Specialist Weight Management Service

Tirzepatide LCS for General Practitioners

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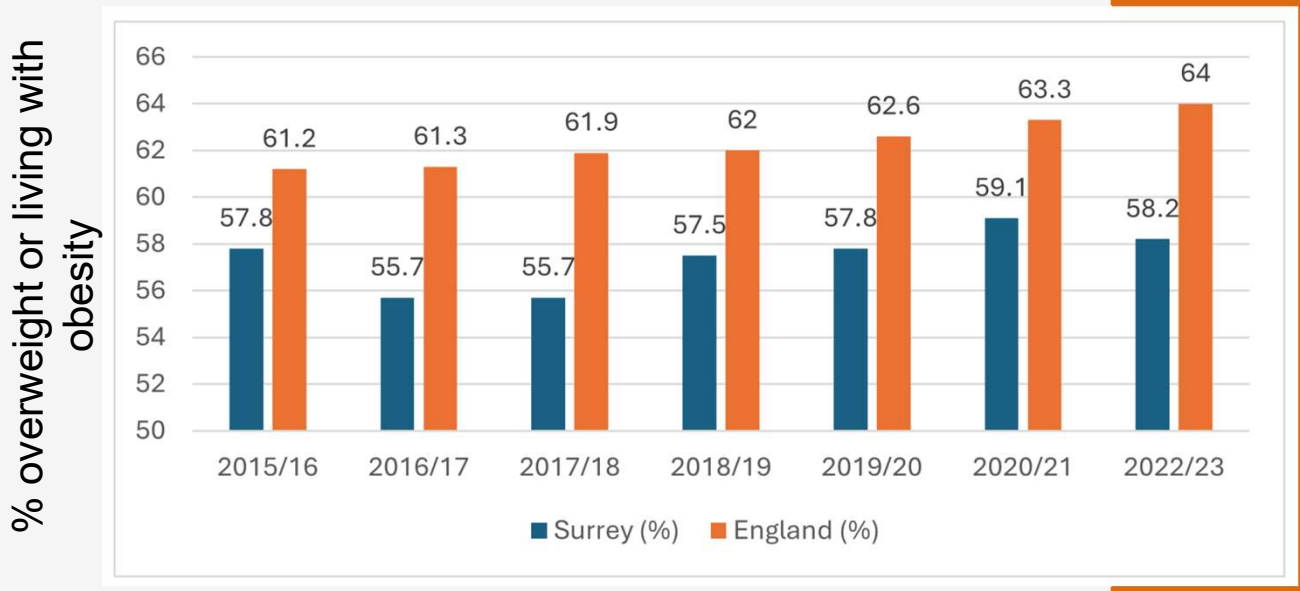
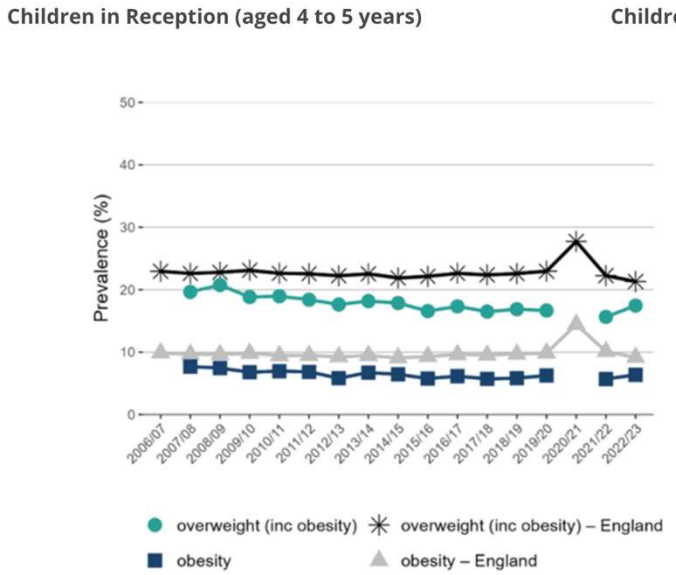
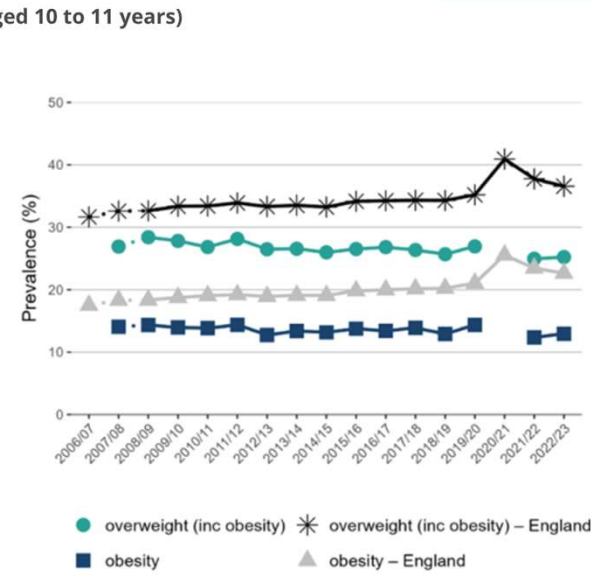
Learning objectives:

- Background on obesity stats for Surrey Heartlands
- How tirzepatide works
- NICE guidance on tirzepatide (Mounjaro) for use in weight loss and the Funding Variation
- Practical guide – dosing, titration, patient support
- Manage Safety and side effects - when to pause, stop or refer and other important considerations
- Assessing suitability for patients meeting tirzepatide eligibility
- Key outcomes from clinical trials – why it is important to consider all options

