Dr. Purvi Chawla

MBBS (Mum),
MS (Pharm Sci, USA),
PG (Diabetology, UK);
PG Endocrinology, UK

- Consultant Diabetologist and Director of Clinical Research - Lina Diabetes Care, Diabetes & Beyond and Mumbai Diabetes Research Centre, Mumbai
- Consultant Diabetologist - VLSR – The Clinic, Bhartiya Arogya Nidhi Hospital, Nanavati Max Super Specialty Hospital & BSES Global Hospital, Mumbai
- Secretary - IDF Women & Diabetes group
- Secretary – All India Association for Advancing Research in Obesity (AIAARO)
- Chair – Diabetes & Women Interest Group, Diabetes India
- Governing council member - RSSDI Maharashtra Chapter
- Scientific Council - Hriday - Focused on T1DM care
- Co and Sub-Investigator - Global/National Clinical Trials at BSES Municipal General Hospital, Mumbai
- Founder and Organizing Chair – Diabetes Research and Solutions since 2022
- Social Media Editor – International Journal for Diabetes In Developing Countries

- **RSSDI Best Women Diabetologist of the year 2025**
- JPEF-USV Diabetes Tech Innovation Award 2022
- ACP – Best Indian Women Educator Award 2022
- TruWellth Health & Wellness Award for Courage, Compassion & Commitment in COVID care, ’21
- DiaCareCON Award 2021 – For Social Media Awareness In Diabetes
- RSSDI-USV Best Innovations Award in Diabetes Care During Challenging Times 2020
- Obesity Warriors, AMOCE Senior Career Physician Award, Rank: Colonel, 2025
- Chief Coordinator - RSSDI TOP 10 and RSSDI Diabetes Bytes

Clinical Management of Obesity – Emerging Approaches

Dr. Purvi Chawla

MBBS (Mum),
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PG Endocrinology, UK

Mechanism and evolution of GLP-1 therapies in obesity management

Obesity is recognised as a disease and a health

Overweight and obesity

Obesity is a medical condition described as excess body weight in the form of fat, when accumulated, this fat can lead to severe health impairments.

2.9 billion people will be living with obesity by 2030.

Obesity meets common criteria of a disease

- An impairment of the normal functioning of some aspect of the body
- Characteristic signs or symptoms
- Harm or morbidity

Yet obesity remains underdiagnosed and undertreated

<20%

People receiving evidence-based anti-obesity treatment*

Obesity is recognised as a disease and a health issue

WORLD OBESITY

obesity canada

aoaso

AMA

Royal College of Physicians

eat right. Academy of Nutrition and Dietetics

Obesity is the root of a lot of chronic diseases

Metabolic, mechanical and mental

Metabolic

Mechanical

Mental

Cancers*

Physical functioning

Depression

Anxiety

Asthma

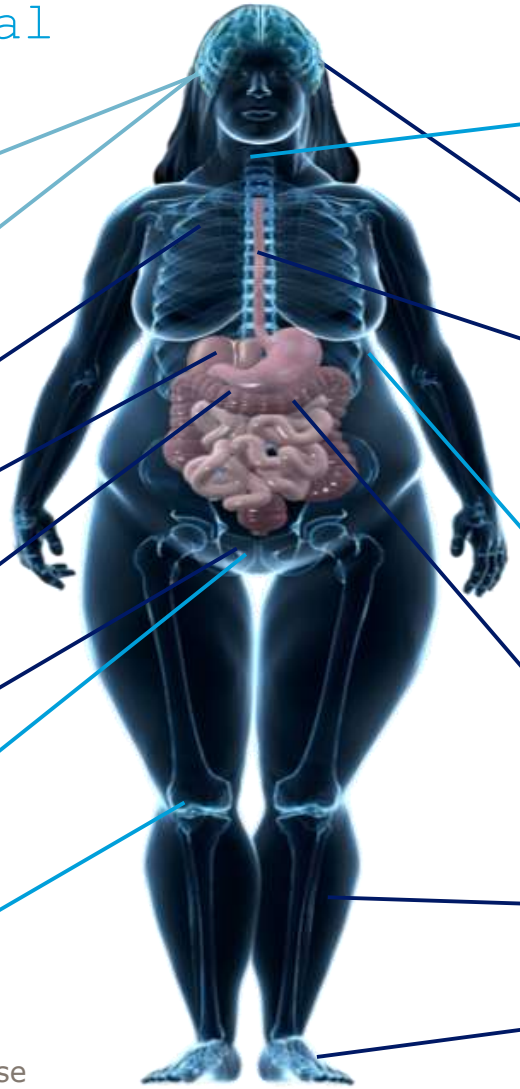
NAFLD

Gallstones

Infertility

Incontinence

Arthrosis



Sleep apnoea

CVD and risk factors
- Stroke
- Dyslipidaemia
- Hypertension
- Coronary artery disease
- Congestive heart failure
- Pulmonary embolism

