Appendix 5: rapid review of evidence for obesity management medications

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Contents

Information about weight management services and the availability of weight-related drug treatments in Suffolk and North East Essex

From 23 June 2025, some people living with obesity may be eligible to access Tirzepatide (Mounjaro®) for weight loss purposes in community settings as outlined in NICE guidelines. For patients in Suffolk and north east Essex, this will be enabled via a Specialist Weight Management Service community outreach model, which is one of the nationally approved delivery models. The community outreach service is not open to new referrals yet as existing patients who were already on the waiting list are being prioritised. The ICB is aiming to enable new referrals later this summer. This service, delivered by East Suffolk and North Essex NHS Foundation Trust (ESNEFT), is a core component of ESNEFT's hospital-led service, the Weight Management and Complex Obesity Service (WMCOS).

Priority patients for the outreach service are those who belong in 'Cohort 1' of the NHS England Interim Commissioning Guidance. These are the patients NHS England consider as having the greatest clinical need and, therefore, only patients from this group will be prioritised in the first year. Please see page 7 of the guidance for the list of priority patients in Cohorts 2 and 3.

Please note that your GP or clinician cannot prescribe obesity management medications. Furthermore, no GP in Suffolk and north east Essex can prescribe these medications for overweight and obesity; they can only be prescribed by the specialist service provider, ESNEFT

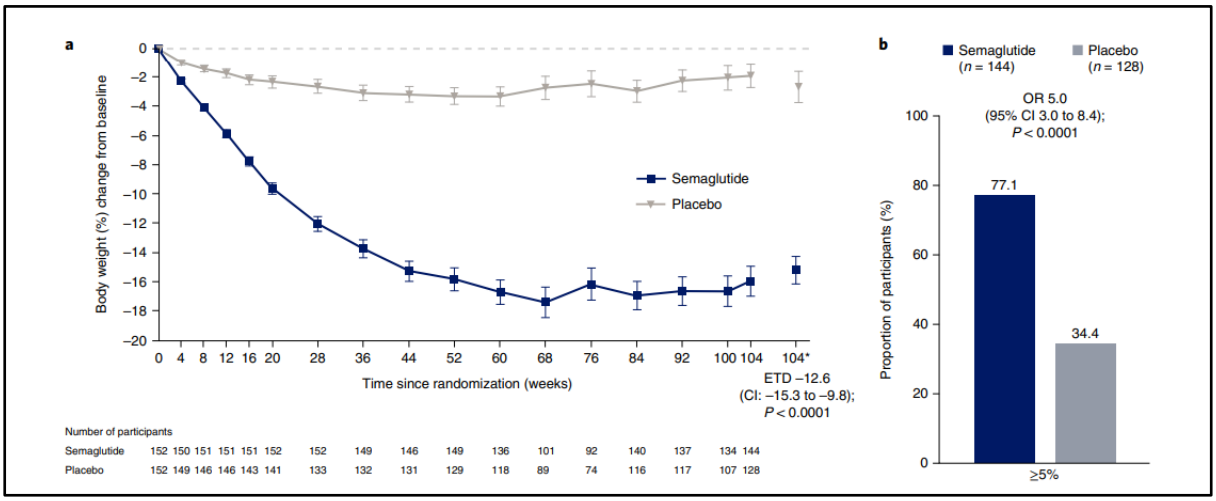
Ozempic (Semaglutide/Wegovy)

In 2023, the obesity management medications Ozempic (also referred to as Semaglutide or Wegovy) was approved for NHS use. NICE has recommended the use of the drug together with a reduced-calorie diet and increased physical activity to adults who have at least 1 weight-related comorbidity and a body mass index (BMI) of at least 35kg/m2. People with an BMI of between 30-34.9 kg/m2, with 1 weight-related comorbidity who are eligible for referral to specialist weight management services could also be prescribed the drug. Semaglutide can only be prescribed for a maximum of two years.