Obesity Data for Surrey 2023/2024



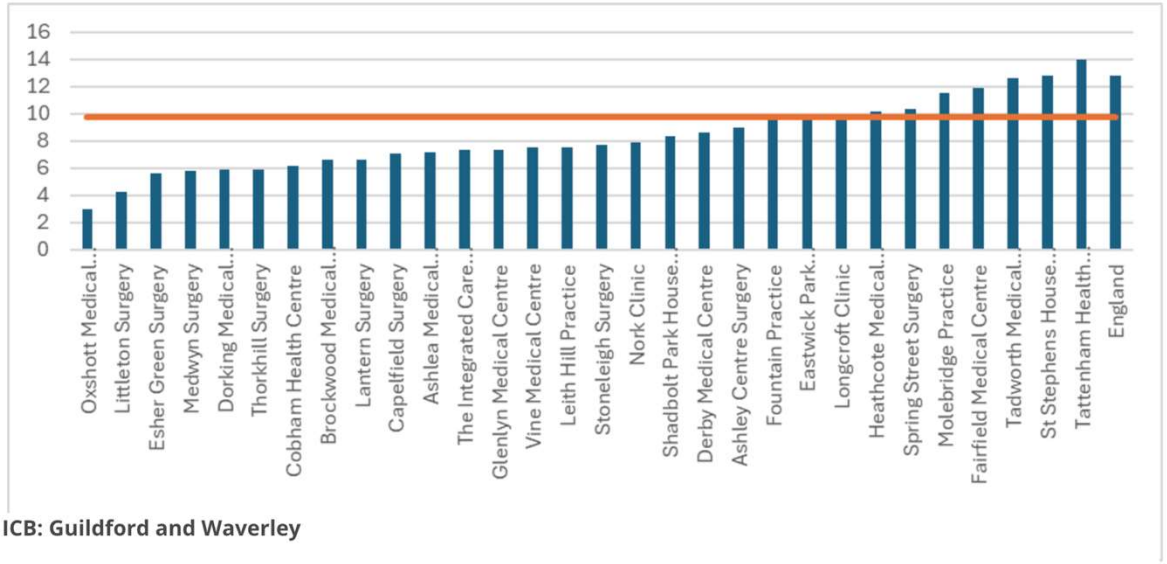




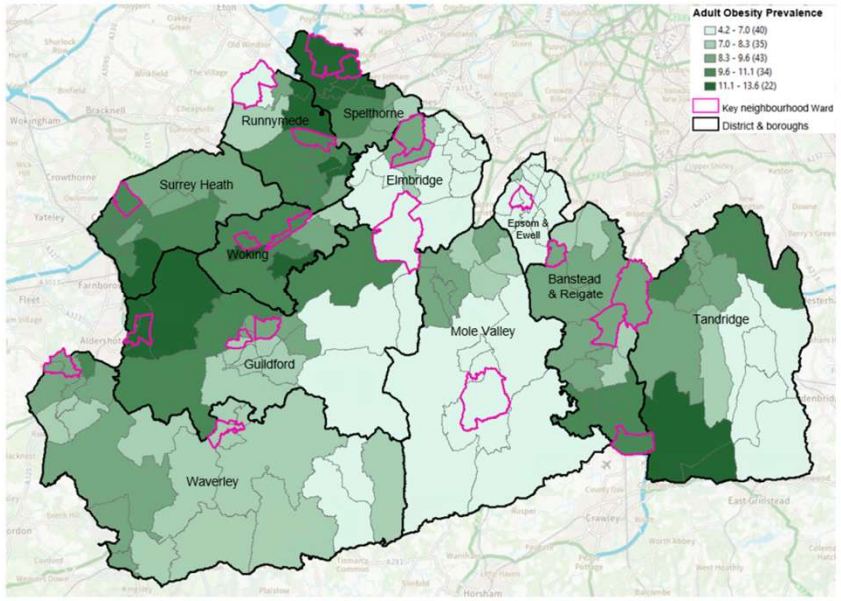
GP practice level data:

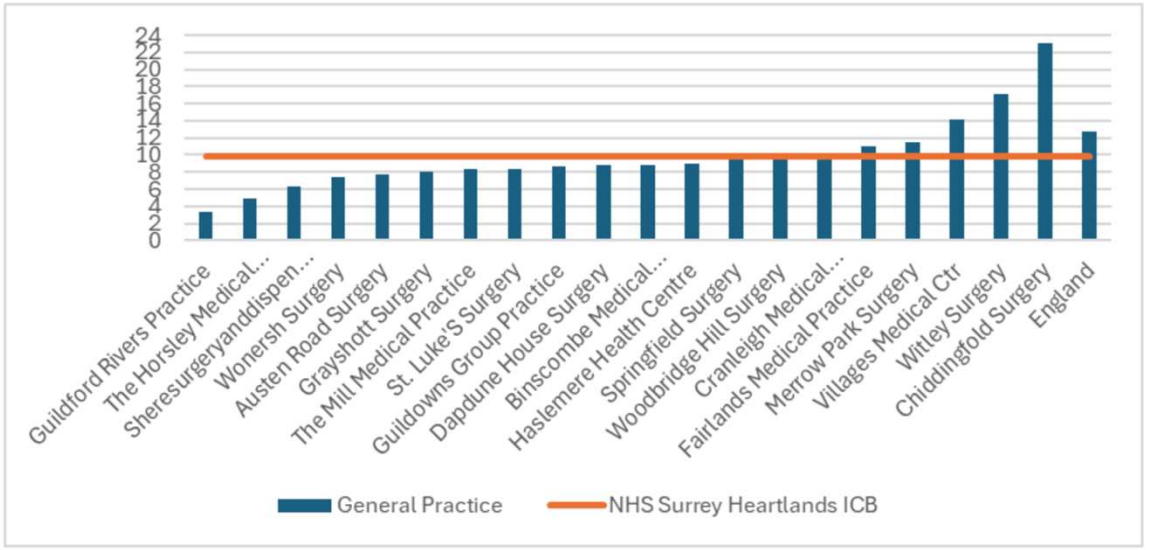
https://www.surreyi.gov.uk/jsna/food-and-health/

