (BMI ≥ 30 kg/m^2) or with overweight (BMI ≥ 27 kg/m^2) and at least one weight-related co-morbidity (treated or untreated): dyslipidaemia, obstructive sleep apnoea, hypertension or CVD. But no diabetes. *Male/female ratio: 22.4%/77.6%	Semaglutide 2.4 mg/week SC (n= 152)	Placebo (n= 152)	* 104 weeks (week 0-104) weight maintenance phase (= treatment phase)	*Percentage change in body weight from baseline to week 104 * Achievement of body weight reduction of ≥5% from baseline to week 104	*Participant-reported control of eating using the CoEQ (= exploratory end point in a subset of trial participants)	* Change in body weight from baseline to week 104 was −14.8% with semaglutide 2.4 mg and −2.4% with placebo (estimated treatment difference, −12.4 percentage points; 95% CI: −16.2 to −8.5; p < 0.0001) * Weight loss of ≥5% from baseline to week 104 in Semaglutide group 74.7% vs. Placebo group 33.3% (p < 0.0001)

					* Race of participants: white (93.1 %), black/Afro-American, Asian, American Indian (6.9%)						
16.	ACC	Bjorner, J. B.; 2023; Denmark	RCT	Low	*Adults (age ≥ 18 years) with obesity (BMI ≥ 30 kg/m^2) or with overweight (BMI ≥ 27 kg/m^2) and at least one weight-related co-morbidity STEP2 trial also DM2; STEP1; 3-4: no DM2 *Male/female ratio: STEP1: 74.1% female STEP2: 51.2% female STEP3: 81% female STEP4: 79% female *Race of participants: STEP1: 75.1% white STEP2: 59.4% white STEP3: 76.1% white STEP4: 83.7% white	Semaglutide 2.4mg SC/week + lifestyle intervention STEP1: 1961 participants were randomized 2:1 to SC semaglutide 2.4 mg or placebo STEP2: 1210 participants were randomized 1:1:1 to SC semaglutide 2.4 mg, SC semaglutide 1.0 mg or placebo STEP3: 611 participants were randomized 2:1 to SC semaglutide 2.4 mg or placebo. STEP4: 902 participants received open-label,	Placebo	*68 weeks * STEP 4 trial: 20w run in period	Change in body weight; Improved health utility (SF-6Dv2 and EQ-5D-3L)	Proportion of participants achieving a reduction in body weight of 10% or more, or 15% or more at week 68 (except for STEP 4); and change from baseline to week 68 in waist circumference, systolic blood pressure and PRO assessments, including the SF 36v2 physical functioning score	SF-6Dv2: STEP 1(ETD: 0.029; 95% CI: 0.012, 0.046) and STEP 4 (ETD: 0.045; 95% CI: 0.025, 0.066), no significance in STEP 2 (ETD: 0.021; 95% CI: -0.002, 0.044) or STEP 3 (ETD: 0.013; 95% CI: -0.014, 0.041) EQ-5D-3L: STEP 1 (ETD: 0.029; 95% CI: 0.018, 0.039), STEP 2 (ETD: 0.023; 95% CI: 0.010, 0.037) and STEP 4 (ETD: 0.034; 95% CI: 0.024, 0.044), but did not reach significance in STEP 3 (ETD: 0.015; 95% CI: -0.001, 0.032) estimated mean weight changes from randomization to week 68 with semaglutide2.4 mg (vs. placebo) for the trial product estimand were (STEP1-4) -16.9% (-2.4%), -10.6% (-3.1%), -17.6% (-5.0%) and -8.8% (6.5%), respectively.

