Obesity Update : Pharmacotherapy

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2025

Disclosures

GP TALKS FOR NOVONORDISK (SAXENDA) AND FOR INOVA (CONTRAVE)
BUT NONE FOR OZEMPIC, WEGOVY OR MOUNJARO….

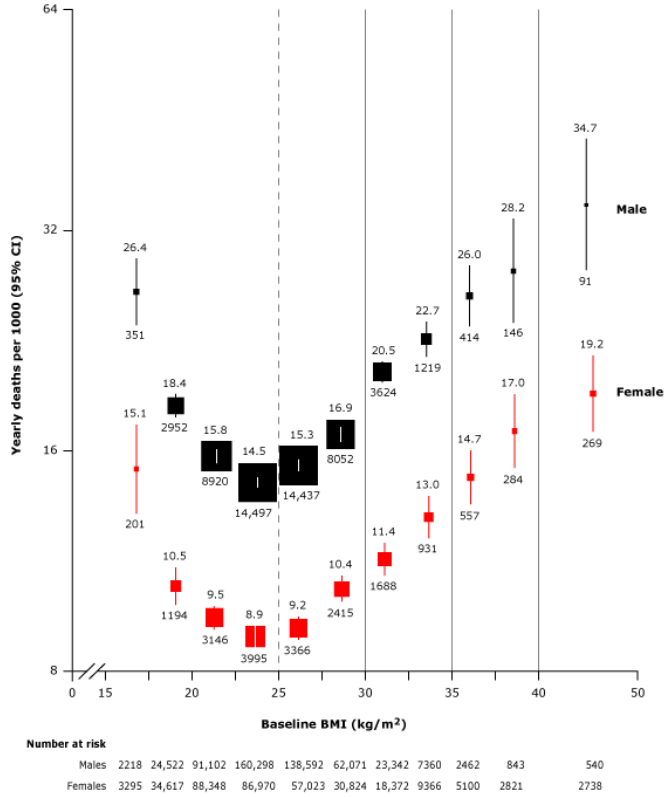
Outline

- Lancet Commission and diagnostic criteria for “Clinical Obesity”
- Recent publications in obesity management
- Currently available medication and how to make best use of them
- New medications coming

Complications

- Obesity is surpassing smoking as the number one cause of preventable disease and disability

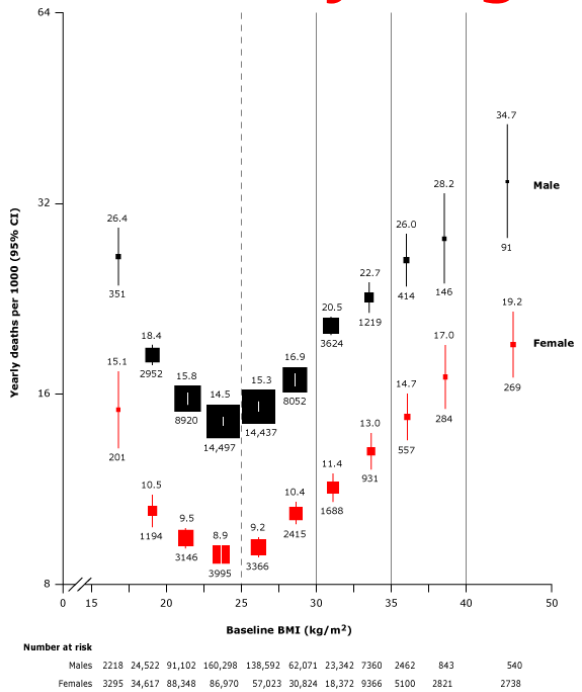
Obesity in adulthood is associated with a striking reduction in life expectancy



- The increased all cause mortality due to increasing BMI is on a continuum
- There is progressively greater mortality as BMI increases >25 kg/m^2
- Mortality is ~ 30 percent higher for every 5 kg/m^2 increment in BMI above 25

Whitlock et al. 2009 Lancet. Body-mass index and cause-specific mortality in 900,000 adults: collaborative analyses of 57 prospective studies. 373:1083

Years of life lost are highest for people who develop obesity at a younger age and live with obesity longer



Excessive mortality is from:
diabetes mellitus, IHD, cerebrovascular disease, CKD, malignancy (breast, endometrial, prostate, liver, kidney, colon)

BMI 30 - 35 kg/m^2, median survival was reduced by two to four yrs

BMI 40 to 45 kg/m^2, ↓by 8 - 10 yrs (*similar to the effects of smoking*)

BMI 55 to 59
~ 14 yrs reduced life expectancy

Whitlock et al. 2009 Lancet. Body-mass index and cause-specific mortality in 900,000 adults: collaborative analyses of 57 prospective studies. 373:1083

Kitihara et al, Association between Class III Obesity (BMI of 40–59 kg/m) and Mortality: A Pooled Analysis of 20 Prospective Studies(external link). *PLOS Medicine*. 11(7), e1001673.

BMI categories

Obesity : BMI > 30

- Class I BMI 30 -35
- Class II BMI 35 to 40
- Class III BMI > 40

"Super Obesity" : BMI > 50

- For avg height male this ~> **150kg**
- Avg height female ~>**135kg**

"Super super obesity" BMI > 60

Lancet Diabetes and Endocrinology commission on OBESITY -> new definitions and diagnostic criteria

1. **Confirm excess adiposity** (reduces risk of "overdiagnosis of obesity" and uses BMI as a screening measure instead of the definer of obesity)

   - If BMI is > 40 then assume excess adiposity
   - If BMI is 30 - 40 then confirm adiposity by one other anthropomorphic measure eg
     - WHR (waist-hip ratio), WHI (waist height ratio), WC (waist circumference)
     - OR Body composition/DEXA scanning (but impractical, expensive)

Rubino et al March 2025 The Lancet Diabetes & Endocrinology Commission
Volume 13, Issue 3 P221-262