Surrey Heartlands ICB: Surrey Downs



Surrey Heartlands ICB: Guildford and Waverley





Type 2 DM
90% of type 2 DM have BMI >23 kg/m2

Hypertension
66% of cases linked to excess weight

Dyslipidaemia
progressive increase above BMI of 21 kg/m2

Liver and gallbladder disease
40% NASH patients are obese

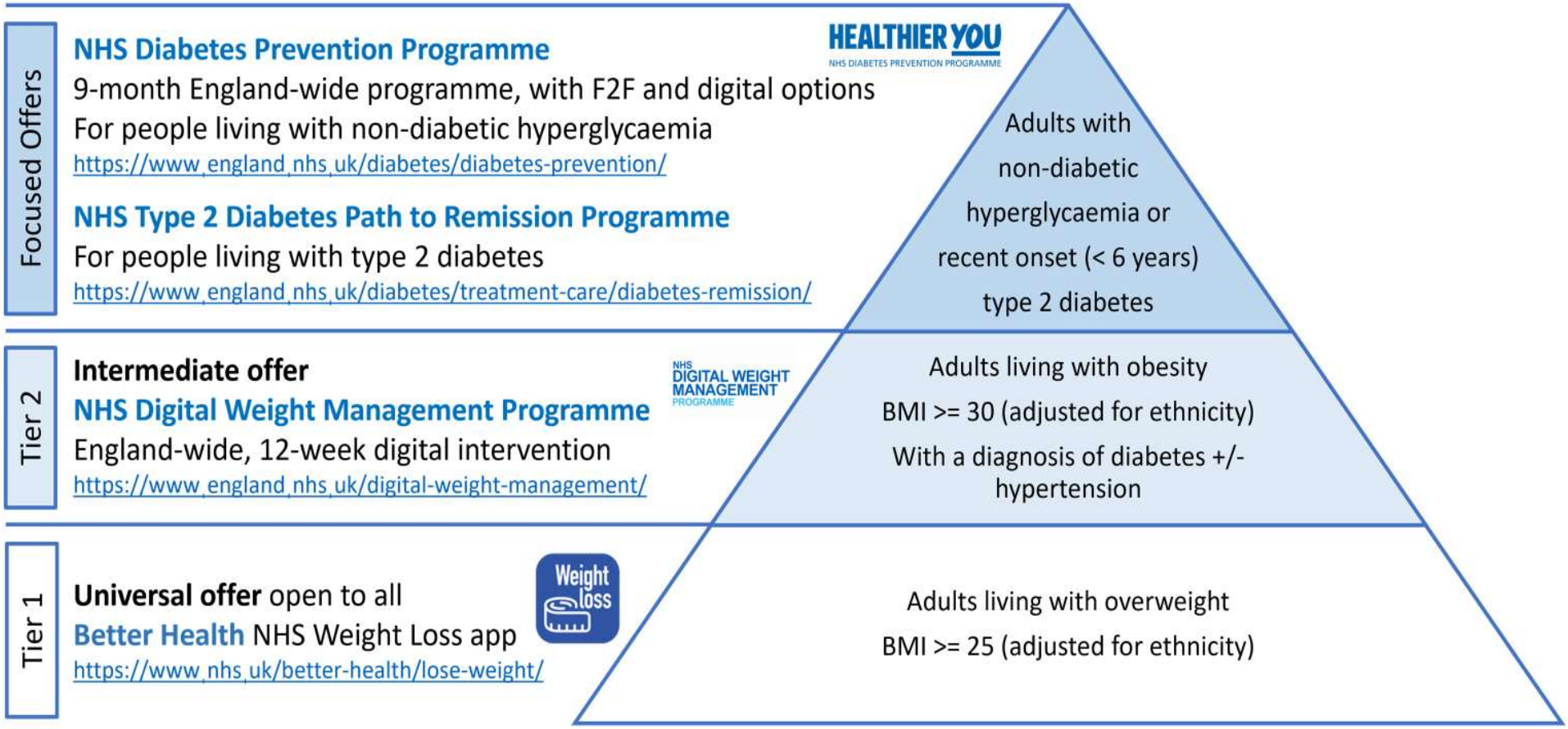
Osteoarthritis

Cancer

CAD and stroke
Twice as likely in obese under 50s

Respiratory problems
OSA
pulm. hypertension

Current therapeutic strategies to reduce body weight



Currently approved drug treatments for weight management

Orlistat 60/120 mg TDS
(Alli®/Xenical®)

Naltrexone 32 mg/ Bupropion 360 mg PR[3]
(Mysimba™)

Liraglutide 3.0 mg daily
(Saxenda®)