Ozempic, clinically, is known as a GLP-1 agonist. This means that the medication mimics the effects of a hormone that occurs naturally in the body called glucagon-like peptide-1. The medication is administered by a subcutaneous injection, meaning that it comes in a pre-filled pen that patients inject themselves with once a week. Ozempic works on multiple organs, to reduce patients food cravings, gastric emptying and glucagon release and increase patients satiety signals and insulin secretion which helps to reduce appetite and improve blood sugar control, ultimately leading to patient weight loss.

The effects of Ozempic are promising. The STEP 5 trial assessed the efficacy and safety of once-weekly subcutaneous Ozempic administration at 2.4 milligram doses compared to placebo (both with behavioural intervention) for long-term treatment of adults with obesity, or overweight with at least one weight-related comorbidity, without diabetes. What was hypothesised was that after 2 years people who took the dose medication once-weekly would see a percentage change in body weight and achievement of weight loss of 5% or more. Figure 1a shows the mean observed change in body weight over time during the in-trial period. Change in body weight from baseline to week 104 was –15.2% with semaglutide and –2.6% with placebo. Figure 1b shows the observed proportions of participants and odds ratio for achieving weight loss of at least 5% from baselines at week 104 for both groups. Results show that Semaglutide-treated participants, compared with placebo, had five times higher odds of losing at least 5% of baseline body weight at week 104 (OR= 5.0). This suggest that Ozempic was more effective than placebo at helping people achieve meaningful weight loss over a two-year period[1].

Figure 1: Comparison of body weight parameters for Ozempic versus placebo (co-primary endpoints; treatment policy estimand)



Source: Nature medicine

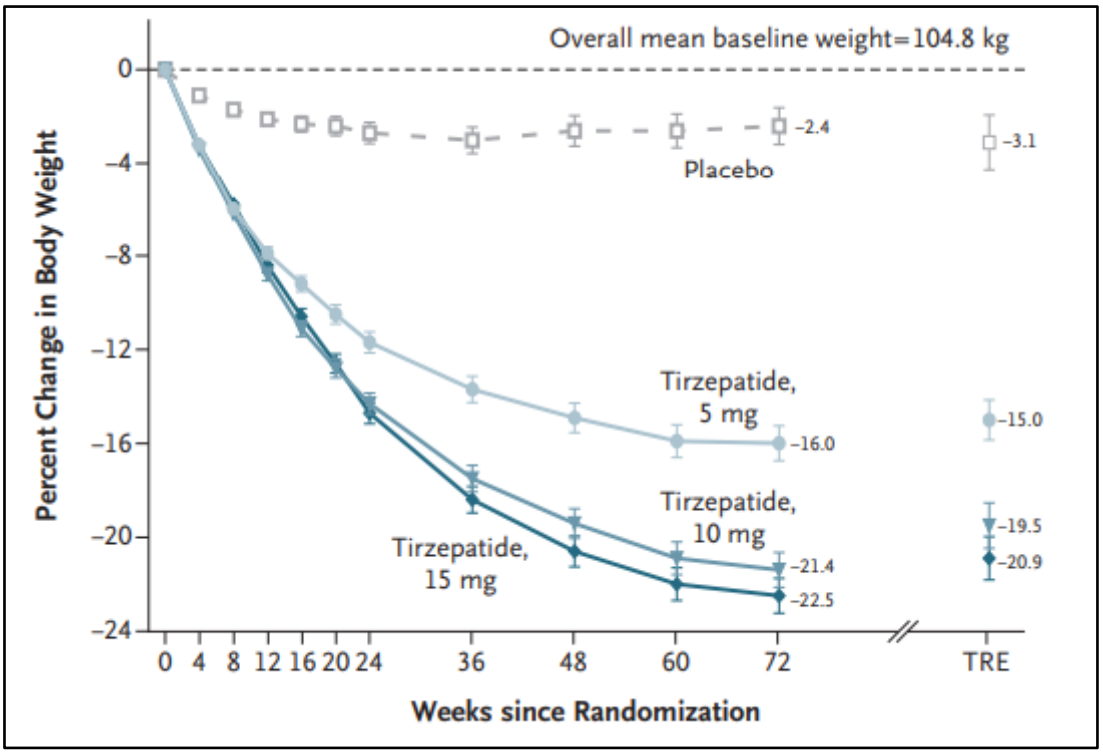
Mounjaro (Tirzepatide)