Waist circumference

- **Increased Risk:**
  - **Men:** > 94 cm
  - **Women:** > 80 cm
- **Substantially Increased Risk:**
  - **Men:** >102 cm
  - **Women:** > 88 cm

https://www.health.gov.au/topics/overweight-and-obesity/bmi-and-waist#waist-measurement

"Clinical Obesity" = excess adiposity with reduced organ function due to obesity OR limitation in function

	Organ, tissue, or body system	Diagnostic criterion (as agreed by commissioners)	Grade of agreement
Adults			
1	CNS	Signs of raised intracranial pressure such as vision loss and/or recurrent headaches	A, 93%
2	Upper airways	Apnoeas/hypopnoeas during sleep due to increased upper airways resistance	U, 100%
3	Respiratory	Hypoventilation and/or breathlessness and/or wheezing due to reduced lung and/or diaphragmatic compliance	U, 100%
4	Cardiovascular (ventricular)	Reduced Left Ventricular systolic function - Heart Failure with Reduced Ejection Fraction - HFrEF	A, 96%
5	Cardiovascular (atrial)	Chronic/recurrent atrial fibrillation	A, 98%
6	Cardiovascular (pulmonary)	Pulmonary artery hypertension	A, 96%
7	Cardiovascular	Chronic fatigue, lower limb edema due to impaired diastolic dysfunction– Heart Failure with Preserved Ejection Fraction - HFpEF	U, 100%
8	Cardiovascular (thrombosis)	Recurrent DVT and/or pulmonary thromboembolic disease	A, 90%
9	Cardiovascular (arterial)	Raised arterial blood pressure	U, 100%
10	Metabolism	The cluster of hyperglycaemia, high triglyceride levels, and low HDL cholesterol levels	U, 100%
11	Liver	NAFLD with hepatic fibrosis	U, 100%
12	Renal	Microalbuminuria with reduced eGFR	A, 96%
13	Urinary	Recurrent/chronic urinary incontinence	U, 100%
14	Reproductive (female)	Anovulation, oligo-menorrhea and PCOS	U, 100%
15	Reproductive (male)	Male hypogonadism	A, 96%
16	Musculoskeletal	Chronic, severe knee or hip pain associated with joint stiffness and reduced range of joint motion	U, 100%
17	Lymphatic	Lower limbs lymphedema causing chronic pain and/or reduced range of motion	A, 98%
18	Limitations of day-to-day activities	Significant, age-adjusted limitations of mobility and/or other basic Activities of Daily Living (ADL=bathing, dressing, toileting, continence, eating)	U, 100%

The cluster of metabolic criteria recommended in this Commission for diagnosis of obesity includes, high triglyceride concentrations, **both diabetic and non-diabetic levels of hyperglycaemia** and low HDL cholesterol.

Rubino et al March 2025 The Lancet Diabetes & Endocrinology Commission Volume 13, Issue 3 P221-262

"Preclinical obesity" : excess adiposity without any limitation in function or end organ dysfunction

However this definition is one of exclusion which can only be used if full screening undertaken:

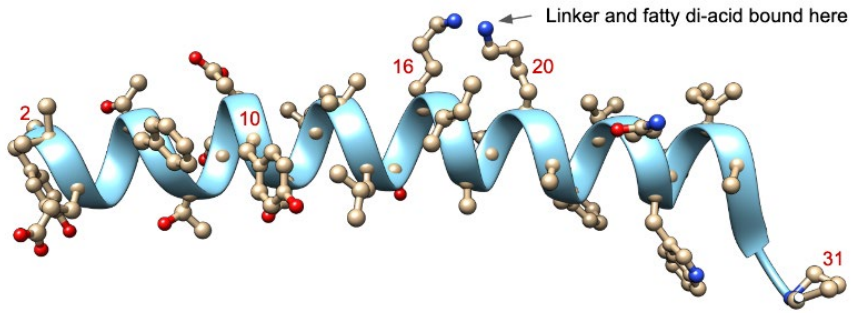
- Measure BP
- Check HbA1C and OGTT/lipid profile/EUC/ urinary microalbumin
- Sleep studies
- Echocardiogram
- ECG/Holter
- Abdo USS/fib 4 score +-fibroscan
- take history regarding urinary and reproductive function
- CT Head if headaches present
- Functional assessment – mobility and independence

What are the clinical implications of preclinical obesity?
People with preclinical obesity should be considered as having a variable, but generally increased, risk (depending on age, ethnicity, familial predisposition, body fat distribution, etc) to develop obesity-related diseases, clinical obesity itself, or both.

Rubino et al March 2025 The Lancet Diabetes & Endocrinology Commission Volume 13, Issue 3 P221-262

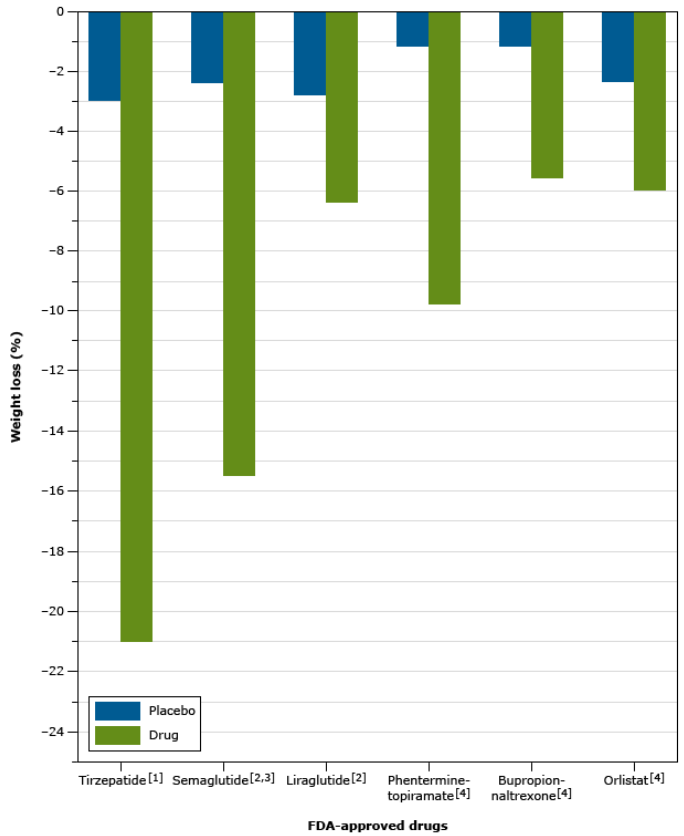
Highly Effective Treatment Options for Obesity