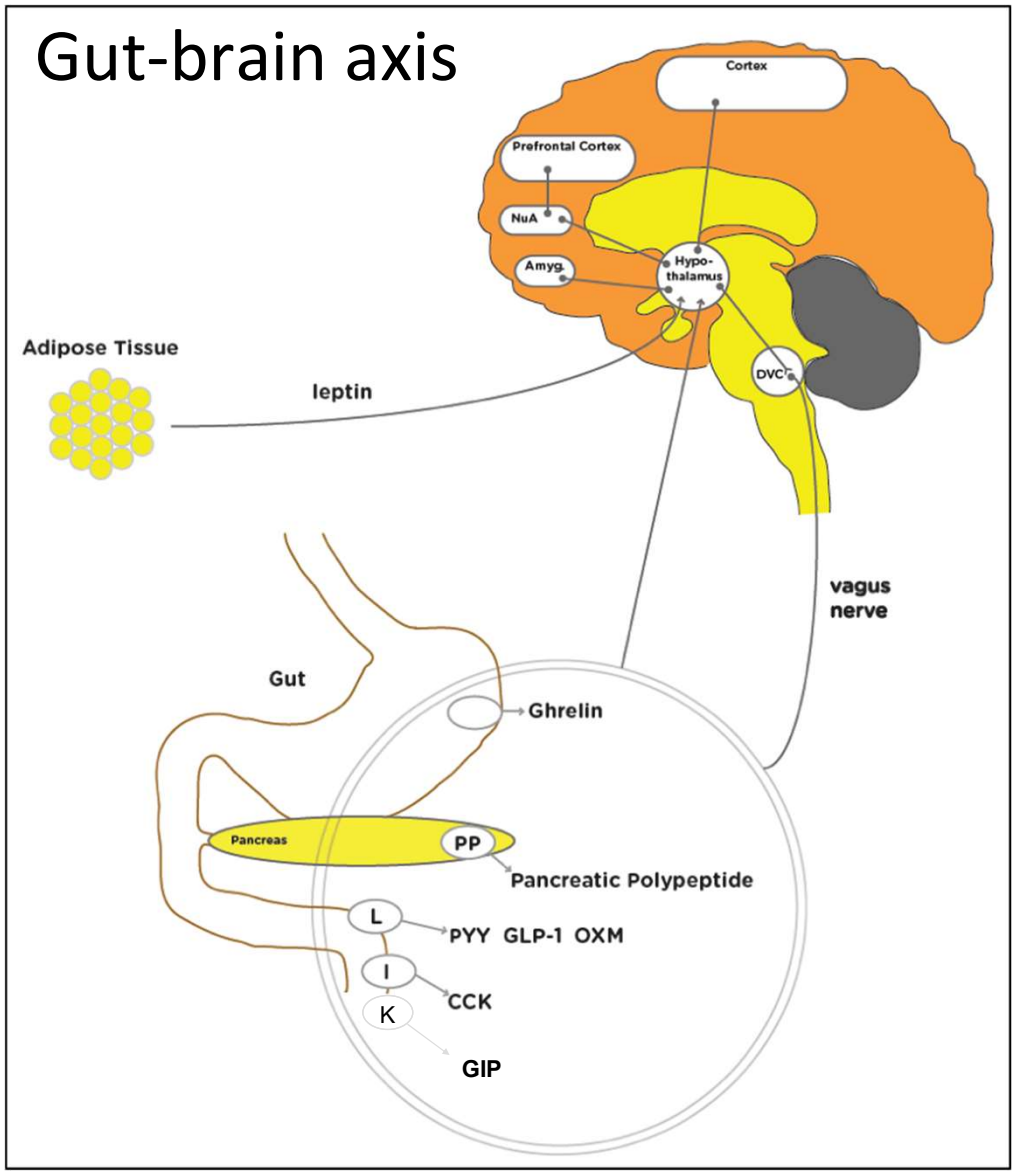
Tirzepatide 15 mg daily
(Mounjaro®)

Metreleptin od

Setmelanotide 1-3mg od
IMCIVREE®

Semaglutide 2.4 mg Weekly
(Wegovy®)

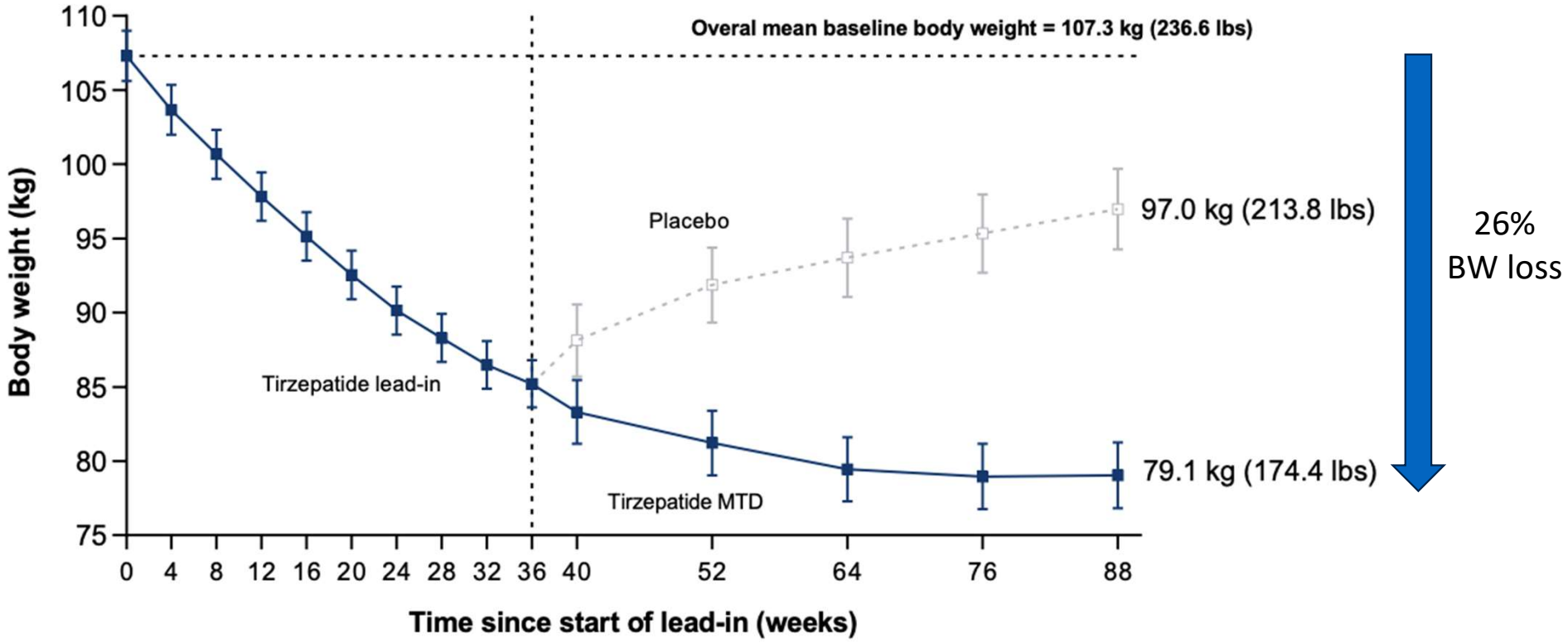
Metreleptin – only for leptin deficiency; Semaglutide – UK, Denmark, Norway ,Germany;
Setmelanotide – only for POMC deficiency, LEPR, MC4R variants – rare genetic causes of obesity



Tirzepatide (Mounjaro):

- GLP-1 and GIP both incretins
- GLP-1 from L cells, GIP from K cells in the gut
- GLP-1 appetite suppressant via vagal afferents and possibly blood stream

Tirzepatide/Mounjaro: SURMOUNT trial – GLP-1/GIP combination



Aronne L et al JAMA Dec 2023

NICE TA 1026: Tirzepatide for Overweight and Obesity

1 Recommendations

1.1 Tirzepatide is recommended as an option for managing overweight and obesity, alongside a reduced-calorie diet and increased physical activity in adults, only if they have:

- an initial body mass index (BMI) of at least 35 kg/m^2 and
- at least 1 weight-related comorbidity.