Chronic back pain

Type 2 diabetes
Prediabetes

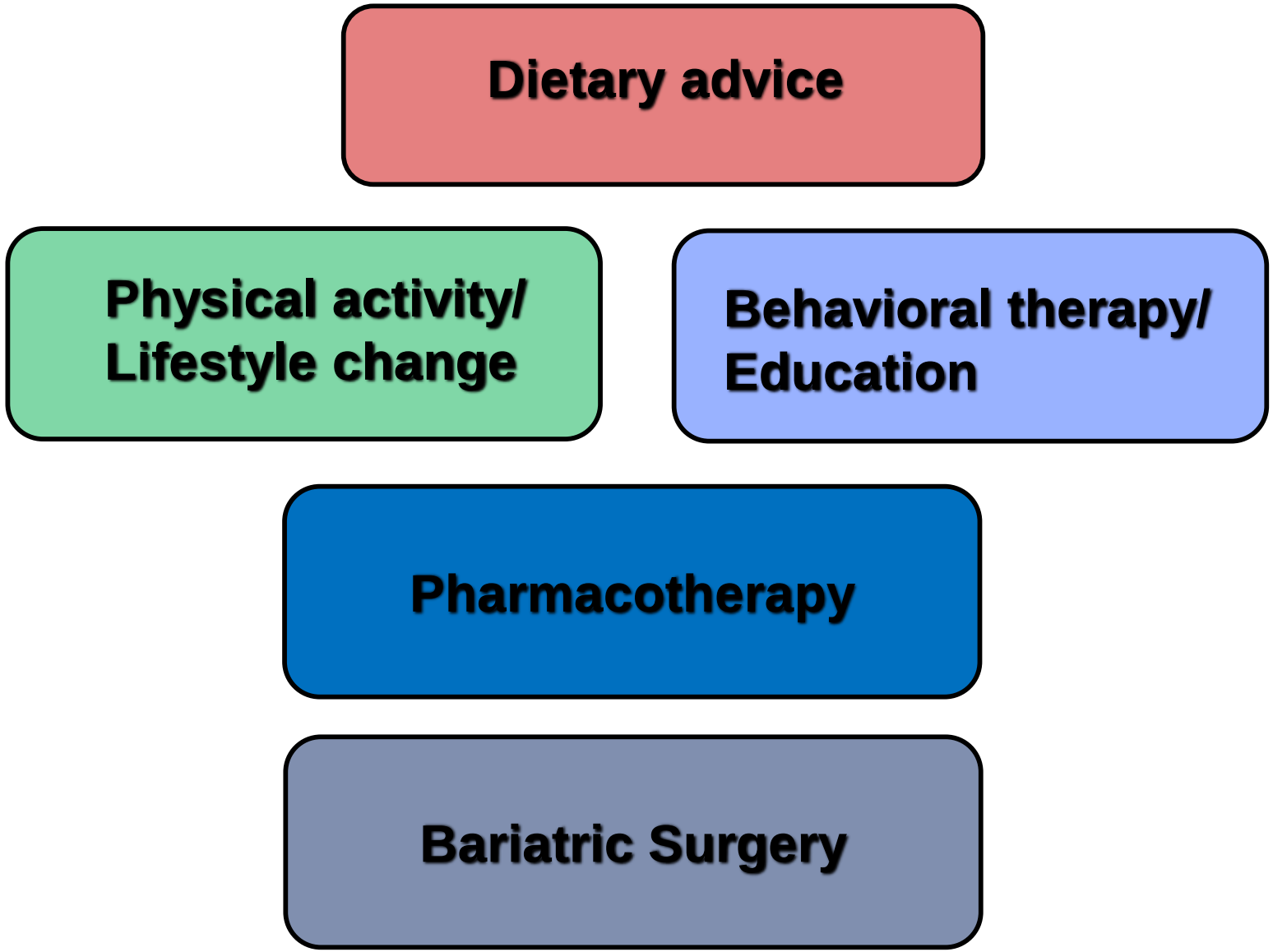
Thrombosis

Gout

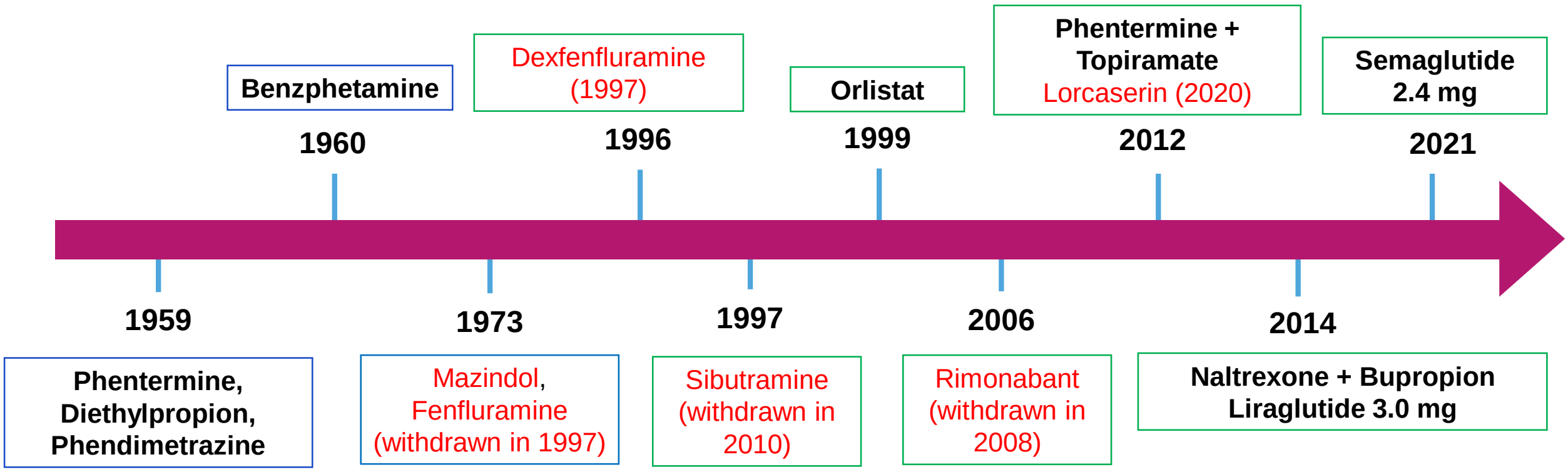
CVD, cardiovascular disease; NAFLD, non-alcoholic fatty liver disease
*Including breast, colorectal, endometrial, esophageal, kidney, ovarian, pancreatic and prostate

Adapted from Sharma AM. *Obes Rev*. 2010;11:808-9; Guh *et al. BMC Public Health* 2009;9:88; Luppino *et al. Arch Gen Psychiatry* 2010;67:220–9; Simon *et al. Arch Gen Psychiatry* 2006;63:824–30; Church *et al. Gastroenterology* 2006;130:2023–30; Li *et al. Prev Med* 2010;51:18–23; Hosler. *Prev Chronic Dis* 2009;6:A48

Current Management Strategies



Global History of Anti-obesity Drugs



Blue box = Short-term use; Green box = Long –term use; Red text = Discontinued.

Gadde. *et al.*, Clinical Chemistry, 2018; 64(1); 118–129.

Drugs Approved for Long Term Use in Weight Management

- Orlista — Available in India
- Phentermine/Topiramate ER
- Naltrexone SR/Bupropi — Available in India
- Liraglutide 3mg
- Lorcaseri — Withdrawn Feb 2020
- Semaglutide 2.4mg once a — Approved June 4,2021 Available in India
- Tirzepatide(Zepbound) once — Approved Nov 8,2023 Available in India

Evolving Therapies for Obesity

- Learnings from Bariatric Surgery
- An intervention leading to increased postprandial levels of multiple entero-pancreatic hormones
- The notion for combining entero-pancreatic hormone-based therapies for obesity

Eka Melson et al. International Journal of Obesity; https://doi.org/10.1038/s41366-024-01473-y.
Published online 01Feb 2024

Evolving Therapies for Obesity

- Numerous entero-pancreatic hormones with diverse metabolic actions are currently under investigation
  - GLP1 RA
  - GIP
  - GIP antagonists
  - Glucagon
  - Amylin
  - Peptide YY (PYY) agonists
- Either alone or in combination with GLP-1 RA
- Aiming to enhance and/or complement the effect of GLP-1 agonism on weight and metabolism

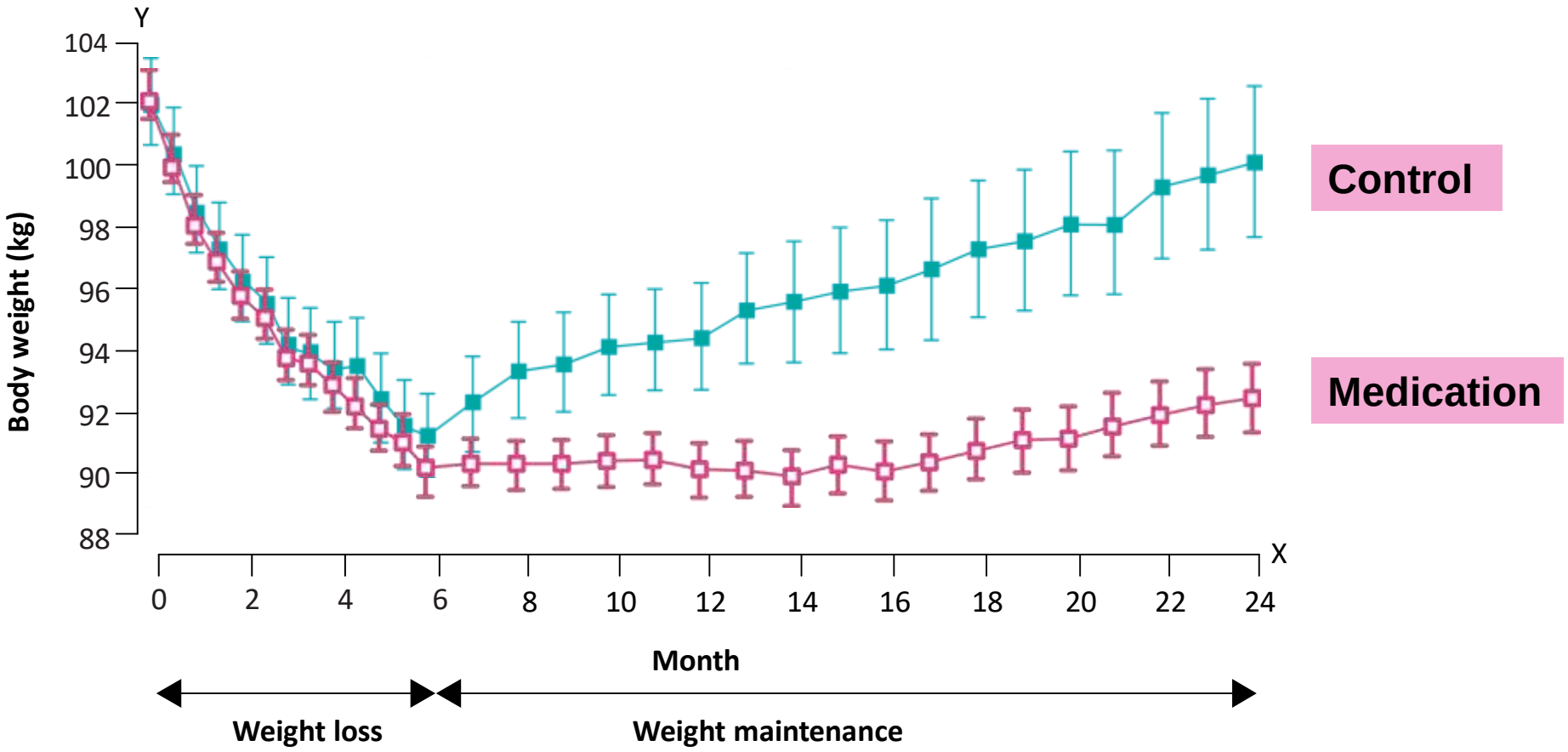
Eka Melson et al. International Journal of Obesity; https://doi.org/10.1038/s41366-024-01473-y. Published online 01Feb 2024

Evolving Therapies for Obesity

- SMART MOLECULES
  - Multiple receptor recognition
  - Balanced effect or selective bias for one receptor
  - Tri- and Tetra-
  - Combining GLP1ra with MAB
  - GLP1ra + PKA
  - Genetic interventions

Eka Melson et al. International Journal of Obesity; https://doi.org/10.1038/s41366-024-01473-y. Published online 01Feb 2024

Is There A Better Way to Manage Obesity?