1. **Guidelines recommend pharmacotherapy if BMI is > 30** or >27 with complications eg T2DM
   - **Semaglutide** 2.4mg weekly -> ave 17% weight loss at 12months ($5500 annually)
   - **Tirzepatide** 5 -15 mg weekly -> ave 20% weight loss at 12 months ($7400 annually)
2. **Treatment is life long**, if medication is ceased, weight regain will occur -> back to original weight
3. **Bariatric surgery is recommended if BMI > 40** or > 35 with complications (> 30% weight loss, v good long term outcomes)
4. **Obesity is a chronic disease, needing lifelong treatment, medical and surgical options, similarly to many other chronic diseases**



Tirzepatide:dual agonist (GLP1 and GIP recptors)
GIP= Glucose-dependent insulinotropic polypeptide

Weight loss outcomes with FDA-approved medications



Weight loss reflects results at 72 weeks (tirzepatide), 68 weeks (semaglutide, liraglutide), or 52 weeks (other medications).

FDA: US Food and Drug Administration.

Data from:

1. *Jastreboff AM, Aronne LJ, Ahmad NN, et al. Tirzepatide once weekly for the treatment of obesity. N Engl J Med 2022; 387:205.*
2. *Rubino DM, Greenway FL, Khalid U, et al. Effect of weekly subcutaneous semaglutide vs daily liraglutide on body weight in adults with overweight or obesity without diabetes: The STEP 8 randomized clinical trial. JAMA 2022; 327:138.*
3. *Wilding JPH, Batterham RL, Calanna S, et al. Once-weekly semaglutide in adults with overweight or obesity. N Engl J Med 2021; 384:989.*
4. *Khera R, Murad MH, Chandar AK, et al. Association of pharmacological treatments for obesity with weight loss and adverse events: A systematic review and meta-analysis. JAMA 2016; 315:2424.*

UpToDate®

Tirzepatide as Compared with Semaglutide for the Treatment of Obesity

in weight at week 72 was −20.2% (95% confidence interval [CI], −21.4 to −19.1) with tirzepatide and −13.7% (95% CI, −14.9 to −12.6) with semaglutide (P<0.001). The least-squares mean change in waist circumference was −18.4 cm (95% CI, −19.6 to −17.2) with tirzepatide and −13.0 cm (95% CI, −14.3 to −11.7) with semaglutide (P<0.001). 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%. The most common adverse events in both treatment groups were gastrointestinal, and most were mild to moderate in severity and occurred primarily during dose escalation.

20% on tirzepatide (15% in diabetics)
15% Semaglutide 2.4mg (10% in diabetics)

CONCLUSIONS

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. (Funded by Eli Lilly; SURMOUNT-5 ClinicalTrials.gov number,

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

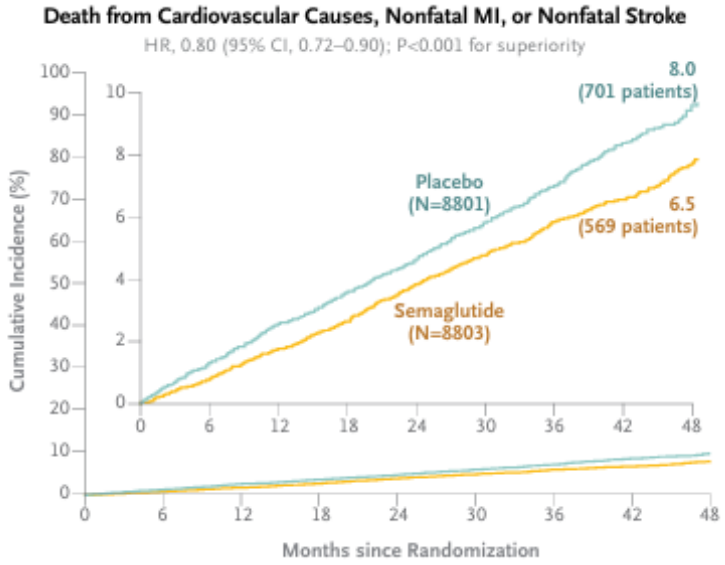
SELECT trial : 20% RRR in CV events in NON-diabetics on Semaglutide (2023)

CLINICAL TRIAL

Design: An international, double-blind, event-driven, randomized, placebo-controlled, superiority trial assessed the safety and efficacy of semaglutide in patients with preexisting cardiovascular disease, overweight or obesity (body-mass index, ≥27), and no history of diabetes.

Intervention: 17,604 adults ≥45 years of age were assigned to receive once-weekly subcutaneous semaglutide (2.4 mg) or placebo. The primary cardiovascular end point was a composite of the first occurrence of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke in a time-to-event analysis.