Use a lower BMI threshold (usually reduced by 2.5 kg/m^2) for people from South Asian, Chinese, other Asian, Middle Eastern, Black African or African-Caribbean ethnic backgrounds.

Setting of Care:

- The committee concluded that it would consider tirzepatide use across both **primary and secondary care settings**

Priority Cohort Phasing Proposal for NICE FV

NHS England

The guidance approach considers comorbidities as the main determinant in clinical prioritisation in association with the BMI rather than BMI leading for clinical factor consideration. This is subject to completion of engagement sessions with final proposal to be published.

FV Year	Estimated Cohort Duration	Cohorts	Proposed Cohort Access Groups	
			Comorbidities	BMI
Year 1	**12mths**	**Cohort I**	**≥4 'qualifying' comorbidities hypertension, dyslipidaemia, obstructive sleep apnoea, cardiovascular disease, type 2 diabetes mellitus**	**≥ 40**
Year 2	**~9mths**	**Cohort II**	**≥4 'qualifying' comorbidities hypertension, dyslipidaemia, obstructive sleep apnoea, cardiovascular disease, type 2 diabetes mellitus**	**≥35 - 39.9**
Year 2/3	**15mths**	**Cohort III**	**3 'qualifying comorbidities hypertension, dyslipidaemia, obstructive sleep apnoea, cardiovascular disease type 2 diabetes mellitus**	**≥ 40**
3 years	**36 months**			
NICE will evaluate relevant evidence generated during the initial guidance implementation period of up to 3 years and review the effectiveness of the service delivery pilots. NICE may then set a revised timeline for the second phase of the guidance implementation period.				
TBC	TBC mths	Cohort IV	≥3 'qualifying comorbidities hypertension, dyslipidaemia, obstructive sleep apnoea, cardiovascular disease, prediabetes Subject to review and potential for change or eligible cohort based on	≥ 40

Royal Surrey County Hospital NHS
NHS Foundation Trust

How to approach the consultation: 12 tips

1. Explain how tirzepatide works, gut hormones – 3 main mechanisms:
    - acts on appetite centres in the brain
    - slows down emptying of stomach so physically feel fuller
    - helps with glucose metabolism

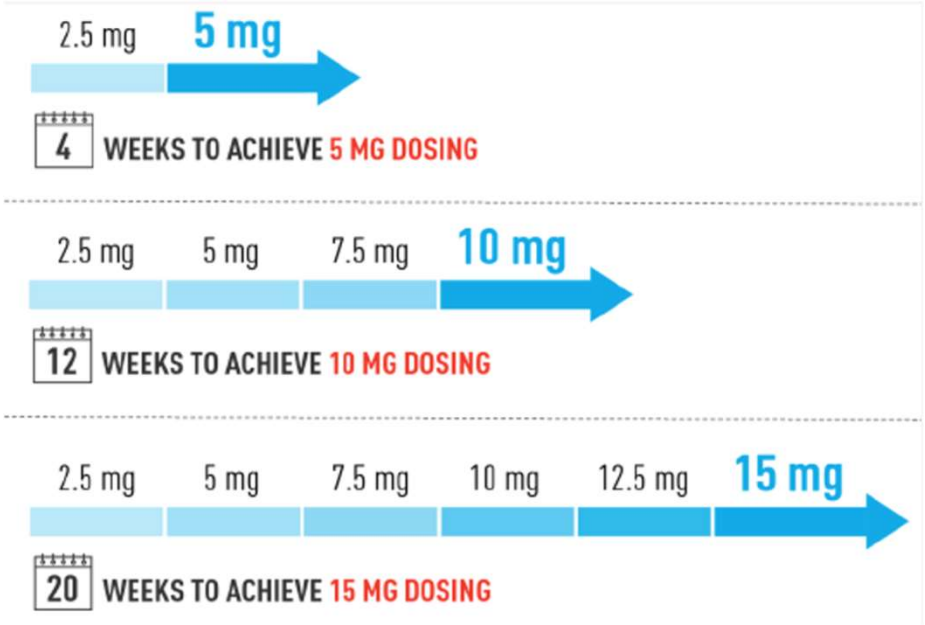
2. Ideal way to lose weight - slow and sustainable. Fast weight loss – reduces basal metabolic rate and ability to 'burn off calories', rise in 'hunger hormones'.

3. Relatively new drug (unlike 'Ozempic' which has been in use for around 15 years) so no long term outcomes or safety data

4. Manage patient expectations about weight loss - clinical trials suggest 20-25% weight loss however real-world data more like 15-20%. Not everybody loses weight – approx. 5% non-responders.

5. Weight loss is over 12-18 mths with most weight loss in first 6 months and then it slows down. No way of knowing ultimately how much weight a patient will lose. (Note: patients with T2DM tend to lose less weight on GLP-1 based drugs).

6. Starting dose 2.5 mg – dose escalation every 4 weeks in 2.5 mg increments, **<u>however:</u>**
   - side-effects may slow this down
   - you don't want rapid weight loss – you want slow and sustainable so may need to slow down



7. Side-effects:

- Common: nausea (smaller portions spread out) and constipation (hydration, fibre, gentle laxatives)
- Less common: diarrhoea and vomiting – can lead to hospitalisation
- Rare: pancreatitis and gallbladder problems (0.2 – 1%) – reported deaths but rare

Side-effects usually for first 24-48 hours after injection and tends to improve with time.