In 2024, a new obesity management medications Tirzepatide (Mounjaro) was approved for NHS use. NICE has recommended the use of the drug together with a reduced calorie diet and increased physical activity in adults who have at least 1 weight-related medical condition and a body mass index (BMI) of at least 35kg/m2. Mounjaro may be stopped if less than 5% of the starting weight has been lost after 6 months of treatment with the highest dose the person can have with manageable side effects.

Similar to Ozempic, Mounjaro also supports a reduction in appetite and blood sugar control, and the medication is administered by a subcutaneous injection.

A phase 3 double-blinded randomised controlled trial assessed the efficacy and safety of trizepatide, in adults were a BMI of 30 or more, or 27 or more and at least one weight-related complication, excluding diabetes. The study assigned 2,359 adults in a 1:1:1 ratio to receive once-weekly, subcutaneous Tirzepatide (5 mg, 10 mg, or 15 mg) or placebo for 72 weeks, including a 20-week dose-escalation period. Coprimary end points were the percentage change in weight from baseline and a weight reduction of 5% or more. The treatment-regimen estimand assessed effects regardless of treatment discontinuation in the intention-to-treat population. Figure 2 shows the percentage change in body weight by week for participants in Tirzepatide and placebo cohorts. Results show that the mean change in weight at week 72 with Tirzepatide was −16.0%, a weight reduction of 16.1 kg (35.5 lb), with the 5-mg dose; −21.4% a reduction of 22.2 kg (48.9 lb), with the 10-mg dose; and −22.5%, a reduction of 23.6 kg (52.0 lb) with the 15-mg dose, and the mean change with placebo was −2.4%, a reduction of 2.4 kg (5.3 lb). Therefore, in this 72-week trial in participants with obesity, 5 mg, 10 mg, or 15 mg of Tirzepatide once weekly provided substantial and sustained reductions in body weight[3].

Figure 2: Percentage change in body weight by week for Tirzepatide and Placebo

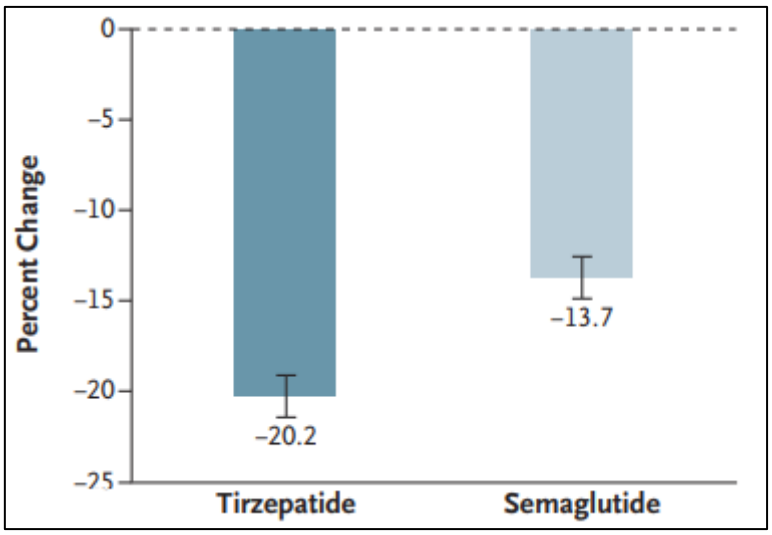


Source: The New England Journal of Medicine

Tirzepatide combines the effect of the GLP-1 agonist used in Ozempic, with GIP- better known as a glucose dependent insulinotropic polypeptide- another naturally occurring hormone which increases insulin sensitivity (also improving blood glucose control) and reduces the secretion of stomach acid, slowing the rate at which food is broken down and digested. Therefore, Mounjaro leads to even greater weight loss as it combines the effects of the GIP and GLP-1 agonist.