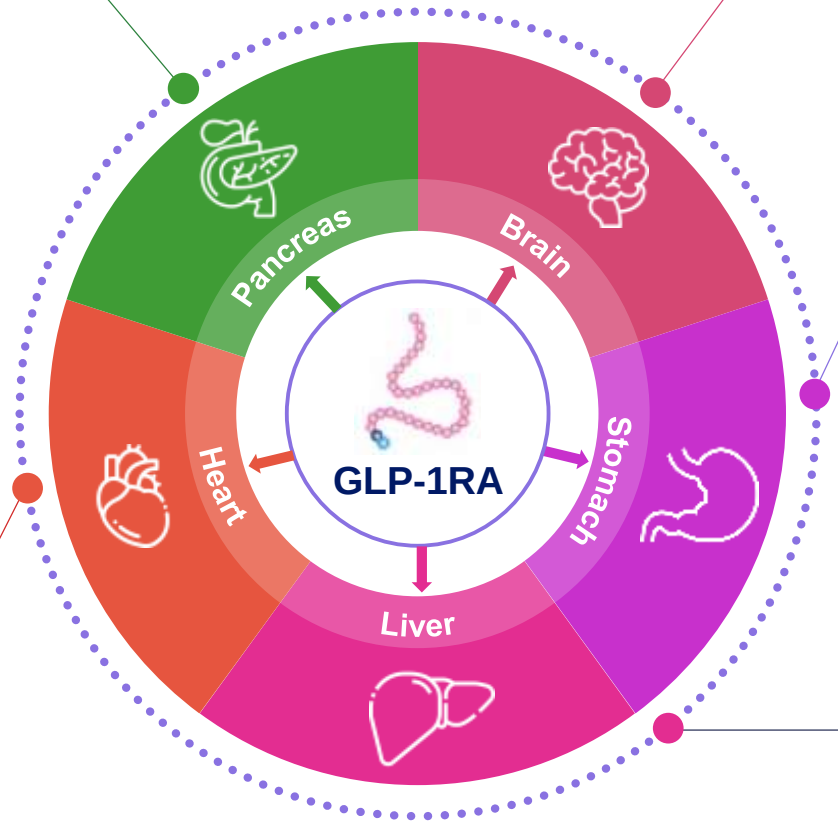


Long-term strategies (such as pharmacotherapy) to counteract this change may be needed to prevent obesity relapse

James *et al. Lancet.* 2000; 356:2119–2125..

GLP-1RAs have multifactorial effects

Pharmacological effects



Pancreas

- ↑ Beta-cell function[1]
- ↓ Beta-cell death[1]
- ↑ Insulin secretion and production[1]
- ↓ Glucose-dependent glucagon secretion[1]
- ↑ Glucose-dependent insulin secretion[1]

Brain

- ↓ Body weight[5]
- ↓ Food intake[6]
- ↑ Satiety[7,8]

Stomach

- ↓ Gastric emptying[9]

Heart

- ↓ Cardiovascular risk[2]
- ↓ Fatty acid metabolism[2]
- ↑ Cardiac function[3]
- ↓ Systolic blood pressure[3]
- ↓ Inflammation[4]

Liver

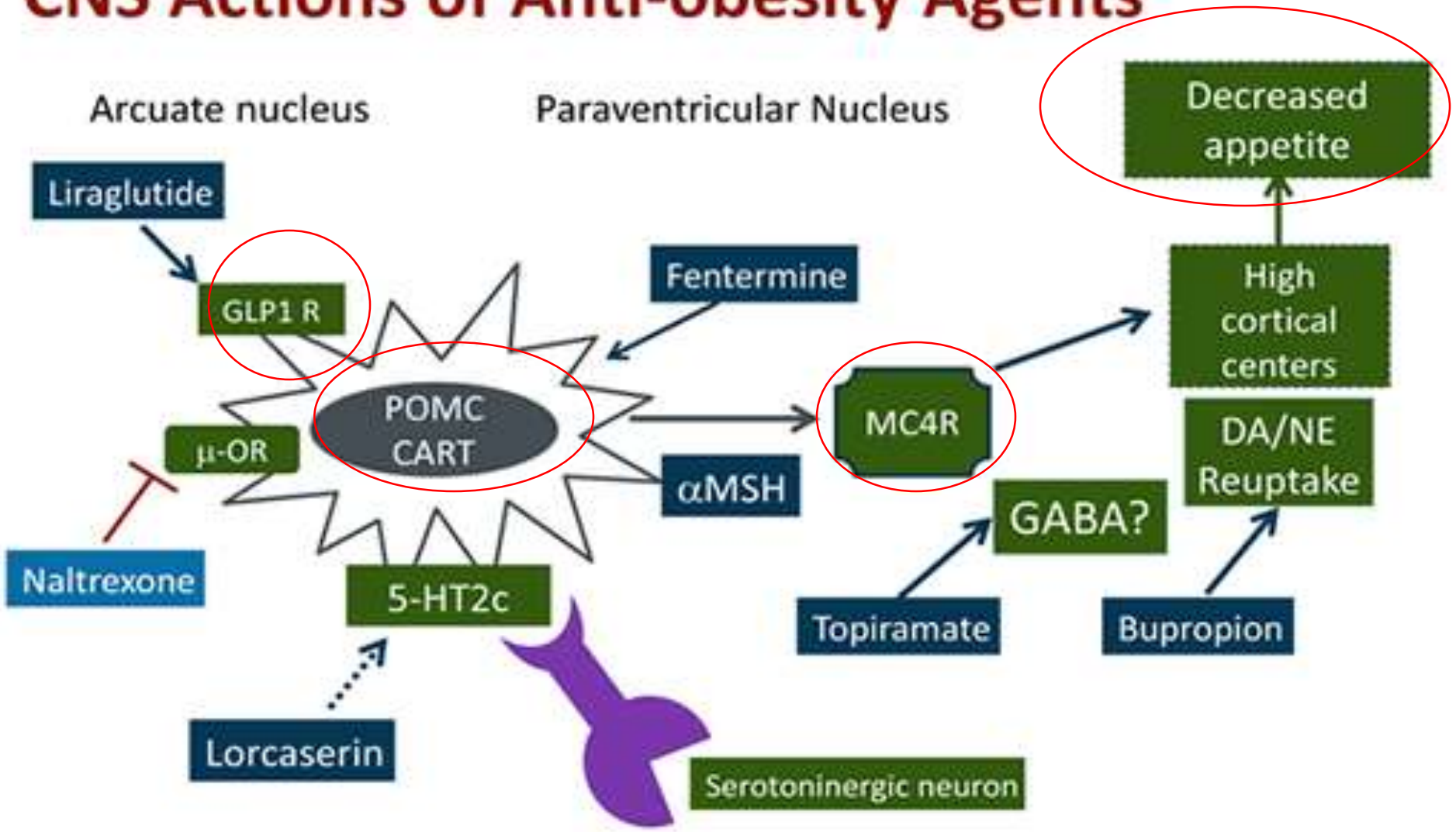
- ↓ Endogenous glucose production[10]
- ↑ Hepatic insulin sensitivity[10]
- ↓ *De novo* lipogenesis[10]
- ↓ Lipotoxicity[10]
- ↓ Steatosis[11]

GLP-1RA, glucagon-like peptide-1 receptor agonist.

1. Campbell JE, DJ Drucker. Cell Metab 2013;17:819–37; 2. Marso SP et al. N Engl J Med 2016;375:311–22; 3. Ryan D, Acosta A. Obesity 2015;23:1119–29; 4. Hogan AE et al. Diabetologia 2014;57:781–4; 5. Baggio LL, Drucker DJ. J Clin Invest 2014;124:4223–6; 6. Bagger JI et al. Clin Endocrinol Metab 2015;100:4541–52; 7. Flint A et al. J Clin Invest 1998;101:515–20; 8. Blundell J et al. Diabetes Obes Metab. 2017;19(9):1242–51; 9. Tong J, D'Alessio D. Diabetes 2014;63:407–9; 10. Armstrong MJ et al. J Hepatol 2016;64:399–408; 11. Armstrong MJ et al. Lancet 2016;387:679–90.