Absolute contra-indication – 'pancreatitis', FHx medullary thyroid ca., MEN2

- Acute pancreatitis – avoid if within last 12 months but if clear precipitant and dealt with – ok to continue with caution
- Caution if symptomatic gallstones – would avoid
- Caution with excess alcohol use
- if significant side-effects: can pause for 2-3 weeks and re-start at lower dose.

Explain symptoms to look out for – pancreatitis and biliary colic/cholesystitis

Other side effects – hair loss (?stress response from weight loss)

8. Other considerations and assessing suitability:
   - COCP and HRT
   - malabsorption – eg vitamin D, B12, folate. Beware of poor diet/smaller portions = risk of malnutrition.
   - other medications eg oral hypoglycaemics, anti-hypertensives
   - if T2DM – recent retinopathy scan
   - pregnancy plans – all women of child-bearing age should be counselled to not get pregnant if on these meds and at least one month prior to conception. Also avoid if breastfeeding.

9. Explain touch points and how often will be reviewed – blood tests annually. Longer term – explain no long-term data but we do know if stopping drug, weight re-gain. We don't know what happens longer term and whether weight re-gain.

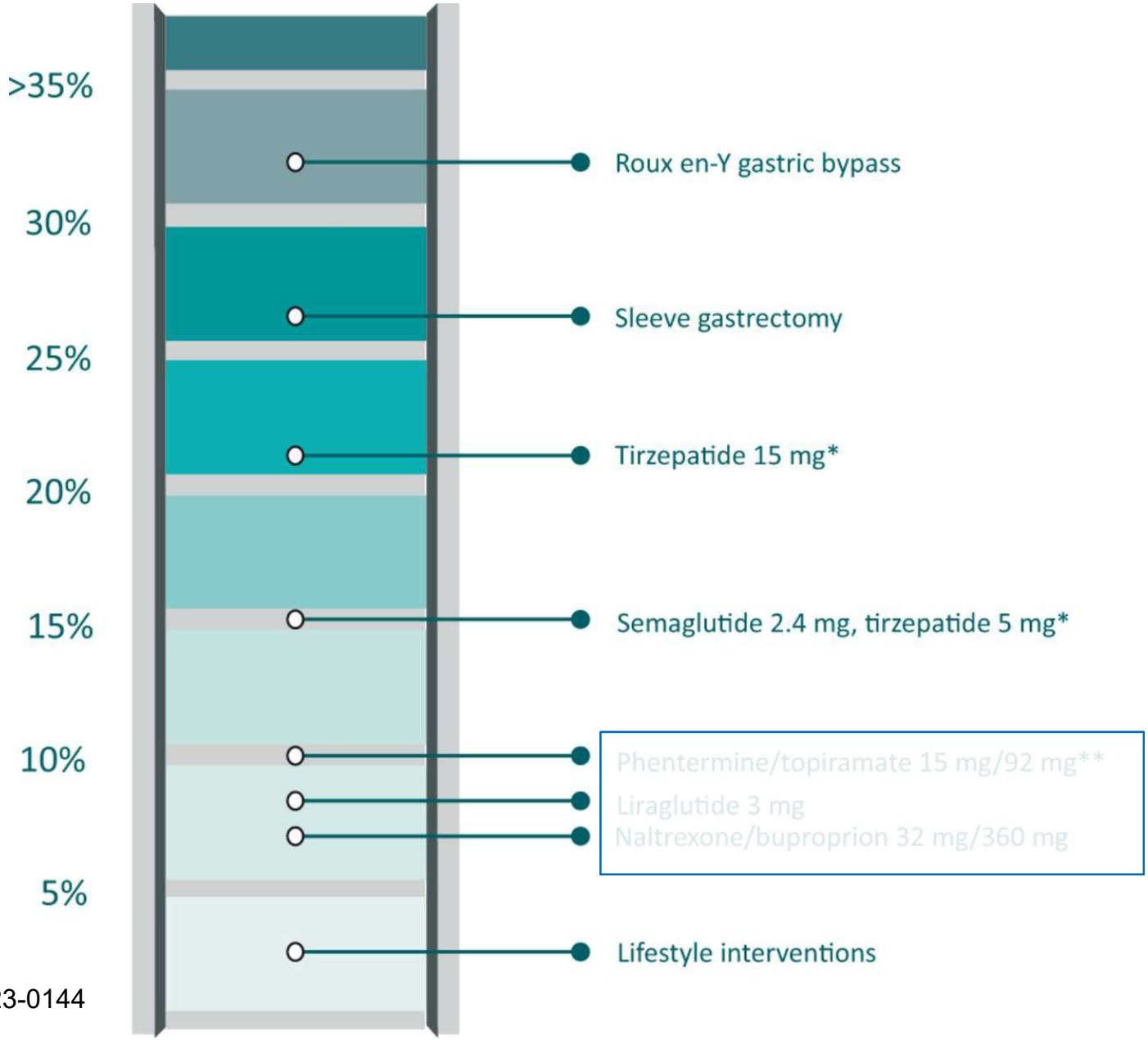
10. Importance of using tirzepatide ‘as a tool’ to help cement healthy lifestyle habits which includes healthy, nutritious diet and being active/exercise – establish by 1 year. Behavioural support.

Diet – high protein, reduce carbohydrates (wholegrain), Eat Well guide, fruit and veg

Exercise – cardiovascular (CMO guidance), but remember resistance training eg bands, weights.

11. Storage and other considerations: once open, can stay at room temperature for 30 days (up to 30 degrees centigrade). Travel – hand luggage, not hold! Ideally keep in fridge.

12. Commonly asked questions – micro dosing, ‘cycling’, taking in different dosing schedule, ‘Ozempic face’, loose skin/muscle mass loss, general anaesthetic.