						once-weekly SC semaglutide during a 20-week run-in period that included a 16-week dose escalation period and 4 weeks on the target semaglutide dose of 2.4 mg. After the run-in period, 803 participants were randomized (2:1) to continued semaglutide 2.4 mg or switched to placebo, for a further 48 weeks.					
17.	ACC	Lundkvist, P.; 2017; Sweden	RCT	Some concerns	*Participants were obese (body mass index [BMI], 30-45 kg/m^2), were aged 18 to 70 years and did not have diabetes *Male/female ratio: 60% female *Race of participants: not specified	Oral dapagliflozin 10 mg once daily (DAPA) and subcutaneous exenatide 2 mg once weekly	Placebo (n=25; completed: 17)	*52weeks (investigator-initiated 24-week, followed by an optional 28-week open-label phase)	Change and percent change in body weight (kg)	Proportions of participants achieving ≥5% and ≥10% body weight loss; changes in waist circumferenc	DAPA + ExQW; 0-24w: − 4.48kg (−6.09, −2.88), 24-52w: −1.21kg (−3.19, 0.78), 0-52w: −5.69kg (−8.63, −2.75) Placebo followed by DAPA+ExQW; 0-24w: −0.34kg (−2.02, 1.33), 24-52w: −3.80kg (−5.85, −1.75), 0-52w: −4.15kg (−7.19, −1.10

						(ExQW) (n=25; completed: 16)				e and waist-to-hip ratio; MRI assessed changes (continued DAPA + ExQW group only) in total adipose and lean tissue volumes, abdominal visceral and subcutaneous adipose tissue volumes, and liver fat percent; changes in HbA1c and fasting plasma glucose; changes OGTT-derived measures (continued DAPA + ExQWgroup only), including 2-hour plasma glucose, proportions with impaired fasting glucose, or impaired glucose	

											tolerance (IGT); changes in seated systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate; and changes in fasting Serum lipids.	
18.	ACC	Rubino, D.; 2024; USA	RCT	Low	*Adults with ≥1 self-reported unsuccessfuldietary attempt to loseweight. In STEP 1, 3 and4, participants had overweight (body mass index [BMI] ≥27 and <30 kg/m^2) with ≥1 treated or untreated weight-related comorbidity, or obesity (BMI ≥30 kg/m^2); no participants had type 2 diabetes. In STEP 2, participants had a BMI of ≥27 kg/m^2 and type 2-diabetes (T2D). *Male/female ratio: STEP1: 74.1% female STEP2: 51.2% female STEP3: 81% female STEP4: 79% female *Race of patients: STEP1: 75.1% white STEP2: 59.4% white STEP3: 76.1% white STEP4: 83.7% white	Semaglutide 2.4mg SC/w (n=2652)	Placebo (n=1530)	*68 weeks (see above)	Change in IWQOL-Lite-CT Physical Function scores and SF-36v2 Physical Functioning scores	See above	IWQOL-Lite-CT Physical Function scores (≥14.6 points) from baseline to Week 68 in STEP 1 with semaglutide 2.4 mg (51.8%) versus placebo (28.3%; p <0.0001) and with semaglutide 2.4 mg versus placebo in STEP 2 (p = 0.0083) Reaching MWPC threshold for SF-36v2 Physical Functioning scores (≥3.7 points): STEP 1; 2 and 4