This has been confirmed in recently published research. A randomised control trial investigated the efficacy and safety of Tirzepatide as compared with Semaglutide in adults with obesity without type 2 diabetes. A total of 750 participants were randomly assigned in a 1:1 ratio to receive the maximum tolerated dose of Tirzepatide (10 mg or 15 mg) or the maximum tolerated dose of semaglutide (1.7 mg or 2.4 mg) subcutaneously once weekly for 72 weeks. The primary end point was the percent change in weight from baseline to week 72. Results found that the least-squares mean percent change in weight at week 72 was -20.2% with Tirzepatide and -13.7% with semaglutide- shown in figure 3. Participants in the Tirzepatide group were more likely than those in the semaglutide group to have weight reductions of at least 10%, 15%, 20%, and 25%. Overall, among participants with obesity but without diabetes, treatment with Tirzepatide was superior to treatment with semaglutide with respect to reduction in body weight and waist circumference at week 72 [2].

Figure 3: Effect of Trizepatide as compared with Semaglutide on Body weight



Source: The New England Journal of Medicine

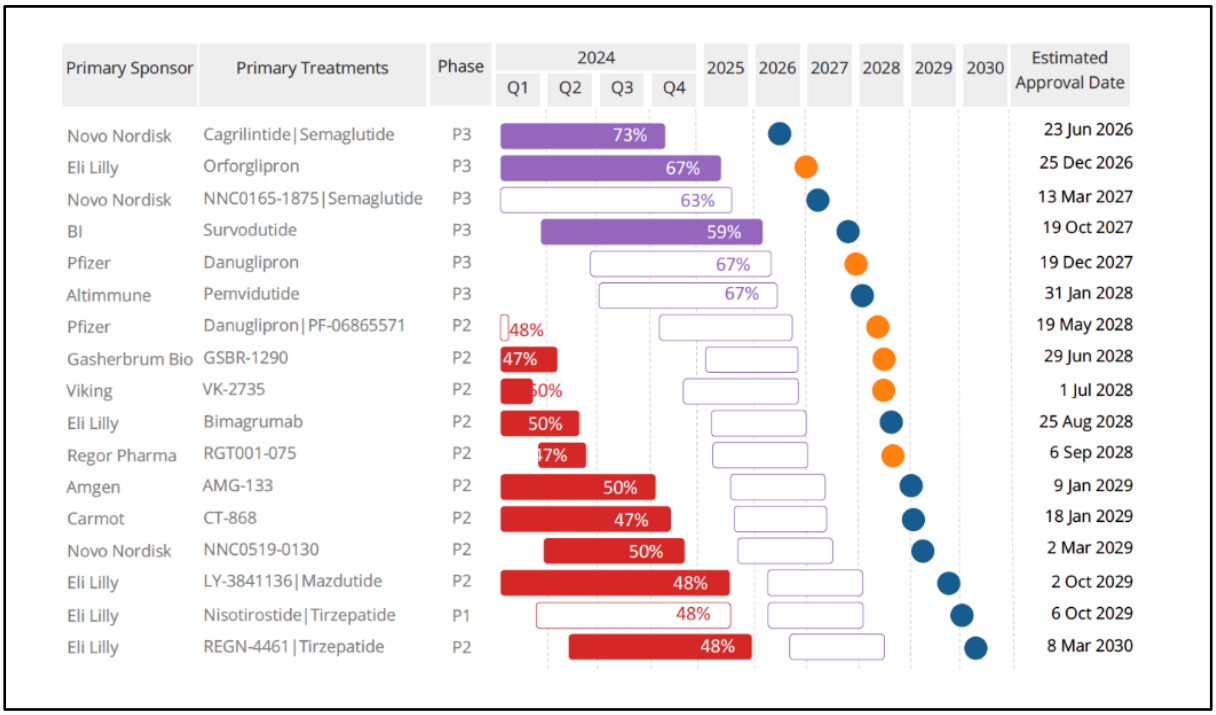
Future of obesity management medicationss