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Clinical approach to patient with obesity:

What is the primary indication for weight loss?

How much weight do they need to lose in order to ‘reverse’ that clinical condition?

Which treatment is most likely to succeed in delivering that outcome according to the evidence available?

Development of the European Association for the Study of Obesity (EASO) Grade-Based Framework on the Pharmacological Treatment of Obesity: Design and Methodological Aspects

Barbara McGowann, Andreea Ciudin, Jennifer L. Baker, Luca Busetto, Dror Dicker, Gema Frühbeck, Gijs H. Goossens, Matteo Monami, Benedetta Ragghianti, Paolo Sbraccia, Borja Martinez-Tellez, Euan Woodward, Volkan Yumuk

Pre-existing comorbid conditions
Type 2 diabetes mellitus
Primary endpoint: complete diabetes remission* *Other critical endpoints*: Body weight reduction (total body weight loss % - TBWL%); lipid and blood pressure profile, and renal function), and improvement of metabolic control (glycosylated hemoglobin - HbA1c and fasting plasma glucose - FPG).
Pre-diabetes
Primary endpoint: normoglycemia restoration* *Other critical endpoints*: Body weight reduction (total body weight loss % - TBWL%); lipid and blood pressure profile, and renal function), reduction of incident diabetes*, and improvement of metabolic control (glycosylated hemoglobin - HbA1c and fasting plasma glucose - FPG).
Established cardiovascular disease
Primary endpoint: Incidence of Major Adverse Cardiovascular Events (MACE)* *Other critical endpoints*: Body weight reduction (total body weight loss % - TBWL%), all-cause and cardiovascular mortality reduction.
Heart failure
Primary endpoint: Reduction of hospital admission for heart failure* *Other critical endpoints*: Body weight reduction (total body weight loss % - TBWL%), incidence of MACE*, improvement of Kansas City Cardiomyopathy Questionnaire clinical summary score, change in 6-minute walking test distance. All-cause and cardiovascular mortality reduction.
Obstructive sleep apnea syndrome (OSAS)
Primary endpoint: OSAS remission (defined as AHI<5 events) *Other critical endpoints*: Body weight reduction (total body weight loss % - TBWL%) and; improvement of parameters evaluating apnea-hypopnea*.
Metabolic dysfunction-associated steatotic liver disease (MASLD)
Primary endpoint: MASLD remission (defined as the improvement of liver fibrosis without worsening steatohepatitis)* *Other critical endpoints*: Body weight reduction (total body weight loss % - TBWL%) and improvement of fibrosis and fat liver indexes.
Knee osteoarthritis (KOA)
Primary endpoint: KOA improvement assessed with scales evaluating osteoarthritis outcome scores (e.g., Western Ontario and McMaster Universities Osteoarthritis Index – pain and physical-function score). *Other critical endpoints*: Body weight reduction (total body weight loss % - TBWL%), improvement of 6-m walking distance, and opioids use.

Bariatric surgery:

Gastric bypass (RYGB) **Sleeve gastrectomy** **One-anastomosis**

Key points:

Low mortality <0.5% - less than elective cholecystectomy or knee replacement

45-60 mins operation Laparoscopic (key hole) Increasing use of robots and same day surgery

NICE Clinical Guideline 189 states the following:

Offer adults a referral for a comprehensive assessment by specialist weight management services providing multidisciplinary management of obesity to see whether bariatric surgery is suitable for them if they:

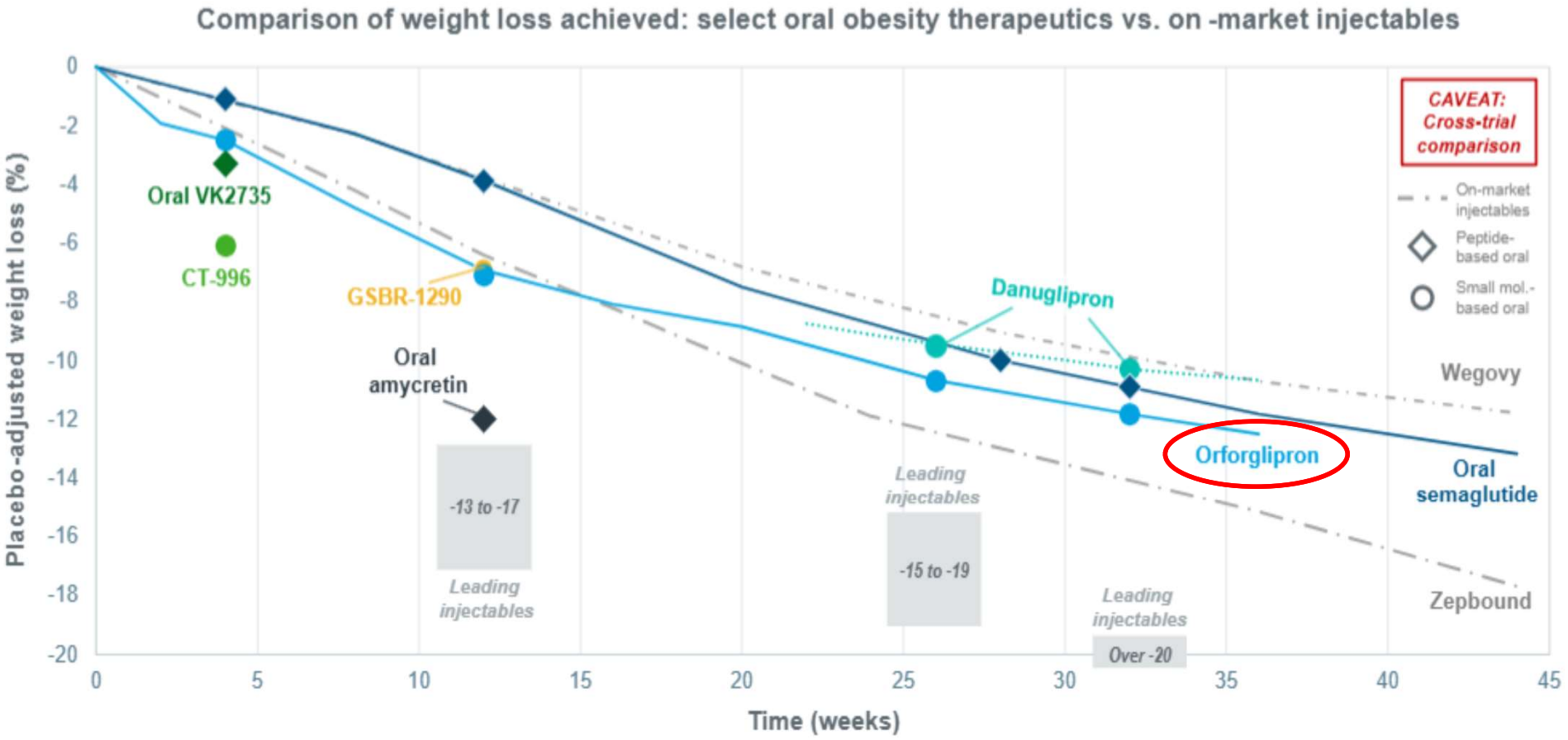
- have a **BMI of 40 kg/m2* or more**, or between **35 kg/m2* and 39.9 kg/m2* with a significant health condition that could be improved if they lost weigh**t and
- agree to the necessary long-term follow up after surgery (for example, lifelong annual reviews).