RESULTS



16000 patients, RCT, placebo controlled

Lincoff AM et al. DOI: 10.1056/NEJMoa2307563

Royal Perth Hospital

Surpass CVOT : outcomes just announced ! Cardiovascular benefit of Tirzepatide

13,000 participants across 30 countries > four and a half years duration

participants were age >40 yrs, HbA1c) of 7.0–10.5 % and a BMI of > 25 kg/m^2

They had established atherosclerotic CV disease, including coronary artery disease, cerebrovascular disease, and peripheral artery disease

Phase 3 cardiovascular outcomes trial **comparing** two incretin therapies (**dulaglutide and tirzepatide) in adults with type 2 diabetes and established atherosclerotic cardiovascular disease.**

"Overall, SURPASS-CVOT demonstrated that Tirzepatide is cardioprotective in participants with established atherosclerotic cardiovascular disease and type 2 diabetes"

significant 8% risk reduction for a composite endpoint of CV death, myocardial infarction (MI), or stroke

favorable, significant effect on secondary endpoints, including changes in estimated glomerular filtration rate, all-cause death, and a composite of CV death, MI, stroke, or coronary revascularization

https://www.springermedicine.com/type-2-diabetes/easd-2025/surpass-cvot-tirzepatide-vs-dulaglutide-cardioprotection-t2d/51483494
https://investor.lilly.com/news-releases/news-release-details/lillys-mounjaro-tirzepatide-gipglp-1-dual-agonist-demonstrated

Tirzepatide for HFpEF and Obesity

-double-blind, randomized, placebo-controlled trial,
-364 patients were assigned to the tirzepatide group and 367 to the placebo group;
-the median duration of follow-up was 104 weeks.
Adjudicated death from cardiovascular causes or a worsening heart-failure event occurred in 36 patients (9.9%) in the tirzepatide group and in 56 patients (15.3%) in the placebo gp (hazard ratio, 0.62; 95% confidence interval [CI], 0.41 to 0.95; P = 0.026).

"Treatment with tirzepatide led to a lower risk of a composite of death from cardiovascular causes or worsening heart failure than placebo .... in patients with heart failure with preserved ejection fraction and obesity".

Packer et al NEJM Jan 2025

Semaglutide improved MASLD related fibrosis

Practice Changing UpDate

GASTROENTEROLOGY AND HEPATOLOGY (August 2025, Modified September 2025)

Semaglutide in metabolic dysfunction-associated steatohepatitis

- For patients with metabolic dysfunction-associated steatohepatitis (MASH) and stage ≥2 fibrosis who do not achieve their weight loss goals with lifestyle interventions alone, we suggest GLP-1-based therapy for treatment of MASH (**Grade 2C**).

Glucagon-like peptide-1 (GLP-1)-based therapies are widely used to treat obesity, and they improve liver inflammation in metabolic dysfunction-associated steatohepatitis (MASH). New data show that a GLP-1 receptor agonist can also improve fibrosis [1]. In an interim analysis of a randomized controlled trial including 800 patients with MASH and stage 2 or 3 fibrosis, the GLP-1 agonist semaglutide for 72 weeks improved liver fibrosis compared with placebo (37 versus 22 percent) and resolved steatohepatitis. These data support our suggestion to use GLP-1-based therapies in patients with MASH. In August 2025, the US Food and Drug Administration approved semaglutide for treatment of MASH [2]. (See "Management of metabolic dysfunction-associated steatotic liver disease (nonalcoholic fatty liver disease) in adults", section on 'GLP-1-based therapies'.)

Up to date

Tirzepatide and Pancreatitis: a meta-analysis

18 RCT's
> 14 000 patients

Obesity Science & Practice

WILEY

Obesity Science and Practice

REVIEW OPEN ACCESS

Pancreatic Safety of Tirzepatide and Its Effects on Islet Cell Function: A Systematic Review and Meta-Analysis

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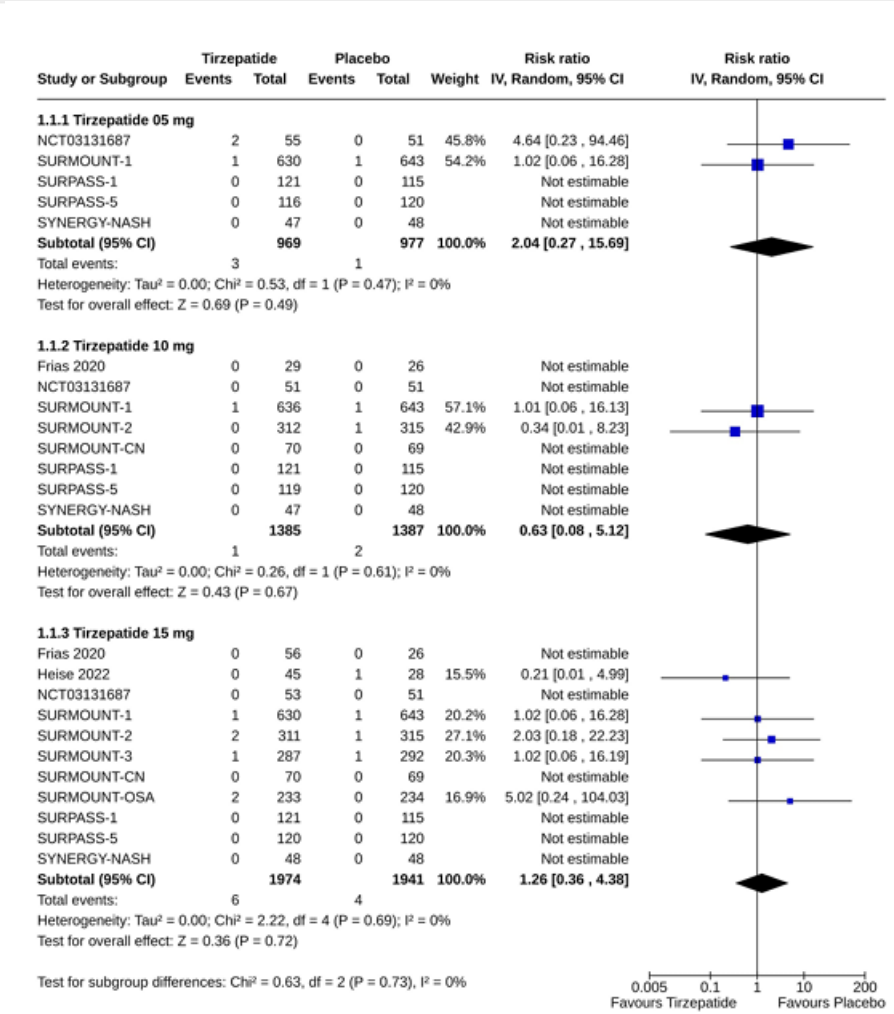
Keywords: insulin resistance | islet cell function | lipase | pancreatic amylase | pancreatitis | tirzepatide