19.	ACC	Rasmus, M. Sandsdal; 2023; Denmark	RCT	Low	*18–65 years of age, BMI 32–43 kg/m^2 *Male/female ratio: 64% female *Race of participants: not specified	Liraglutide 3.0mg/d + exercise (n=49); Liraglutide 3.0mg/d (n=49)	Exercise (n=48); Placebo(n =49)	*8+ 52weeks	Weight loss	Prespecified secondary outcome = primary outcome of this study: Metabolic syndrome severity z-score (MetS-Z), abdominal obesity and inflammation marker high sensitivity C-reactive protein (hsCRP)	After 1 year: MetS-Z was unchanged in the placebo and exercise groups; MetS-Z decreased by 0.37, P < 0.001, in the liraglutide group and by0.48, P < 0.001, in the combination group After 1 year: android and gynoid fat percentages were unchanged in the placebo group; the exercise group decreased android fat percentage by 2.6%-points, P = 0.022, and the liraglutide group decreased android fat percentage by 2.8%-points, P = 0.006; combination group decreased android fat percentage by 6.1%-points (P < 0.001) HsCRP decreased only in the combination group compared with placebo (by 43%, P = 0.03).
20.	ACC	Kahn, S.; 2024	RCT	Low	*Age >45 years and overweight or obesity and established CVD *Male/female ratio: 72.3% male *Race of participants: 84% white	Semaglutide 2.4mg SC/w (n=8803)	Placebo (n=8801)	* 152 ± 56 weeks and follow-up 176 ± 40 weeks	HbA1c and proportions achieving biochemical normoglycemia (HbA1c <5.7%) and progressing to biochemical diabetes (HbA1c<6.5%).	Weight loss	HbA1c increased similarly in both arms, with a mean difference of 20.32 percentage points (95% CI20.33 to20.30;23.49 mmol/mol [23.66 to23.32]) and with the difference favouring semaglutide throughout the study (P < 0.0001). Body weight plateaued at 65 weeks and was 8.9% lower with semaglutide. At week 156, a greater proportion treated with semaglutide were normoglycemic (69.5% vs. 35.8%; P < 0.0001) and a smaller proportion had biochemical diabetes by week 156 (1.5% vs. 6.9%; P < 0.0001).
21.	ED	Hany, M.; 2024; Egypt	RCT	High	* Patients aged between 18 and 60 years, and insufficient weight loss (IWL) or weight	Liraglutide 3.0mg/day SC (n=38)	Placebo (n=31)	* Month 0-6: treatment phase	Weight loss benefit after cRYGB:	/	Liraglutide group experienced better WL with a significantly higher mean %TWL at 1 month (10.27 ± 1.39 vs.

					regain (WR) after previous long sleeve gastrectomy (LSG) as indications for conversional Roux-en-Y Gastric Bypass (cRYGB). IWL was defined as excess weight loss (%EWL) of less than 50% through 18 months after LSG, WR was defined as a reported weight increase after achieving greater than 50% of % EWL. *Male/female ratio: 20/49 (=29%/71%) *Race of participants: no information available			*Month 6-12: post-treatment follow-up phase	weight loss measured by total weight loss (%TWL) and excess weight loss (%EWL)		8.41 ± 2.08), at 6 weeks (12.65 ± 1.77 vs. 10.47 ± 2.23), at 6 months (18.29 ± 1.74 vs. 15.58 ± 1.65), and at 12 months 24.15 ± 2.35 versus 22.70 ± 2.13 (all P < 0.001). For % EWL, this was also significantly higher in the liraglutide group at all time points. A %TWL of greater than 20% at 6 months of treatment was recorded in six (15.8%) patients in the liraglutide group and none in the placebo group (P = 0.029).
22.	ED	McGowan, B.; 2024; UK *STEP 10*	RCT	Low	*Participants aged 18 years or older with a BMI of 30 kg/m² or higher and prediabetes according to UK National Institute for Health and Care Excellence criteria (defined as having at least one of the following at screening: HbA1c of 6·0–6·4% [42–47 mmol/mol] or fasting plasma glucose [FPG] of 5·5–6·9 mmol/L). *Male/female ratio: 60/147 (=29%/71%) *Race of participants: 88% White, 4% Asian, 4% Black or African American, <1% American Indian or Alaska Native, 2% other	Semaglutide 2.4mg/week SC (n=138), with diet and physical activity counselling	Placebo (n=69), with diet and physical activity counselling	*Week 0-52: treatment-phase *Week 52-80: post-treatment follow-up phase	Percentage change in body weight and proportion of participants reverting to normoglycaemia (HbA1c <6·0% [<42 mmol/mol] and FPG <5·5 mmol/L) at week 52	Proportion of participants at week 52 who had a weight loss of at least5%, at least 10%, at least15%, and at least20%	There was a significantly greater reduction in body weight with semaglutide2·4 mg than with placebo at week 52 (–13·9% [SD 0·7] vs –2·7% [0·6]; estimated treatment difference –11·2% [95% CI –13·0 to –9·4]; p<0·0001). Greater proportions of participants reverted to normoglycaemia at week 52 with semaglutide 2·4 mg than with placebo (103 [81%] of 127 vs nine [14%] of 64; odds ratio 19·8 [95% CI 8·7 to 45·2]; p<0·0001).
23.	ED	O'Neil, P.; 2018; USA	RCT	Some	*Adults who were 18 years or older without diabetes, and with a body-mass index (BMI) of 30	Semaglutide SC once a	Liraglutide 3.0mg/day SC	*Week 0-52: treatment-phase	Relative percentage change in	Categorical weight loss of 5% or	Estimated mean weight loss was –2·3% for the placebo group versus –6·0% (0·05 mg), –8·6% (0·1 mg), –