Clinical Benefits: Weight loss, Glycemic control, Cardiometabolic outcomes

CNS Actions of Anti-obesity Agents

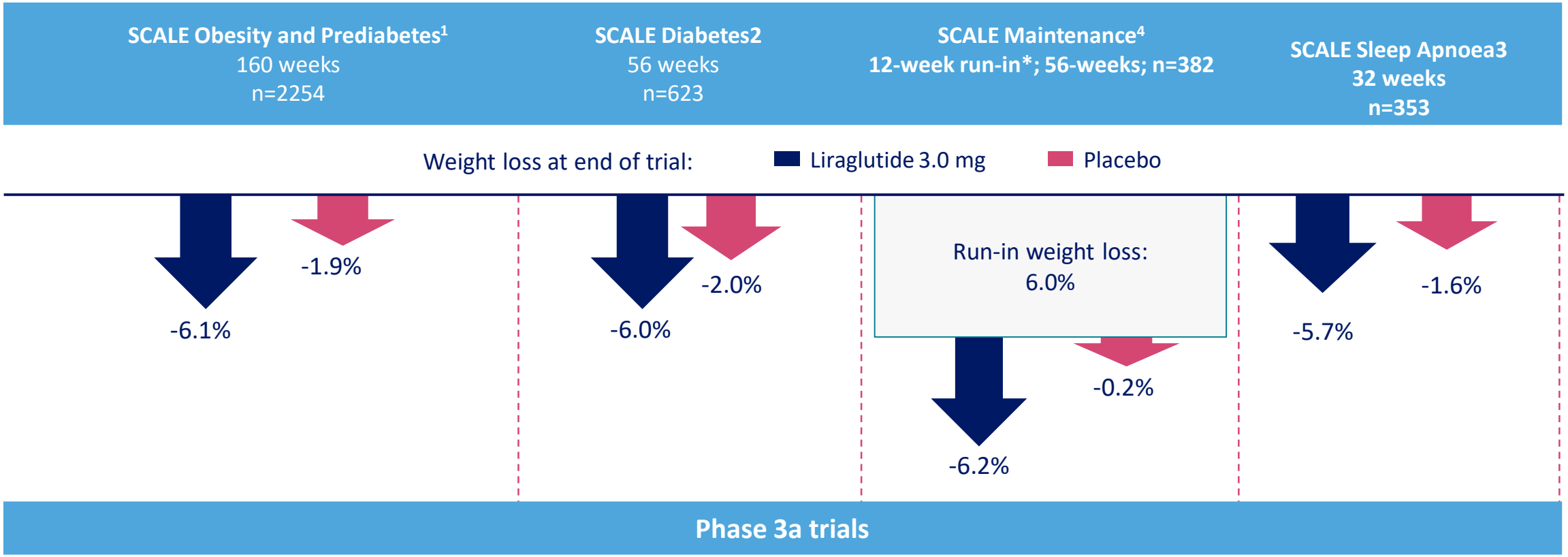


CART = cocaine- and amphetamine-regulated transcript; DA = dopamine; GABA = gamma-aminobutyric acid; MC4R = melanocortin receptor 4; NE = norepinephrine; POMC = pro-opiomelanocortin

Boughton CT, et al. *Br J Pharmacol*. 2013:170;1333-1348.
Sumithran P, et al. *Clin Sci (Lond)*. 2013:124:231-241,

Liraglutide 3.0 mg for weight management

Summary of phase 3a trial results



Data are observed means; last observation carried forward at end of trial; n, number of individuals contributing to the analysis
**Low calorie diet (total energy intake 1200–1400 kcal/day)*
1. le Roux CW et al. Lancet. 2017;389:1399–1409; 2. Davies et al. JAMA 2015;314:687–99; 3. Blackman et al. Int J Obes (Lond) 2016;40:1310–19; 4. Wadden et al. Int J Obes (Lond) 2013;37:1443–51

Role of GLP-1RA -Semaglutide

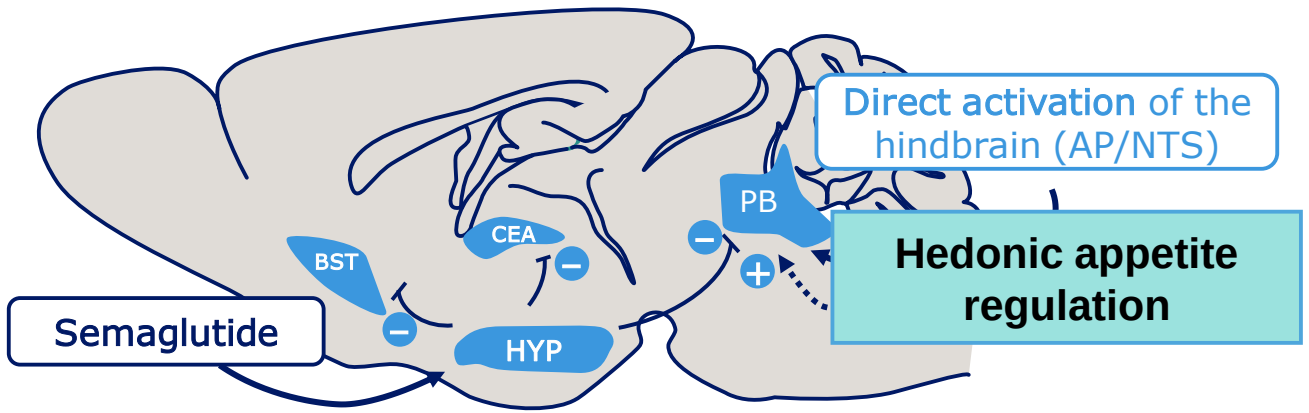
Semaglutide is a human GLP-1 analogue

- 94% homology to human GLP-1
- $t_{½}$ of approximately 1 week

Amino acid substitution at position 8 (alanine to alpha-aminoisobutyric acid) protects against DPP-4 degradation[1]

Spacer and C-18 fatty di-acid chain to lysine in position 26 provide strong binding to albumin

Amino acid substitution at position 34 (lysine to arginine) prevents C-18 fatty di-acid binding at the wrong site

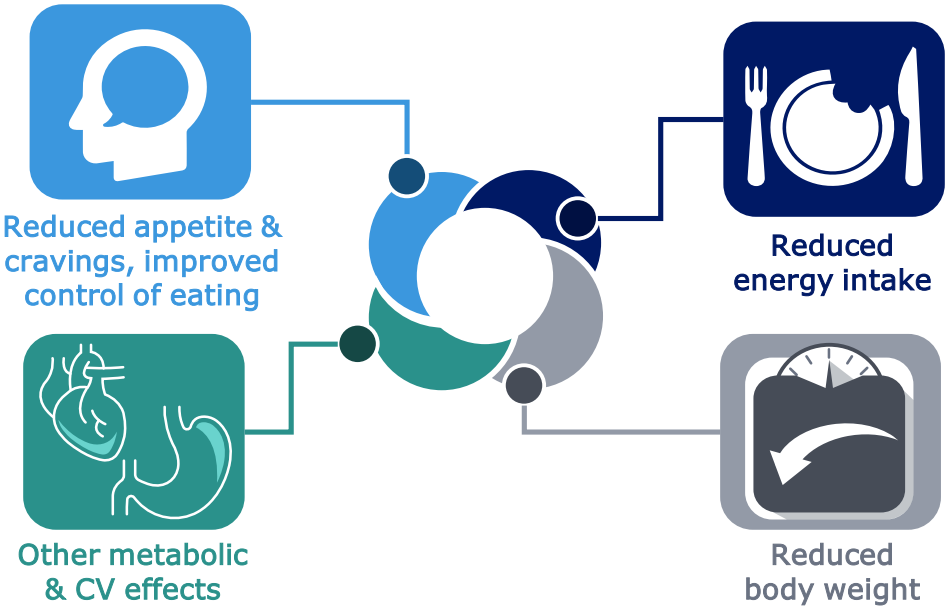


Direct activation of the hindbrain (AP/NTS)

Direct activation of the hypothalamus (HYP)

Hedonic appetite regulation

Homestatic appetite regulation



AP/NTS, area p -1, glucagon-like peptide-1; t1/2, half life.

Adapted from C

Higher weight loss has been seen with Semaglutide 2.4 mg

Up to

18%

mean weight loss with semaglutide **2.4 mg**

≥20%

weight loss in **>1 in 3** patients[2]

Sustained

weight loss over

4 years

with **Wegovy®**[3]

Wegovy® is indicated in people with BMI

- 30 kg/m² or greater (obesity) or
- 27 kg/m² or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia).