In 2023 NICE update the guidance to state people should be offered a comprehensive assessment for bariatric surgery:

- without the requirement for all non-surgical interventions to be exhausted first, or
- If already be under the management of tier 3 services.

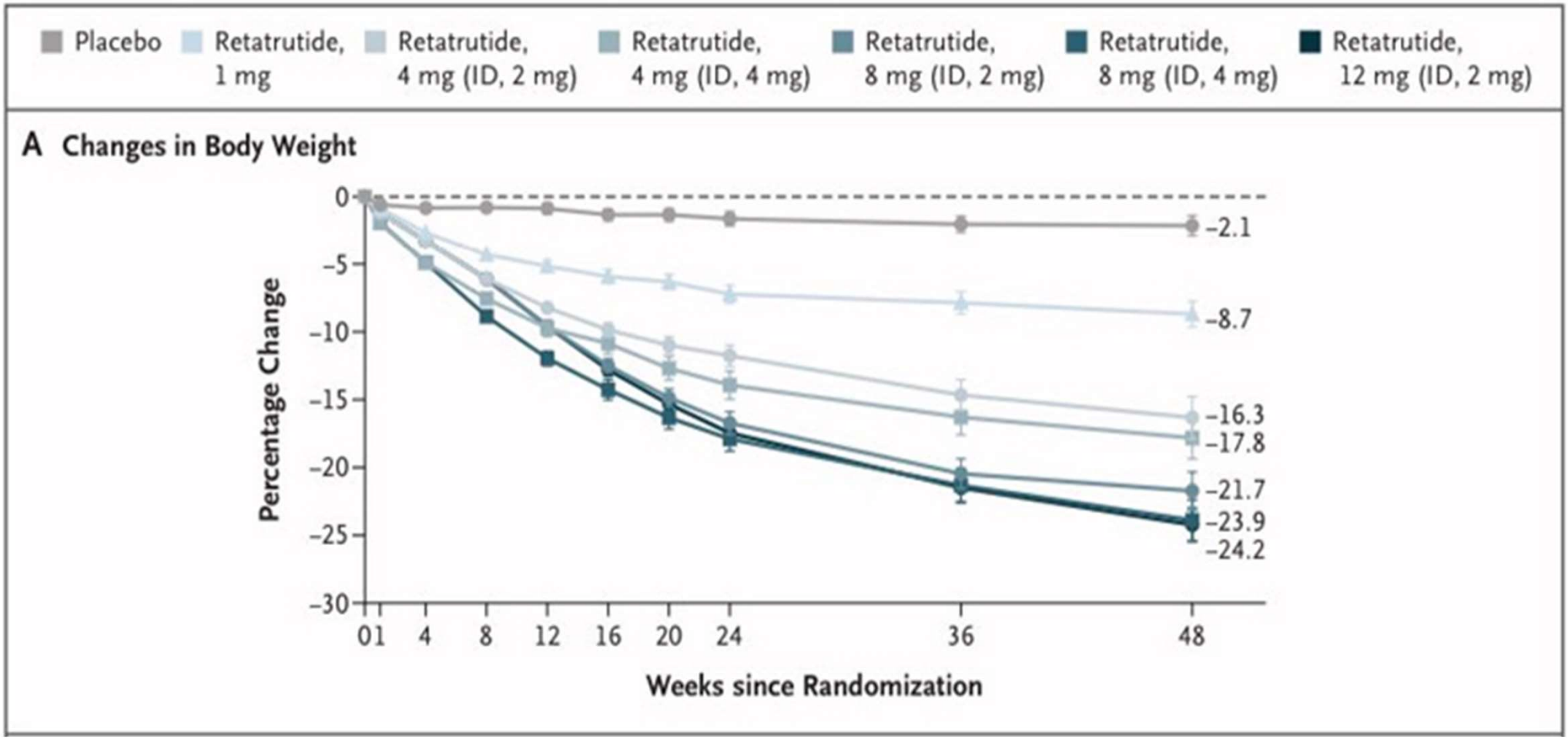
https://www.nice.org.uk/guidance/ng246 - Jan' 25

Emerging landscape of oral obesity therapeutics



Note: Weight loss shown was achieved at highest dose; Examples of efficacy-leading injectables in development: CT-388, retatrutide, MariTide
Source: Company reports and press releases; scientific publications; IQVIA EMEA Thought Leadership analysis

Orforglipron: oral GLP-1 agonist



[Triple–Hormone-Receptor Agonist Retatrutide for Obesity — A Phase 2 Trial | New England Journal of Medicine]

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Any Questions?

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