				concerns	kg/m^2 or more that was not of endocrine aetiology (e.g., Cushing's syndrome). *Male/female ratio: 338/619 (=35%/65%) *Race of participants: 73% White, 6% Black or African American, 3% other, 18% not applicable	day [0.05 mg, 0.1 mg, 0.2 mg, 0.3 mg, 0,3mg FE, 0.4 mg or 0.4mg FE] (resp. n=103, n-102, n=103, n=103, n=102, n=102, n=103), with dietary and physical activity counselling	(n=103) or placebo (n=136), with dietary and physical activity counselling	*Week 52-59: post-treatment follow-up phase	bodyweight from baseline to week 52	more or 10% or more from baseline	11·6% (0·2 mg), –11·2% (0·3 mg), and –13·8% (0·4 mg) for the semaglutide groups. All semaglutide groups versus placebo were significant (unadjusted p≤0·0010) and remained significant after adjustment for multiple testing (p≤0·0055). Mean bodyweight reductions for 0·2 mg or more of semaglutide versus liraglutide were all significant (–13·8% to –11·2% vs –7·8%). Estimated weight loss of 10% or more occurred in 10% of participants receiving placebo compared with 37–65% receiving 0·1 mg or more of semaglutide (p<0·0001 vs placebo).
24.	ED	Wadden, T.; 2020; USA *SCALE-IBT*	RCT	High	*Patients aged ≥18 years, with stable body weight (maximum 5-kg self-reported weight change within 90 days before screening) and BMI ≥ 30 kg/m^2, without diabetes *Male/female ratio: 47/235 (=16,7%/83,3%) *Race of participants: 82% White, 16% Black, 2% Asian	Liraglutide 3.0mg/day SC (+IBT = intensive behavioural therapy) (n=142)	Placebo (+IBT) (n=140)	*Week 0-56: treatment phase *Week 56-60: post-treatment follow-up phase	Change in body weight (percent) from baseline to week 56 and the proportion of participants who lost ≥5% of baseline body weight	The proportion of participants who lost >10% or >15% of baseline body weight at week 56 and the proportion who lost ≥4% of baseline body weight at week 16	At week 56, mean weight loss with liraglutide 3.0 mg plus IBT was 7.5% and 4.0% with placebo combined with IBT (estimated treatment difference [95% CI] –3.4% [–5.3% to –1.6%], P=0.0003). Significantly more individuals on liraglutide 3.0 mg than placebo achieved ≥5% weight loss (61.5% vs. 38.8%; odds ratio [OR] 2.5% [1.5% to 4.1%], P=0.0003), >10% weight loss (30.5% vs. 19.8%; OR 1.8% [1.0% to 3.1%], P=0.0469), and >15% weight loss (18.1% vs. 8.9%; OR 2.3% [1.1% to 4.7%], P=0.0311).
25.	ED	Knop, F.; 2023; Denmark *OASIS 1*	RCT	Low	*Adults (aged 18 years or older) with a BMI of at least 30 kg/m^2, or at least 27 kg/m² with one or more bodyweight-relatedcomplications or comorbidities (hypertension, dyslipidaemia, obstructive sleep apnoea,	Semaglutide 50mg/day PO (n=334), plus lifestyle intervention	Placebo (n=333), plus lifestyle intervention	*Week 0-68: treatment phase *Week 68-75: post-treatment follow-up phase	Percentage change in bodyweight from baseline to week 68 and whether participants reached a	Whether participants reached at least 10%, 15%, and 20% bodyweight reduction	The estimated mean bodyweight change from baseline to week 68 was –15·1% (SE 0·5) with oral semaglutide 50 mg versus –2·4% (0·5) with placebo (estimated treatment difference −12·7 percentage points, 95% CI −14·2 to −11·3; p<0·0001). More participants reached bodyweight reductions of at least 5% (269 [85%] of