Data are for the in-trial period. BW, body weight; IBT, intensive behavioural therapy.

1. Wilding et al. N Engl J Med 2021; doi:10.1056/NEJMoa2032183; 2. Davies et al. Lancet, 2021; doi.org/10.1016/S0140-6736(21)00213-0: 3. Wadden et al. JAMA. doi:10.1001/jama.2021.1831; 4. Rubino et al. JAMA. 2021 Apr 13;325(14):1414-1425. doi: 10.1001/jama.2021.3224. 5. Garvey et al. Nat Med 28, 2083–2091 (2022); 6. Kadowaki et al. The Lancet Diabetes & Endocrinology 2022., 7. Mu, Y., et al. The Lancet Diabetes & Endocrinology, 2024. 12(3): p. 184-1958. Rubino et al. JAMA 2022; 327(2): 138-150

Semaglutide 1mg reduces A1c by 2.8% in people with high baseline A1c levels

2.8%

PROVEN TO BE SUPERIOR VS OTHER ANTI DIABETIC AGENTS

- Vs SGLT-2i*
- Vs basal insulin*
- Vs DPP-4i*
- Vs other GLP-1 RAs*
- In drug-naïve T2D

4 Out of 5

PwT2D achieved A1c

<7%

A1C reduction seen in patients whose baseline A1C was more than 9%
SUSTAIN 7.Pratley RE et al. Lancet Diabetes Endocrinol 2018;6:275–86; Aroda VR et al. Diabetes & metabolism. 2019 Oct 1;45(5):409-18.

82% participants achieved HbA1c target of <7% with Semaglutide 2.4mg

In people with overweight/obesity and T2D – STEP 2

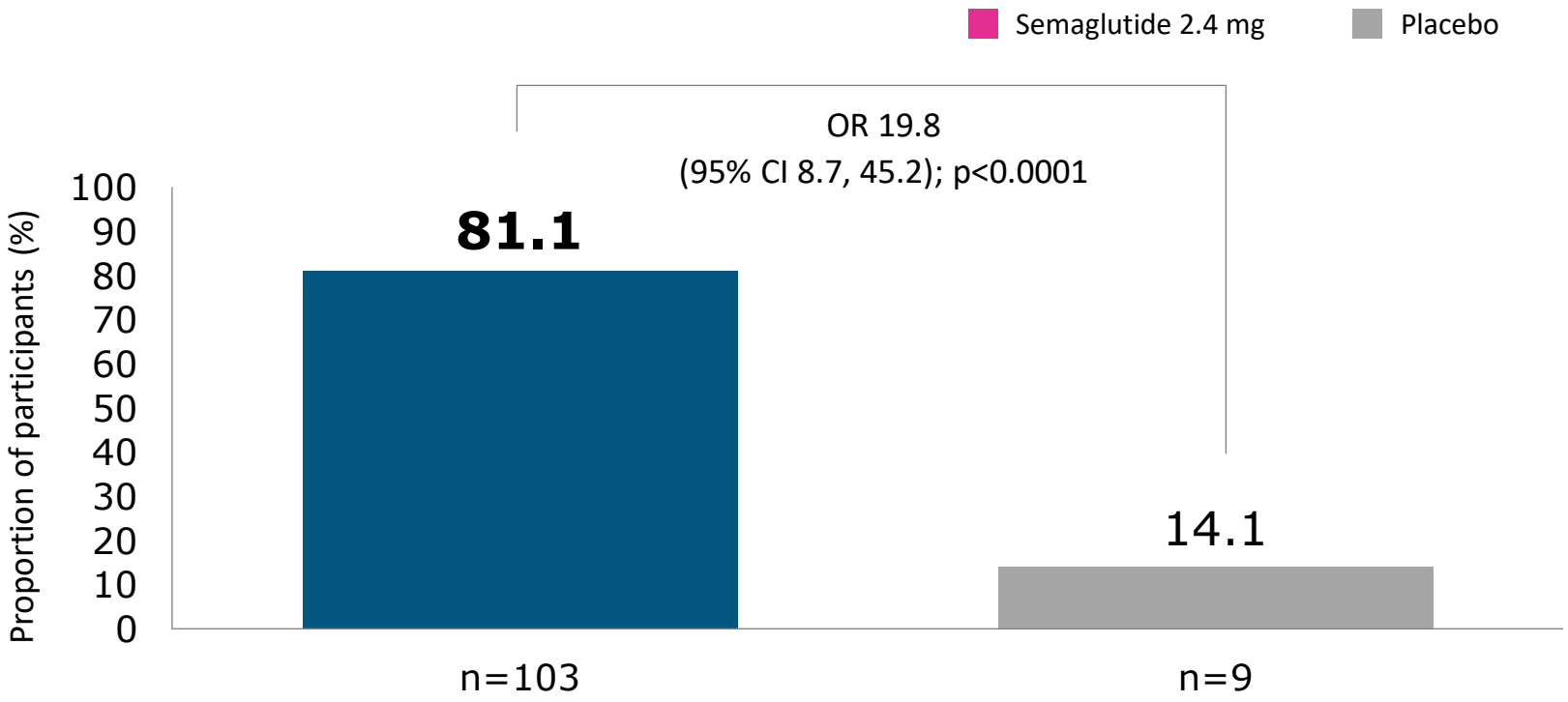
1.9 % **reduction in A1c at 68 weeks**

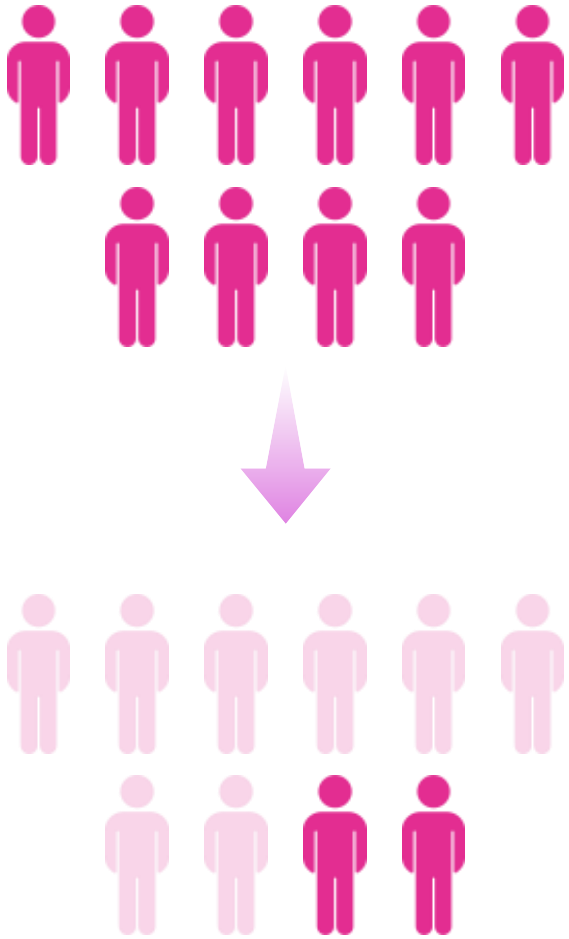
Note: Davies et al. Lancet 2021;397:971-84.