Several companies are developing oral GLP-1 formulations, including Novo Nordisk, Pfizer, and smaller firms. Figure 4 shows the clinical timing, risk, and approval estimates for upcoming GLP-1 U.S. launches. Oral drugs are designated as orange dots and blue designates the injectable treatments. Results show that there may be one to two GLP-1 launches annually starting in 2026, with the first oral entrant expected by 2027. Injectable GLP-1 drugs will continue to be developed, with Novo Nordisk advancing multiple candidates. It is anticipated that there will be around seven actual launches in the US by 2030 after risk-adjustment[4].

Key up-coming medications to note include:

- **Retatrutide:** a triple agonist that targets GLP-1, GIP and glucagon. By adding more hormones, which may show achievements of even greater weight loss[5].
- **Orforglipron:** This is an oral medication rather than an injection. One of the drawbacks of Ozempic and Mounjaro are that they're administered by subcutaneous injection. These are not acceptable to everyone and also need to be refrigerated. Therefore, with similar promising phase 3 trial results this medication is both more acceptable to patients and more feasible from a logistical point of view[6].
- **Bimagrumbab:** This medication supports muscle development. The rapid weight loss achieved by these medications shows that you do not only lose fat, but you also lose lean mass and muscle. Therefore, this medication can support muscle development, mitigating some of those effects and protecting lean and muscle mass[7].

Figure 4: Clinical timing, risk, and approval estimates for upcoming GLP-1 U.S. launches. Oral drugs are designated as orange dots and blue designates the injectable treatments



Source: Ozmosi

Long term sustainability of obesity management medications

Although these obesity management medications are promising and achieve higher weight loss reductions than previously seen, they are not a silver bullet for the obesity epidemic.

These medications are not suitable for everyone. Not everyone wants to take medication, or administrate via subcutaneous injection, and there are several noted side effects, mainly gastrointestinal- such as abdominal bloating, abdominal pain, constipation, diarrhoea, flatulence (gas) or burping, indigestion, and nausea and vomiting. Even though the side effects may not severely endanger participants living with these may be a burden to individuals quality of life[1,3].

The medications are also at a high cost (up to £300 per month). With a large eligible population, there is limited NHS availability to reach every person qualifying for this medication. This may lead to an increased gap in inequality as those who can afford to may wish to pay privately for the medication available[8].

The medications are also not a complete replacement for current healthy weight management initiatives. They require behavioural support to ensure participants[1,3]:

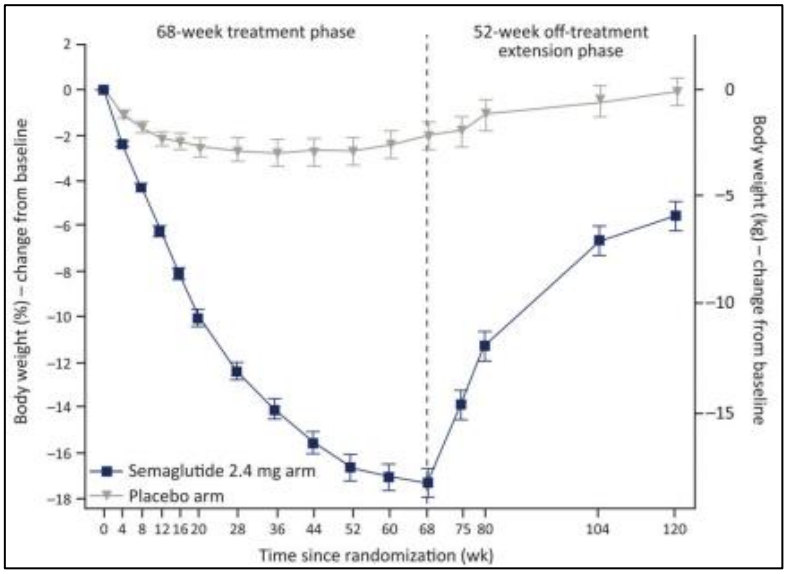
- are attaining adequate nutrition, despite the reduced appetite
- are preserving strength and lean mass
- have the tools to mitigate side effects effectively
- have mental wellbeing support throughout the process