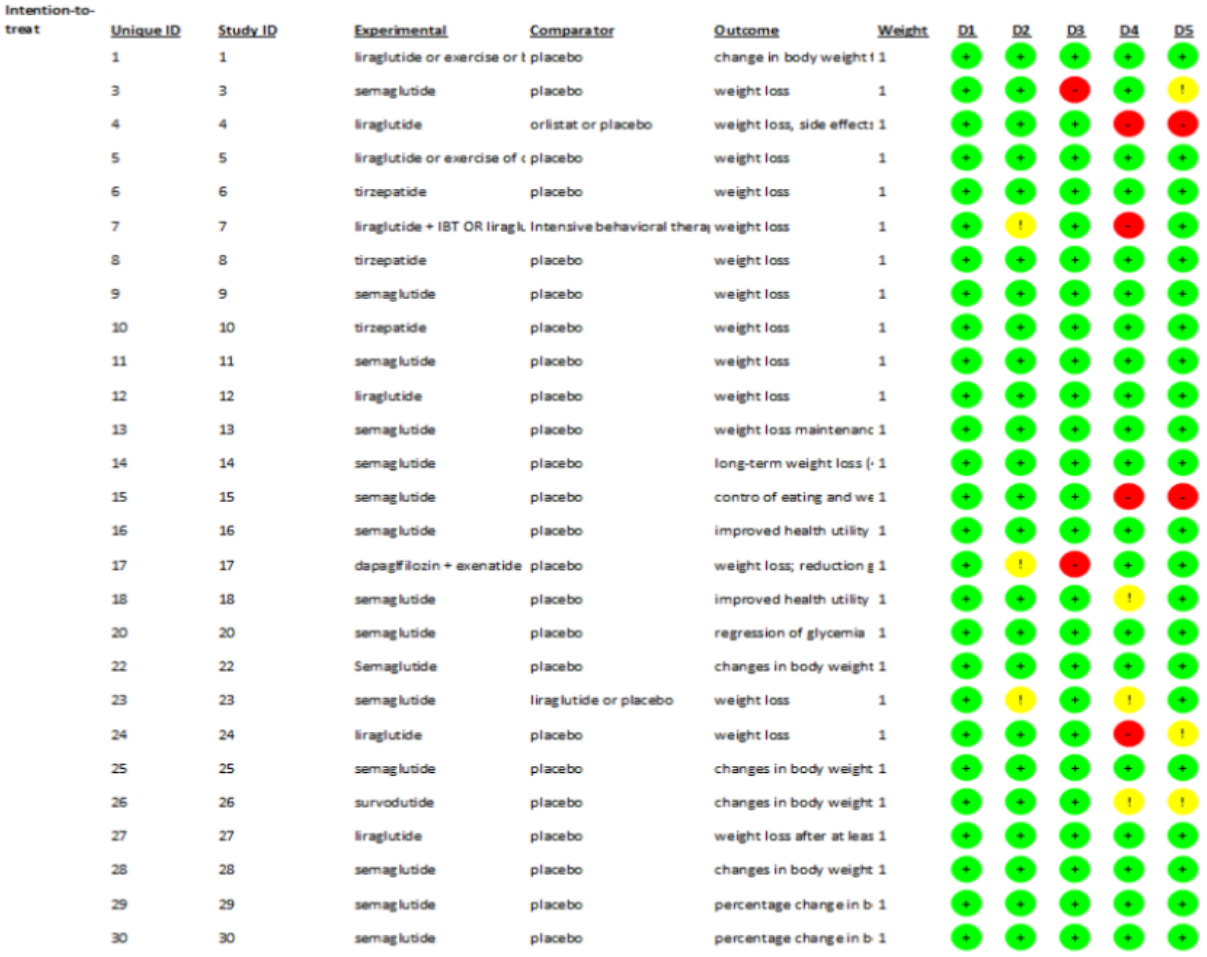
					or cardiovascular disease), without type 2 diabetes. *Male/female ratio: 182/485 (=27%/73%) *Race of participants: 74% White, 11% Asian, 6% Black or African American, 9% other				bodyweight reduction of at least 5% at week 68	from baseline at week 68	317 vs 76 [26%] of 295; odds ratio [OR] 12·6, 95% CI 8·5 to 18·7; p<0·0001), 10% (220 [69%] vs 35 [12%]; OR 14·7, 9·6 to 22·6), 15% (170 [54%] vs 17 [6%]; OR 17·9, 10·4 to 30·7), and 20% (107 [34%] vs 8 [3%]; OR 18·5, 8·8 to 38·9) at week 68 with oral semaglutide 50 mg versus placebo.
26.	ED	Le Roux, C.; 2024; Ireland	RCT	Some concerns	*Adults (aged ≥18 to <75 years) with a BMI of 27 kg/m² or greater, a stable bodyweight of 70 kg or greater (females) or 80 kg or greater (males), and with HbA1c less than 6·5% (without diabetes) at screening. *Male/female ratio: 122/262 (=32%/68%) *Race of participants: 78% White, 10% Asian, 10% Black or African American, 1% multiple, 1% Native Hawaiian or Pacific Islander, <1% American Indian or Alaska Native	Survodutide SC once a week (0.6mg, 2.4mg, 3.6mg or 4.8mg) (resp. n=77, n=78, n=76, n=76), with dietary and physical activity counselling	Placebo (n=77), with dietary and physical activity counselling	*Week 0-46: treatment phase *Week 46-49: post-treatment follow-up phase	Percentage change in bodyweight from baseline to week 46	The achievement of bodyweight reductions of 5% or greater, 10% or greater, and 15% or greater at week 46	Mean (95% CI) changes in bodyweight from baseline to week 46 were −6·2% (−8·3 to −4·1; 0·6 mg); −12·5% (−14·5 to −10·5; 2·4 mg); −13·2% (−15·3 to −11·2; 3·6 mg); −14·9% (−16·9 to −13·0; 4·8 mg); −2·8% (−4·9 to −0·7; placebo)
27.	ED	Lofton, H.; 2024; USA	RCT	Low	*Subjects (at least 18 years of age) 18-120 months post-RYGB, who achieved at least 25% total body weight loss (TBWL) status-post-RYGB and regained at least 10 % TBWL after reaching nadir weight (NW). Without diabetes *Male/female ratio: 19/113 (=14,4%/85,6%)	Liraglutide 3.0mg/day SC (n=89), with lifestyle counselling	Placebo (n=43), with lifestyle counselling	*Week 0-56: treatment phase	Proportion of subjects losing at least 5%, 10%, 15% and 20% TBWL after56 weeks, and achieving weight lower than their nadir weight (NW)	/	The change in %TBWL from baseline to 56-weeks was -8.8 (8.5, 229.2 to 9.7) and 1.1 (3.5, 27.9 to 5.99) in the liraglutide and placebo groups, respectively. 76% and 17% of subjects achieved 5% TBWL at 56 weeks in the liraglutide and placebo groups, respectively; 51% and 26.0% of the liraglutide group achieved 10% and 15 % TBWL, respectively. None of the placebo group lost 10% TBWL. Twenty-one percent of subjects receiving liraglutide surpassed