>80% with pre-diabetes reversed to normoglycaemia

In people with overweight/obesity and pre-diabetes – STEP 10

Reversion to normoglycaemia at week 52



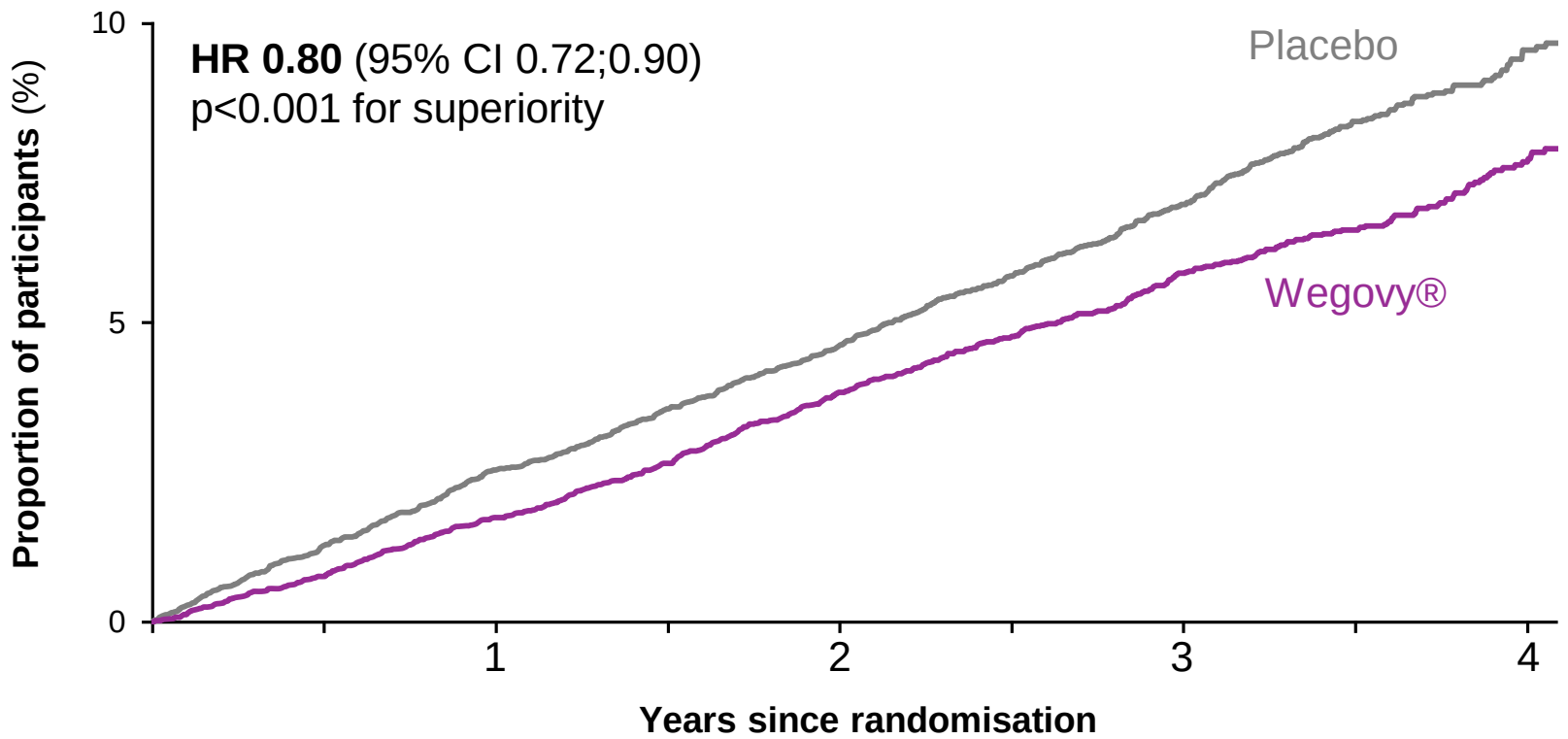


Note: McGowan, B et al. Obes Facts 2024;17(suppl 1):72

Semglutide2.4mg reduced the risk of MACE by 20% vs placebo

SELECT
In people with BMI ≥27 kg/m² and CVD without T2D

Primary outcome: Time from randomisation to first occurrence of 3-point MACE*



Adapted from Lincoff AM et al. *N Engl J Med* 2023;389:2221−32. *Defined as cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke. Efficacy analyses are based on the intention-to-treat population.
BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; MACE, major adverse cardiovascular events; OW, once-weekly; s.c., subcutaneous.Lincoff AM et al. *N Engl J Med* 2023;389:2221−32.

Semaglutide 2.4mg (Wegovy®) has demonstrated improvements to multiple modifiable risk factors known to drive CV outcomes[1-5]

Waist circumference

Reduction Up to

6.3 inches

CRP

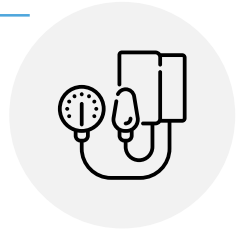
Up to

-63.4%

SBP

Up to

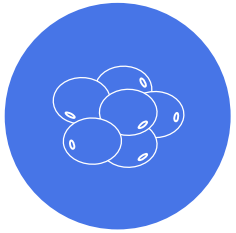
-10.9 mmHg



DBP

Up to

-5.3 mmHg



Triglycerides

Up to

-22%

*Tretament policy estimand (since trialproduct estimand of 20% or more weight loss end pioint was npt calculated in STEP 2) CV, cardiovascular; HbA1c, glycated haemoglobin; hs-CRP, high sensitivity C-reactive protein.

1. Lincoff AM et al. N Engl J Med 2023;359:2221–32; 2. Marso SP et al. N Engl J Med 2016;375:1834–44; 3. McGuire DK et al. N Engl J Med 2025;392:2001–12; 4. Perkovic V et al. N Engl J Med 2024;391:109–21;
5. Mulvagh SL et al. Presented at the European Society of Cardiology 2025, 29 August–1 September 2025, Madrid, Spain.

Proposed Roles of GIP and GLP-1 in Regulation of Metabolism[1,2,*]

GLP-1 activity

Central nervous system

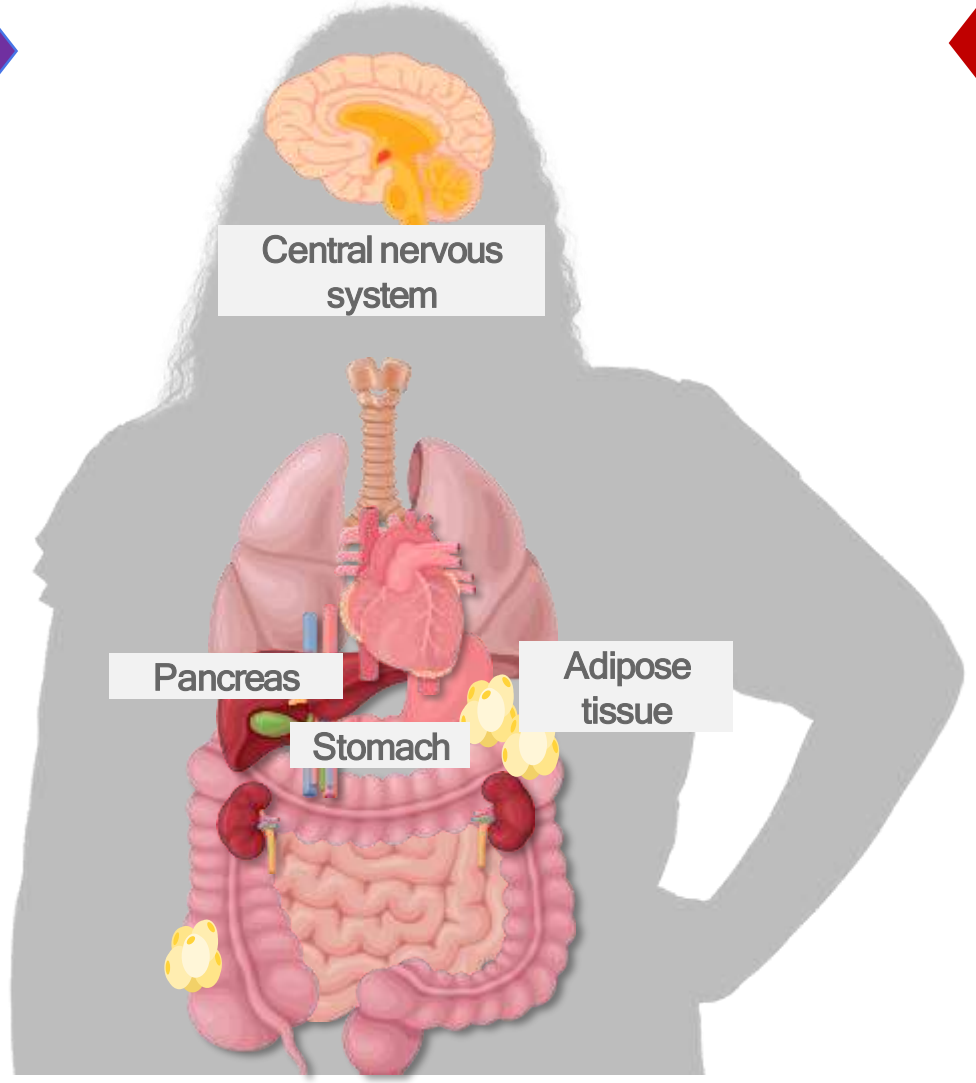
- ▼ Reduced food intake
- ▲ Increased satiety
- ▲ Increased nausea

Pancreas

- ▲ Increased insulin secretion
- ▼ Reduced glucagon

Stomach

- ▼ Delayed gastric emptying



GIP activity

Central nervous system

- ▼ Reduced food intake*
- ▼ Decreased nausea

Pancreas

- ▲ Increased insulin secretion
- ▲ Increased glucagon secretion in a glucose-dependent way