ABSTRACT

Background: Endogenous glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) regulate islet cell function. GLP-1 receptor agonists (GLP-1RAs) have been associated with an elevated risk of acute pancreatitis. Data on the pancreatic safety of tirzepatide (a dual GLP-1 and GIP agonist) and its effects on islet cell function in randomized controlled trials (RCTs) are scarce. Moreover, no meta-analysis has comprehensively examined such effects of tirzepatide.

Methods: Electronic databases were searched for RCTs with tirzepatide as the intervention and a placebo or active comparator as the control. The primary outcome was adjudication-confirmed pancreatitis; secondary outcomes were the percent changes from baseline in serum pancreatic amylase, lipase, insulin, C-peptide, glucagon, and homeostasis model assessment of insulin resistance (HOMA2-IR).

Results: Seventeen RCTs with 18 published reports involving 14,645 subjects were analyzed. Over a follow-up duration of 12–72 weeks, tirzepatide had identical risks of pancreatitis to placebo (tirzepatide 5 mg: RR 2.04, 95% CI [0.27–15.69], $p = 0.49$; 10 mg: RR 0.63, 95% CI [0.08–5.12], $p = 0.67$; and 15 mg: RR 1.26, 95% CI [0.36–4.98], $p = 0.72$). Tirzepatide was also associated with comparable risks of pancreatitis to insulin and GLP-1RAs. However, tirzepatide (at all doses) caused greater increases in pancreatic amylase and lipase than placebo and insulin. Individuals on tirzepatide 15 mg and GLP-1RAs had similar risks of having increased lipase levels. The percent reductions in fasting insulin were greater with tirzepatide 10 and 15 mg than with



tE 1 | Forest plot highlighting the proportions of study subjects with pancreatitis: tirzepatide versus placebo.

Acute pancreatitis

The frequency of adjudication-confirmed acute pancreatitis reported in phase 3a clinical trials was 0.2% for Wegovy and <0.1% for placebo, respectively.

Management of CKM syndrome

dual use of SGLT2i and GLP-1RA ?

1. **Cardiovascular-Kidney-Metabolic** (CKM) syndrome
   - The 2023 European Society of Cardiology Guidelines for the management of cardiovascular disease in patients with diabetes recommended concomitant use in high-risk patients
   - How to prescribe both ?
2. **Approach 1**
   - Prescribe an SGLT2 for one of the cardiac or renal PBS indications:
   - HFpEF, HFrEF, CKD with albuminuria
   - Then prescribe Semaglutide on PBS for their T2DM
3. **Approach 2**
   - The patient pays for their SGLT2 privately (eg 20mg Empaglifozin take ½ daily)
   - And receives Semaglutide on PBS for their T2DM

Non PBS prescribing ie private script

1. If your patient has obesity and T2DM and is not losing adequate amount of weight on PBS Ozempic, then use wegovy to “top up” to a weight loss dose, eg add Wegovy 1mg

2. If your patient has obesity plus Type 1 DM or impaired glucose tolerance they should still be high priority to receive incretin therapy for weight loss.
   - Try getting them private script ozempic

3. Full dose Semaglutide : 2.4mg via Wegovy = $91 a week.
4. Full dose Tirzepatide : 15mg weekly = $173 per week.
5. But if they are responding to lower doses then no need to escalate to full dose

Counting clicks to reduce weekly cost of Wegovy (Semaglutide)

Wegovy 0.25mg/Dose FlexTouch Pen 1.5mL -...	Wegovy 0.5mg/Dose FlexTouch Pen 1.5mL -...	Wegovy 1.0mg/Dose FlexTouch Pen 3mL -...	Wegovy 1.7mg/Dose FlexTouch Pen 3mL -...	Wegovy 2.4mg/Dose FlexTouch Pen 3mL -...
$249.99	**$249.99**	**$249.99**	**$369.99**	**$369.99**
Private	Private	Private	Private	Private

eg buy the 2.4mg pen but use for 8 weeks instead of 4
= $46 a week for the 1.2mg weekly dose (37 clicks)

https://wegovycalculator.com/

ANZCA Australian and New Zealand College of Anaesthetists

GESA Gastroenterological Society of Australia

NACOS National Association of Clinical Obesity Services

ads Australian Diabetes Society

Clinical Practice Recommendations regarding patients taking GLP-1 receptor agonists and dual GLP-1/GIP receptor co-agonists prior to anaesthesia or sedation for surgical and endoscopic procedures.

Recommendations relating to GLP-1RAs and GLP-1/GIPRAs and sedation or anaesthesia:

- All patients should be asked about the use of GLP-1RAs and GLP-1/GIPRAs prior to [illegible] or sedation for surgical and endoscopic procedures and be involved in discussion and planning regarding the risk of aspiration.
- Elective preprocedural cessation of GLP-1RAs and GLP-1/GIPRAs is not recommended [illegible] risks hyperglycaemia in people with diabetes and may compromise weight control where patients are taking GLP-1RAs and GLP-1/GIPRAs for this indication.
- Patients should be asked about the use of other medications and medical conditions which may [illegible] symptoms and delay gastric emptying, such as, but not limited to bowel dysmotility, gastroparesis, and Parkinson's disease.
- Preprocedural diet modification with 24-hour clear fluid diet, followed by standard 6-hour fasting, should be recommended for all patients receiving GLP-1 RAs and GLP-1/GIPRAs.
- Risk mitigation options should be undertaken for those who have not withheld solids for 24 hours. These include detection of residual gastric contents, prokinetic agents, modification of anaesthesia, or deferral of procedure (see figure and explanatory notes).