					*Race of participants: 57,5% White, 26% Black or African American, 1,5% Asian, 2% Native Hawaiian or other Pacific Islander, 3% more than 1 race, 3% unknown/not reported, 7% other						postoperative NW. No subjects on placebo met this goal.
28.	ED	Rubino, D.; 2022; USA *STEP 8*	RCT	Low	*Adults (at least 18 years of age) with body mass index of 30 or greater or 27 or greater with 1 or more weight-related comorbidities (hypertension, dyslipidaemia, obstructive sleep apnoea or cardiovascular disease), without diabetes *Male/female ratio: 73/265 (=21,6%/78,4%) *Race of participants: 74% White, 19% Black or African American, 4% Asian, 3% other	Semaglutide 2.4mg/week SC (n=126) or liraglutide 3.0mg/day SC (n=127), with diet and physical activity	Placebo (n=85), with diet and physical activity	*Week 0-68: treatment phase *Week 68-75: post-treatment follow-up phase	Percentage change from baseline in body weight at week 68, for semaglutide vs liraglutide	Achievement of 10% or more, 15% or more and 20% or more weight loss at week 68, for semaglutide vs liraglutide	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 {95% CI, 3.5 to 19.1}], respectively; all P < .001).
29.	ACC	Wadden, T.; 2021; USA	RCT	Low	*18 years or older, reported 1 or more unsuccessful dietary efforts to lose weight, and had either body mass index (BMI) of 27 or higher with at least 1 weight related comorbidity (cardiovascular disease, dyslipidaemia, hypertension, or obstructive sleep apnoea) or BMI of 30 or higher. Participants were excluded if they had diabetes, glycated haemoglobin levels of 6.5% or more (≥48 mmol/mol), self-reported	Semaglutide 2.4mg SC/w (n=407)	Placebo (n=204)	*68weeks	Percentage change in body weight and the loss of 5% or more of baseline weight by week 68	The proportions of participants achieving weight reductions of at least 10% or 15%, and the change from baseline to week 68 in waist circumference, systolic	At week 68, the estimated mean weight change from baseline was −16.0% with semaglutide vs–5.7% with placebo (difference, −10.3 percentage points [95% CI, −12.0 to −8.6]; P < .001) Semaglutide-treated participants were significantly more likely to have lost at least 5% of baseline body weight at week 68 vs placebo (P < .001 for both estimands), with 86.6% of participants in the semaglutide group vs 47.6% in the placebo group The proportion of participants reporting adverse events was similar in the semaglutide and placebo groups (95.8% and 96.1%, respectively)