Adipose tissue

- ▲ Increased insulin sensitivity*
- ▲ Increased lipid-buffering capacity*
- ▲ Increased blood flow
- ▲ Increased storage capacity*
- ▼ Reduced proinflammatory immune-cell infiltration

*Demonstrated in preclinical research

Glucose-dependent insulin secretion

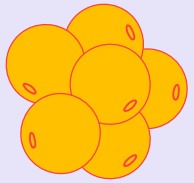
In healthy individuals, **GIP** is estimated to contribute **50-71%** of the incretin effect[1]

Pancreas

Glucose-dependent glucagon secretion

Direct action on the alpha cell[2]

Insulin-dependent fatty acid uptake and mobilization



FAT

Regulation of lipolysis and lipogenesis; direct action on adipocytes[3,4]

GIP

Inhibition of food intake, antiemetic and neuroprotective effects

CNS

Actions in hypothalamus and brainstem[7]

Antiemetic and neuroprotective effects[8,9]

Increased adipose and splanchnic blood flow

Vasculature

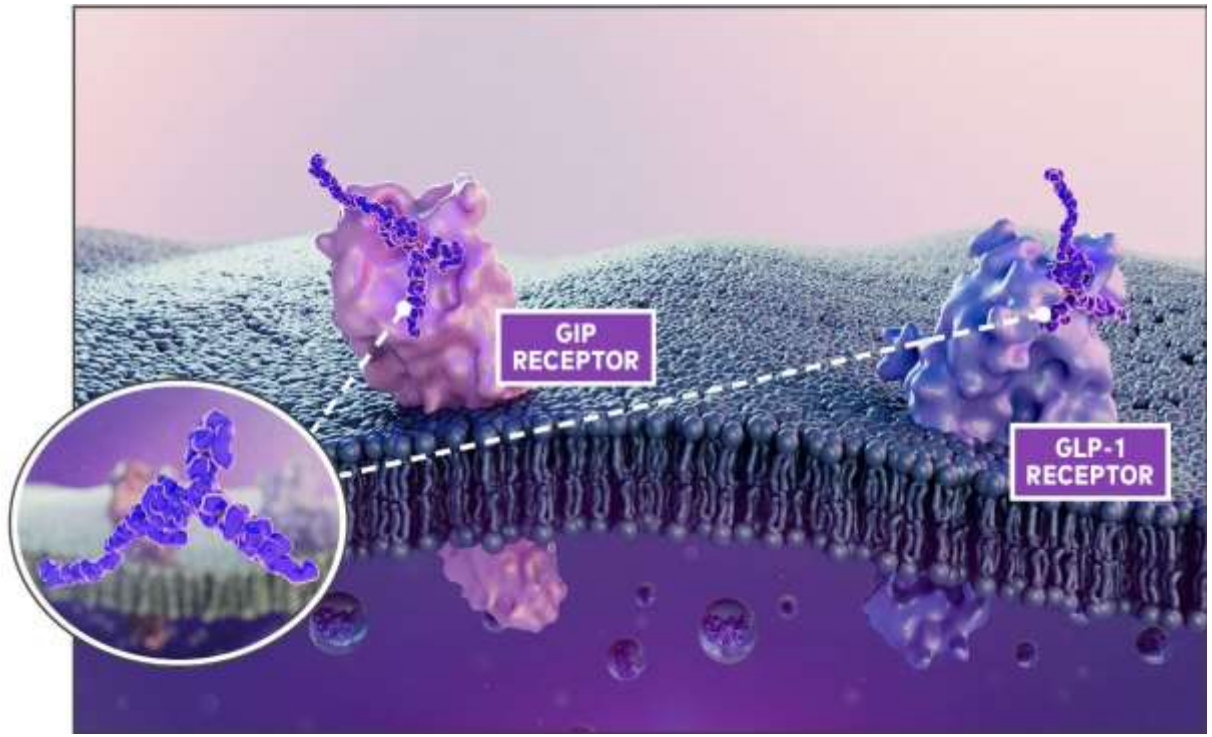
Insulin-dependent increase in adipose tissue blood flow[5]

Direct effects on endothelial cells[6]

1. Gasbjerg et al (2019), *Diabetes* 68:906-917. 2. Gylfe et al. (2014) *Diab Res Clin Pract* 103(1):1-10 3. Yip and Wolfe (2000) Life Sci 66:91-103. 4. Regmi et al (2024) Cell Metab 36:1534-495. Asmar et al (2016) *J Clin Endocirnol Metab* 10:3155-62. 6. Ding et al (2004) Am J Physiol Endocrinol Metab 286:E773-9 7. Adriaenssens (2023) *JCI Insights* 8:e164921. 8. Borner et al (2021) *Diabetes* 70:2545-2553.. 9. Adriaenssens (2020) *Peptides* 125:170194.

Tirzepatide Is a Single Molecule Designed to Activate Both the GIP and GLP-1 Receptors[1]

Structure	Based on the **native GIP sequence**[1,2]
Receptor activity	**Activity on the GIP receptor is similar to the native GIP hormone**, whereas **activity on the GLP-1 receptor is lower compared to the native GLP-1 hormone**[2]
Mean half-life	**Approximately 5 days**, enabling once-weekly dosing[3]
Dose adjustment	**No dose adjustment** of Tirzepatide is recommended for **patients with renal or hepatic impairment**[2]



*Tirzepatide has not been studied in patients with end-stage renal and liver disease.

GIP=glucose-dependent insulinotropic polypeptide; GLP-1=glucagon-like peptide-1.

1. Tirzepatide, India Prescribing Information. Updated Mar 2025.

Tirzepatide – Approved Indications

1 Type 2 Diabetes

Tirzepatide is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise

- as monotherapy when metformin is considered inappropriate due to intolerance or contraindications
- in addition to other medicinal products for the treatment of diabetes. [1]

2 • Chronic Weight Management

- Tirzepatide is indicated as an adjunct to a reduced-calorie diet and increased physical activity for weight management, including weight loss and weight maintenance, in adults with an initial Body Mass Index (BMI) of
  - ≥ 30 kg/m^2 (obesity) or
  - ≥ 27 kg/m^2 to < 30 kg/m^2 (overweight) in the presence of at least one weight-related co-morbid condition (e.g., hypertension, dyslipidaemia, obstructive sleep apnoea, cardiovascular disease, prediabetes, or type 2 diabetes mellitus).

1. Tirzepatide (once weekly) India PI Updated Mar 2025

Tirzepatide for Weight Management Was Evaluated in a Robust Clinical Trial Program Involving >5800 Participants[1]

SURMOUNT-1[1,2]	**Weight management**	Tirzepatide 5 mg Tirzepatide 10 mg Tirzepatide 15 mg Placebo	2539 participants	72 weeks	Double-blind
SURMOUNT-2[1,3]	**Weight management with T2D**	Tirzepatide 10 mg Tirzepatide 15 mg Placebo	938 participants	72 weeks	Double-blind
SURMOUNT-3[1,4]	**Weight management after intensive lifestyle modification**	Intensive lifestyle program (12 weeks) → Tirzepatide max tolerated dose[a] Intensive lifestyle program (12 weeks) → Placebo	806 participants	84 weeks	Double-blind
SURMOUNT-4[1,5]	**Weight reduction maintenance**	Tirzepatide max tolerated dose[a] (36 weeks) → Tirzepatide max tolerated dose[a] Tirzepatide max tolerated dose[a] (36 weeks) → Placebo	783 participants	88 weeks	Double-blind
SURMOUNT-5[1,6]	**Weight reduction compared to Semaglutide MTD**	Tirzepatide MTD[a] Semaglutide MTD[b]	750 participants	72 weeks	Open Label

[a] Tirzepatide MTD - 10 mg or 15 mg [b] Semaglutide MTD – 17 mg or 2.4 mg | T2D=Type 2 Diabetes.