/GIPRAs is not recommended, and [illegible]ks hyperglycaemia in where patients are taking GLP-1RAs and GLP-1/GIPRAs for

d by standard 6-hour fasting, should be RAs

Royal Perth Hospital

nature > news feature > article

NEWS FEATURE | 12 February 2025

Dozens of new obesity drugs are coming: these are the ones to watch

Next-generation obesity drugs will work differently from Ozempic and Wegovy — aiming to deliver greater weight loss with fewer side effects.

By Elie Dolgin

2028 and beyond	Monlunabant	Novo Nordisk	An oral drug that inhibits the CB1 cannabinoid receptor.

Nature https://www.nature.com/articles/d41586-025-00404-9

Retatrutide *a novel triple receptor agonist (GIP, GLP1, glucagon)*

"Retatrutide is a unimolecular hybridized peptide containing amino acid residues from all three separate peptides, resulting in a peptide that favors GIPR activity but has balanced activity between GLP-1R and the glucagon receptor.

Retatrutide (12 mg) recently achieved approximately one quarter ***(−24.2%) total body weight loss over the course of 48 weeks in overweight and obese patients without T2D*** *which is relative to the −20.9% reduction by tirzepatide in 72 weeks during the SURMOUNT-1 trial*

Retatrutide seems to be a leading candidate to induce massive body weight reduction in the shortest amount of time and represents the leading candidate to equivalate, or perhaps surpass, the achievements of bariatric surgery*."*

https://www.sciencedirect.com/science/article/pii/S2666634023003677

Cagrilintide : long acting amylin analogue

"CagriSema"

Cagrilintide Semaglutide combination drug

What's New

Cagrilintide with semaglutide for obesity (August 2025)

Glucagon-like peptide-1 (GLP-1)-based agents are increasingly used for the treatment of obesity, and multiple combination therapies targeting GLP-1 along with other gastrointestinal hormones are under investigation. Cagrilintide is a long-acting amylin analogue that helps regulate appetite. In a randomized trial including 3417 patients with a BMI of ≥30 kg/m^2 or ≥27 kg/m^2 with ≥1 weight-related complication, treatment with combination cagrilintide 2.4 mg-semaglutide 2.4 mg led to greater weight loss compared with either agent alone or placebo after 68 weeks [1]. Combination therapies such as cagrilintide-semaglutide offer promise for even greater weight loss efficacy than traditional GLP-1 monotherapy; this regimen remains investigational at this time. (See "Obesity in adults: Drug therapy", section on 'Investigational agents'.)

Uptodate 17/10/25

% change in body weight over 68 weeks **-20.4%** with cagrilintide-semaglutide as compared with -3.0% with placebo (estimated difference, -17.3 percentage points; 95% confidence interval, -18.1 to -16.6; P<0.001).

Obesity Management: Barriers to Effective treatment

1. **Lack of PBS funding for pharmacotherapy for obesity Rx**
2. **Lack of a multi-disciplinary obesity clinic with subsidised pharmacotherapy** (Perth and Adelaide are the only major cities in Australia without an obesity service)
3. **Insufficient funding for the public list for bariatric surgery** and a more restrictive age cut off in WA (< 55 yrs) compared to other centres VIC, NSW, QLD and SA (60-65 yrs)
4. **Misconceptions among health care professionals**
   - For eg that diet and exercise alone could be effective and sustainable to achieve high degree weight loss with starting BMI > 30
5. **Attitudes among health care professionals**
   - *"lifestyle problem" "lack of self control" "the patient doesn't want to lose weight"*

Other areas of priority (in my opinion)

1. Public health measures including a sugar tax
2. Early and aggressive treatment of adolescents and young adults with clinical obesity *(PCH have requested incretins be added to the hospital formulary for > 12 yrs)*
3. Accurate measurement of height, weight, BMI for every inpatient to detect all patients with clinical obesity and flag BMI > 30
4. Recording of Clinical Obesity as a diagnosis in the medical record is important for funding, coding and data linkage research into the true (inpatient) costs of severe clinical obesity
5. Future planning for increased inpatient numbers with severe obesity BMI > 50 – a dedicated bariatric unit with ?15 beds and specialized equipment, trained and increased staff for turns etc and manual handling

Summary: the physicians role in obesity management

1. **Screen for features of clinical obesity and complications** after confirming excess adiposity
   - sleep study, Echo, holter, liver USS, biochemistry and urinary microalbumin,
2. **Prescribe highly effective medication or refer for bariatric surgery** (http://joondalupbariatricservices.com.au/wa-weight-loss-surgery.asp)
   - Guidelines recommend pharmacotherapy if BMI is > 30 or >27 with complications eg T2DM
   - **Semaglutide** 2.4mg weekly -> ave 17% weight loss at 12months ($5500 annually)
     - Try get all patients with T2DM and excess adiposity onto pbs funded Semaglutide (Ozempic)
   - **Tirzepatide** 5 -15 mg weekly -> ave 20% weight loss at 12 months ($7400 annually)
   - Treatment is life long, if medication is ceased, weight regain will occur
   - With > 15% loss of body weight you can expect significant benefits : remission T2DM, HTN, fatty liver, remission of OSA, less joint pain, improvement in heart failure, slowing of CKD progression, improvement in QOL
   - Both agents confer cardiovascular protection, independent of degree of weight loss
3. Ensure MDT approach : close cooperation with allied health and commence VLCD via dietician
4. **Advocate for better access to affordable and life saving treatment for our patients**

Thank you

Extra slides

Appendix 1: EOSS Staging Tool

EOSS: EDMONTON OBESITY STAGING SYSTEM - *Staging Tool*

STAGE 0

- **NO** sign of obesity-related risk factors
- **NO** physical symptoms
- **NO** psychological symptoms
- **NO** functional limitations

Case Example:
Physically active female with a BMI of 32 kg/m², no risk factors, no physical symptoms, no self-esteem issues, and no functional limitations.