					bodyweight change greater than 5kg within 90 days before screening, or prior or planned obesity treatment with surgery or a weight loss device. *Male/female ratio: 81% female *Race of participants: 76.1% white					blood pressure, and physical functioning score assessed by the 36-Item Short Form Health Survey (SF-36)	
30.	ACC	Wilding, J.; 2021; USA (16 countries)	RCT	Low	*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, dyslipidaemia, obstructive sleep apnoea, or cardiovascular disease Without diabetes *Male/female ratio:73.1-76% female *Race of participants: 74.4-76.2% white	Semaglutide 2.4mg SC/w (n=1306)	Placebo (n=655)	*68weeks	The percentage change in body weight and weight reduction of at least 5%	Achievement of a reduction in body weight of 10% or more and 15% or more by week 68 and the change from baseline to week 68 in waist circumference, systolic blood pressure, physical functioning score on the 36-item Short Form Health Survey (SF-36), version 2, and physical function score on the Impact of Weight	The estimated mean weight change at week 68 was −14.9% with 2.4-mg semaglutide, as compared with −2.4% with placebo (estimated treatment difference, −12.4 percentage points; 95% CI, −13.4 to −11.5; P<0.001). Participants who received semaglutide were more likely to lose 5% or more, 10% or more, 15% or more, and 20% or more of baseline body weight at week 68 than those who received placebo (P<0.001 for the 5%, 10%, and 15% thresholds; the 20% threshold was not part of the statistical testing hierarchy) 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 difference, −12.7 kg; 95% CI, −13.7 to −11.7)