Importantly, when the medications are stopped participants will see weight regain.

Figure 4 shows the change from baseline in body week by weight for participants within the 68-week treatment period and 52-week off-treatment extension phase from the STEP 1 trial extension. Results show that after treatment withdrawal, body weight regain was observed in both the semaglutide and placebo arms. Participants regained a mean of 11.6 percentage points of body weight in the semaglutide arm versus 1.9 percentage points in the placebo arm. However, the net mean body weight loss over the

full duration of the main treatment phase and off-treatment extension phase (from week 0 to week 120) was 5.6% in the semaglutide arm versus 0.1% in the placebo arm, suggesting that utilisation of semaglutide still supports a 5% reduction in body weight 1-year after treatment has stopped[9].

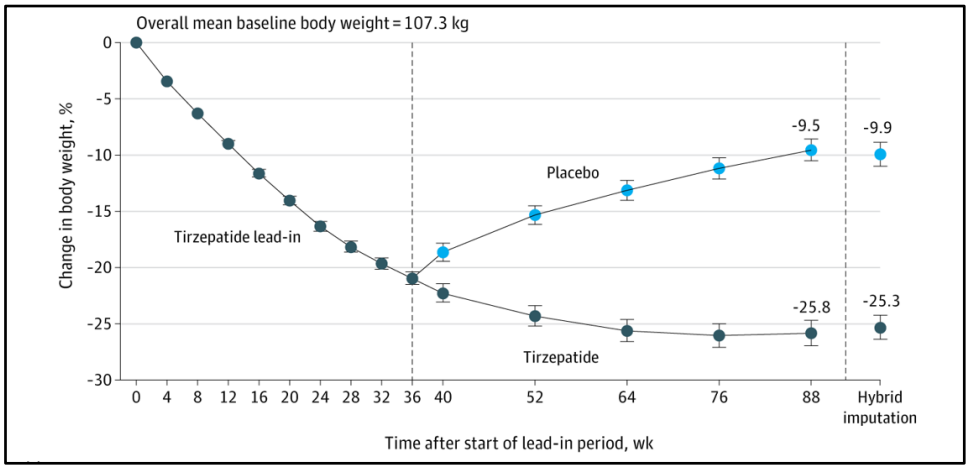
Figure 5: Change from baseline in body weight by week for participants within the 68-week treatment period and 52-week off-treatment extension phase from the STEP 1 trial extension



Source: PubMed

Similarly, in participants with obesity or overweight, withdrawing Tirzepatide led to substantial regain of lost weight, whereas continued treated maintained and augmented initial weight reduction. Figure 5 shows the percentage change in body weight across the 88 week period of a phase 3 randomised withdrawal clinical trial conducted at 70 sites in 4 countries with a 36 week, open-label Tirzepatide lead-in followed by a 52 week, double blind, placebo-controlled period. Results show that the mean percent weight change from week 36 to week 88 was −5.5% with Tirzepatide vs 14.0% with placebo (difference, −19.4%) 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. However, the overall mean weight reduction from week 0 to 88 was 25.3% for Tirzepatide and 9.9% for placebo, suggesting that after 52 weeks participants were still able to reduce their weight by over 5% when not taking the medication[10].

Figure 6: Percentage change in body weight (week 0-88)



Source: JAMA

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