Class I, Stage 0 Obesity
EOSS score
WHO Obesity Classfication

STAGE 1

- Patient has obesity-related **SUBCLINICAL** risk factors
(borderline hypertension, impaired fasting glucose, elevated liver enzymes, etc.)
- OR -
- **MILD** physical symptoms - patient currently not requiring medical treatment for comorbidities
(dyspnea on moderate exertion, occasional aches/pains, fatigue, etc.) *- OR -*
- **MILD** obesity-related psychological symptoms and/or mild impairment of well-being
(quality of life not impacted)

Case Example:
38 year old female with a BMI of 59.2 kg/m², borderline hypertension, mild lower back pain, and knee pain. Patient does not require any medical intervention.

Class III, Stage 1 Obesity

WHO CLASSIFICATION OF WEIGHT STATUS (**BMI** kg/m²)

Obese Class I ..... 30 - 34.9
Obese Class II ..... 35 - 39.9
Obese Class III ..... ≥40

Stage 0 / Stage 1 Obesity

Patient ***does not meet clinical criteria for admission*** at this time.
Please refer to primary care for further preventative treatment options.

STAGE 2

- Patient has **ESTABLISHED** obesity-related comorbidities requiring medical intervention
(HTN, Type 2 Diabetes, sleep apnea, PCOS, osteoarthritis, reflux disease) *- OR -*
- **MODERATE** obesity-related psychological symptoms
(depression, eating disorders, anxiety disorder) *- OR -*
- **MODERATE** functional limitations in daily activities
(quality of life is beginning to be impacted)

Case Example:
32 year old male with a BMI of 36 kg/m² who has primary hypertension and obstructive sleep apnea.

Class II, Stage 2 Obesity

STAGE 3

- Patient has **significant** obesity-related end-organ damage (myocardial infarction, heart failure, diabetic complications, incapacitating osteoarthritis) *- OR -*
- **SIGNIFICANT** obesity-related psychological symptoms
(major depression, suicide ideation) *- OR -*
- **SIGNIFICANT** functional limitations
(eg: unable to work or complete routine activities, reduced mobility)
- **SIGNIFICANT** impairment of well-being
(quality of life is significantly impacted)

Case Example:
49 year old female with a BMI of 67 kg/m² diagnosed with sleep apnea, CV disease, GERD, and suffered from stroke. Patient's mobility is significantly limited due to osteoarthritis and gout.

Class III, Stage 3 Obesity

STAGE 4

- **SEVERE** (potential end stage) from obesity-related comorbidities *- OR -*
- **SEVERELY** disabling psychological symptoms *- OR -*
- **SEVERE** functional limitations

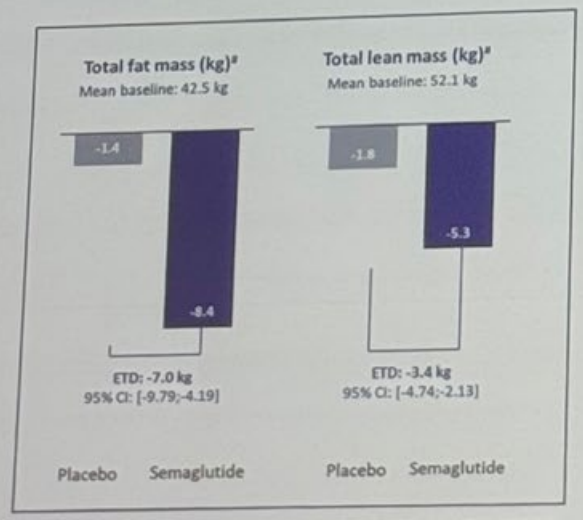
Case Example:
45 year old female with a BMI of 54 kg/m² who is in a wheel chair because of disabling arthritis, severe hyperpnea, and anxiety disorder.

Class III, Stage 4 Obesity

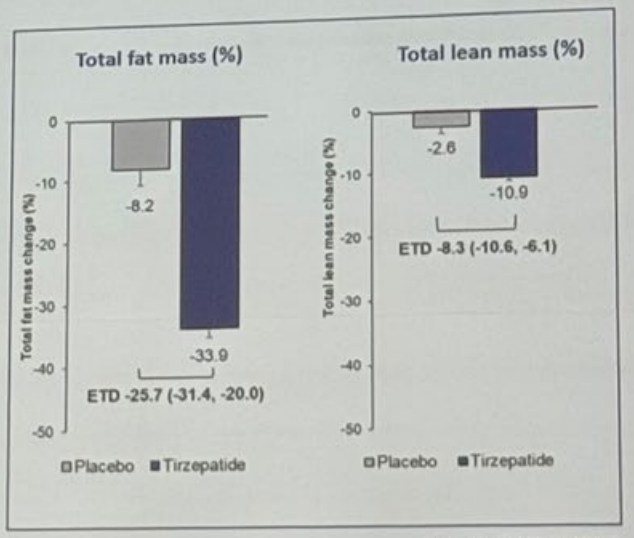
Alberta Health Services
UNIVERSITY OF ALBERTA

Sharma AM & Kushner RF, *Int J Obes* 2009

Changes in body composition with weight loss



Wilding *NEJM* 2021



Jastreboff *NEJM* 2022

- Approximately 25% of weight loss will be fat-free mass after **any** weight loss intervention
- Ratio of fat mass to fat-free mass improves after weight loss interventions
- Self-reported physical function improves after weight loss interventions
- Skeletal muscle mass accounts for ~50% of fat-free mass – lack of data on changes in skeletal muscle mass or strength after we
- There are no head-to-head RCTs comparing body composition changes after GLP-1 based medications vs other interventions

Slide credit to Dr Priya Sumithran, Endocrinologist , head of the Obesity and Metabolic medicine group Monash University

1. Naltrexone-bupropion is a reasonable option for individuals who smoke, have untreated depression and obesity, and want treatment for both conditions. It may also benefit people with obesity and comorbid alcohol use disorder given naltrexone's indication for treating the latter.
2. And combination therapy:

Effect of combined GLP-1 analogue and bupropion/naltrexone on weight loss: a retrospective cohort study.