										on Quality of Life–Lite Clinical Trials Version (IWQOL-Lite-CT) questionnaire	

IV. Overview of the risk of bias assessment (using Cochrane RoB 2 tool)



Intention-to-treat	Unique ID	Study ID	Experimental	Comparator	Outcome	Weight	D1	D2	D3	D4	D5
	1	1	liraglutide or exercise or t	placebo	change in body weight t	1	+	+	+	+	+
	3	3	semaglutide	placebo	weight loss	1	+	+	-	+	!
	4	4	liraglutide	orlistat or placebo	weight loss, side effects	1	+	+	+	-	-
	5	5	liraglutide or exercise of c	placebo	weight loss	1	+	+	+	+	+
	6	6	tirzepatide	placebo	weight loss	1	+	+	+	+	+
	7	7	liraglutide + IBT OR liragl	Intensive behavioral thera	weight loss	1	+	!	+	-	+
	8	8	tirzepatide	placebo	weight loss	1	+	+	+	+	+
	9	9	semaglutide	placebo	weight loss	1	+	+	+	+	+
	10	10	tirzepatide	placebo	weight loss	1	+	+	+	+	+
	11	11	semaglutide	placebo	weight loss	1	+	+	+	+	+
	12	12	liraglutide	placebo	weight loss	1	+	+	+	+	+
	13	13	semaglutide	placebo	weight loss maintenanc	1	+	+	+	+	+
	14	14	semaglutide	placebo	long-term weight loss (·	1	+	+	+	+	+
	15	15	semaglutide	placebo	contro of eating and we	1	+	+	+	-	-
	16	16	semaglutide	placebo	improved health utility	1	+	+	+	+	+
	17	17	dapagliflozin + exenatide	placebo	weight loss; reduction g	1	+	!	-	+	+
	18	18	semaglutide	placebo	improved health utility	1	+	+	+	!	+
	20	20	semaglutide	placebo	regression of glycemia	1	+	+	+	+	+
	22	22	Semaglutide	placebo	changes in body weight	1	+	+	+	+	+
	23	23	semaglutide	liraglutide or placebo	weight loss	1	+	!	+	!	+
	24	24	liraglutide	placebo	weight loss	1	+	+	+	-	!
	25	25	semaglutide	placebo	changes in body weight	1	+	+	+	+	+
	26	26	survodutide	placebo	changes in body weight	1	+	+	+	!	!
	27	27	liraglutide	placebo	weight loss after at leas	1	+	+	+	+	+
	28	28	semaglutide	placebo	changes in body weight	1	+	+	+	+	+
	29	29	semaglutide	placebo	percentage change in b	1	+	+	+	+	+
	30	30	semaglutide	placebo	percentage change in b	1	+	+	+	+	+

Per-protocol	Unique ID	Study ID	Experimental	Comparator	Outcome	Weight	D1	D2	D3	D4	D5	Overall
	2	2	liraglutide or excercise or	placebo	changes in body weight	1	+	!	+	-	-	-
	19	19	liraglutide	exercise or placebo	metabolic syndrome; a	1	+	!	+	+	!	!
	21	21	liraglutide	placebo	weight loss benefit afte	1	+	!	+	-	!	!

Conflict of Interest

The author reports no conflict of interest.

Financial Disclosure

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Ethical Approval

What is the efficacy of the different agents used for treating obesity in adults (in the non-diabetic population)?

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Faculteit/opleiding:	Faculteit Geneeskunde - Master in de huisartsgeneeskunde
Studiefase:	eerste fase
Academiejaar:	2024-2025
Korte omschrijving / abstract:	Welke indicaties worden er vooropgesteld voor behandeling met Orlistat? Welke indicaties worden er vooropgesteld voor behandeling met glp1-agonist (Ozempic, Rybelsus en Saxenda)? Welke indicaties worden er vooropgesteld voor behandeling met Natrexon en Bupropion (Mysimba)? Hoe verhoudt medicamenteuze aanpak zich met niet-medicamenteuze aanpak? Kunnen we medicatie combineren? Hoe verhoudt medicamenteuze aanpak zich met bariatrische chirurgie?
Gewenste taal van communicatie:	nl
Promotor:	Professor Geert Goderis (u0047213)
Copromotor:	Ine Ine Laurys (u0093805)
Organisatie:	KU Leuven
Dienst:	Academisch Centrum voor Huisartsgeneeskunde
Discipline:	Masterproef
Extra groepsleden:	Elke Dobbelaere elke.dobbelaere@student.kuleuven.be r0675217 Ann-Charlotte Claus anncharlotte.claus@student.kuleuven.be r0714796 Sylvie-Anne Duroo sylvieanne.duroo@student.kuleuven.be r0694061

De verstrekte informatie toont aan dat het onderzoek in het kader van de masterproef een zuivere literatuurstudie betreft en dat er op geen enkele wijze gebruik wordt gemaakt van proefdieren, proefpersonen of menselijk lichaamsmateriaal.

Dit type onderzoek vereist geen goedkeuring van een gemachtigde commissie voor medische ethiek.

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