AU
Naude J, Zentner A, Suresh P, Bittman J, Khan NA

SO
Int J Obes (Lond). 2024;48(8):1118. Epub 2024 May 9.

OBJECTIVELittle is known about the effect of a multi-drug weight loss strategy in obesity treatment, particularly combining bupropion/naltrexone and glucagon-like peptide 1 (GLP-1) analogue. The purpose of this study was to evaluate if there are any additive effects of prescribing bupropion/naltrexone on top of GLP-1 analogue as weight loss therapy.

METHODSThis was a retrospective cohort study of adult patients with a body mass index (BMI) ≥ 30 kg/m2 prescribed GLP-1 analogue therapy at an obesity specialist clinic in Vancouver, Canada. We compared a 6 and 12-month change in total body weight loss (TBWL) for those receiving monotherapy from the initiation of GLP-1 analogue therapy with those receiving combination therapy from the initiation of bupropion/naltrexone added-on therapy. Patients prescribed combination therapy were stratified into responder (loss of≥ 5% TBWL) and non-responder (TBWL < 5%) subgroups based on initial response to the GLP-1 analogue alone for any amount of time.

RESULTSThe mean weight loss among patients prescribed GLP-1 analogue monotherapy at 12 months was 11.42 kg, SD 9.95 (9.6% TBWL). There was no significant difference between these two treatment strategies overall (HR 0.88, 95% CI 0.68 to 1.14, p = 0.35). However, when stratified by response to initial GLP analogue therapy, the addition of bupropion/naltrexone was associated with a statistically significant reduction in weight in both the responder (4.3% TBWL (p < 0.01)) and non-responder groups (4.0% TBWL (p < 0.01)).

CONCLUSIONSGLP-1 analogues are an effective treatment for weight loss, and the addition of bupropion/naltrexone is associated with greater weight loss including in patients who are initially non-responsive to GLP-1 analogues.

Challenges for inpatients with BMI > 50

Challenges for inpatients with BMI > 50 Patient 1

49 yr old M

Class III Obesity, “super super bariatric”, 365 kg BMI 120

3 admissions in 18 months: total of 11 months LOS

PHx: OSA on BiPAP, atrial fibrillation, lipodermatosclerosis, recurrent cellulitis (inc ICU admission with sepsis)

Unable to access accommodation, equipment failure (frame, bed), cellulitis, pressure areas (feet)

Commenced on Tirzepatide March 2025. Weight loss 20kg over 8 weeks down to 347kg

IPA for 18 months supply. If he loses total of 20% initial body weight, then will reach 290kg,

upper GI will consider bariatric surgery if close to 280kg.

Challenges for inpatients with BMI > 50 Patient 2

Challenges for inpatients with BMI > 50 Patient 2

60-year-old male

- Class III obesity, 225kg, BMI 78 (peak weight 270kg in 2017)

1. Obstructive sleep apnoea (2009, AHI ? 48, didn't tolerate CPAP).
2. Pendulous L sided abdominal pannus with recurrent infective panniculitis (2017, April 2020, Sep 2020, Oct 2020 (56 day admission) Mar 2023, Feb 2024 (27 day admission).
3. Recurrent cellulitis (admissions Nov 2018, Mar 2019, Mar 2023).
4. Chronic LL Lymphoedema, venous stasis, lower limb ulceration.
5. Verrucous lymphedema/venous stasis dermatitis of posterior thighs with intermittent skin breakdown and blood loss
   5.1 Excisional biopsy (under spinal block), 15/07/2019 of R thigh verrucous lesions, intraoperative finding of chronic venous stasis : large veins and high pressure. Planned excision of buttock/gluteal crease abandoned due to patient discomfort. Histology: venous eczema and proliferation
   5.2 CT angiogram : abnormal /highly vascular soft tissue in the region of the (R) thigh ulcer with prominent vessels arising from the superficial femoral artery.
6. Chronic iron deficiency anaemia since 2018, due to chronic bleeding at posterior thighs (multiple iron infusions)
7. (L) ankle venous ulcer (admission in 2024).
8. AKI complicating admissions with cellulitis, panniculitis
9. GORD.
10. Hypertension
11. Subarachnoid haemorrhage, grade 1, 2005.
12. Psoriasis (in remission)
13. Osteoarthritis

Progress/current admission

His current admission = 410 days length of stay.
He had a fall and fractured his left fibula head -> conservative management.
-very deconditioned, pain at the fracture site, poor balance, unable to mobilise
-further inpatient falls despite physiotherapy, fear of falling
-opinion of our rehabilitation physician :the large asymmetrical abdominal pannus affects his balance and is a major factor in his slow progress with rehabilitation.

Progress: lost 20 kg on a VLCD (very low calorie diet) with optifast from 225-> 205kg over 6/12.
-commenced on Tirzepatide in Dec 2024 and has lost nearly 30kg, – down to 177kg at last weigh
-his IPA was 6 months supply and runs out soon.
-Bariatric surgery requested. Pt > age limit of 55 yrs -> for further exec level discussion