1. le Roux CW, et al. Obesity (Silver Spring). 2023;31(1):96-110. 2. Jastreboff AM, et al. N Engl J Med. 2022;387(3):205-216. 3. Garvey WT, et al. Lancet. 2023;402(10402):613-626. 4. Wadden TA, et al. Nat Med. 2023;29:2909-2918 5. Aronne LJ, et al. JAMA 2024; 331(1): 38–486. Louis J. Aronne, M.D., et al. Tirzepatide as Compared with Semaglutide for the Treatment of Obesity,N Engl J Med. 2025; doi: 10.1056/NEJMoa2416394

Summary

Tirzepatide significantly reduced body weight by an average of

- **16.0%[1,*] with 5mg**
- **22.5%[1,*] with 15 mg**

Tirzepatide MTD demonstrated superior **weight** reduction vs **Semaglutide MTD** of **21.6%[3]** vs **15.4%[3]**

Improvements in key cardiometabolic parameters

- Blood pressure
- Waist Circumference
- Triglycerides
- HDL cholesterol[1,#]

The most common adverse reactions were **gastrointestinal** in nature and were **mostly mild to moderate**

*P<0.001 vs baseline. Mean % change in weight vs baseline (co-primary endpoint) at 72 weeks was -16.0% and -21.4% for the 5 mg and 10 mg doses respectively. Mean % change in weight vs placebo at 72 weeks was -13.5%, -18.9%, -20.1% for the 5 mg, 10 mg and 15 mg doses respectively (P<0.001 vs placebo, adjusted for multiplicity).[1,2]
Tirzepatide is not indicated for the treatment of hypertension and or dyslipidemia

GI=gastrointestinal; HDL=high-density lipoprotein.

1. Tirzepatide, India Prescribing Information. Updated Mar 2025.. 2. Jastreboff AM, et al. N Engl J Med. 2022;387(3): 205-216 (and supplementary appendix). 3. Louis J. Aronne, M.D., et al. Tirzepatide as Compared with Semaglutide for the Treatment of Obesity,N Engl J Med. 2025; doi: 10.1056/NEJMoa2416394

Patient selection and Real applicability

Semaglutide has been studied in **>3,500** participants from **INDIA***

	SEMAGLUTIDE s.c. 2.4mg = Total 858		SEMAGLUTIDE s.c. 1.0mg = Total 1246		ORAL SEMAGLUTIDE = Total 1667	
COMPLETED	STEP 1 semaglutide | treatment effect in people with obesity	117	SUSTAIN 2 SEMAGLUTIDE UNABATED SUSTAINABILITY IN TREATMENT OF TYPE 2 DIABETES	95	PIONEER 8 Peptide InnOvation for Early diabEtes tReatment	51
	STEP 2 semaglutide | treatment effect in people with obesity	164	SUSTAIN 4 SEMAGLUTIDE UNABATED SUSTAINABILITY IN TREATMENT OF TYPE 2 DIABETES	83	PIONEER 6 Peptide InnOvation for Early diabEtes tReatment	201
	SELECT semaglutide | effects of cardiovascular outcomes in people with overweight or obesity	492	SUSTAIN 7 SEMAGLUTIDE UNABATED SUSTAINABILITY IN TREATMENT OF TYPE 2 DIABETES	130	PIONEER+ Peptide InnOvation for Early diabEtes tReatment	214
	STEP-HFpEF-DM	55	SUSTAIN 8 SEMAGLUTIDE UNABATED SUSTAINABILITY IN TREATMENT OF TYPE 2 DIABETES	50	PIONEER REAL India Peptide InnOvation for Early diabEtes tReatment	388
		Total 828	SUSTAIN 11 SEMAGLUTIDE UNABATED SUSTAINABILITY IN TREATMENT OF TYPE 2 DIABETES	346	SOUL semaglutide | cardiovascular outcomes trial	788
			NN9535-1821	60		Total 1642
			FLOW semaglutide | renal outcomes trial	231		
			STRIDE semaglutide | study in peripheral arterial disease	33		
				Total 1028		
ONGOING	ESSENCE semaglutide | effects and outcomes in NASH	30	FOCUS semaglutide | diabetic retinopathy outcomes trial	218	PIONEERTEENS	25
		Total 30		Total 218		Total 25

*Based on Novo Nordisk data file

novo nordisk®

ONCE-WEEKLY wegovy® semaglutide injection 2.4 mg

Which patients in your practice are suitable for Semaglutide 2.4mg?

Wegovy®, as an adjunct to a reduced-energy diet and increased physical activity, is suitable for adults & adolescent.

Chronic weight management
(≥18 years) with an initial BMI of

≥27 kg/m² (overweight) with at least one weight-related comorbidity.

OR

≥30 kg/m² (obesity) with no requirement for a weight-based comorbidity.

Chronic weight management
(≥12 years) with

- obesity*
- body weight above 60 kg.

Wegovy® 2.4 mg is indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established cardiovascular disease and either obesity or overweight.

Note: **BMI:** body mass index.

1. Wegovy® (Wegovy® 2.4 mg) Approved Product Information. 2. Madhu, S V & Kapoor, Nitin & Sambit, Das & Raizada, Nishant & Sanjay, Kalra. (2022). ESI Clinical Practice Guidelines for the Evaluation and Management of Obesity In India. Indian journal of endocrinology and metabolism. 26. 295-318. 10.4103/2230-8210.356236. 3. Deshpande NR et al. . Consensus on Current Landscape and Treatment Trends of Obesity in India for Primary Care Physicians. J Assoc Physicians India. 2023 Oct;71(10):69-77. *Obesity (BMI ≥95th percentile) as defined on sex- and age-specific BMI growth charts (CDC.gov)

Semglutide 2.4 mg is the clinically proven maintenance dose for weight management

4 doses in each pen

Start

0.25 mg

Weeks 1-4

Month 1

Step Up

0.5 mg

Weeks 5-8

Month 2

1.0 mg

Weeks 9-12

Month 3

1.7 mg

Weeks 13-16

Month 4

Stay

2.4 mg

Weeks 17 onwards

Month 5

The therapeutic maintenance dose of 2.4 mg weekly is reached with a stepwise 4-weekly dose titration schedule.[1]

The dose escalation of 4-week intervals can help reduce the likelihood of gastrointestinal-related side effects and can be delayed in the case of significant gastrointestinal symptoms.[1]

1. Wegovy® (semaglutide 2.4 mg) Approved Product Information.
2. Wilding JPH, et al. N Eng J Med. 2021;384:989–1002. 3. Rubino D, et al. JAMA. 2021;325:1414–25. 4. Garvey WT, et al. Nat Med. 2022;28:2083–91.

Semaglutide 2.4mg safety profile is consistent with the GLP-1 RA class

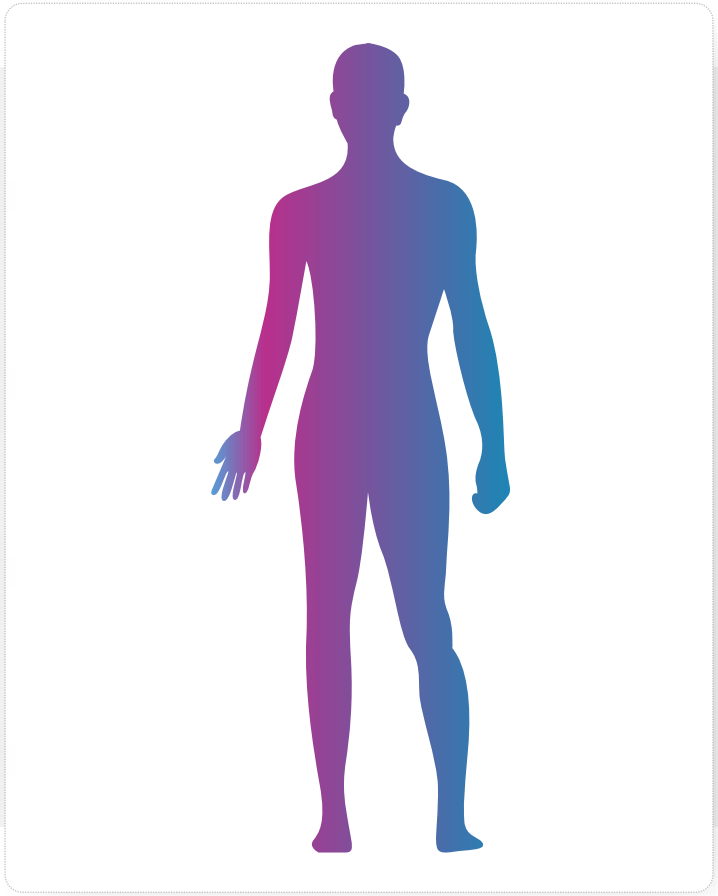
STEP trials

Well tolerated, safety profile similar to other GLP-1RAs (4.3% discontinuation)

GI AEs, were the most commonly reported AEs:

Observed rates of hypoglycaemia in STEP 2 were 6.2% vs 2.5%

Cholelithiasis was reported in 1.6% patients receiving semaglutide 2.4 mg (vs 1.1%)



Very few events of pancreatitis (0.2% vs <0.1%)

No increased risk of malignant neoplasms

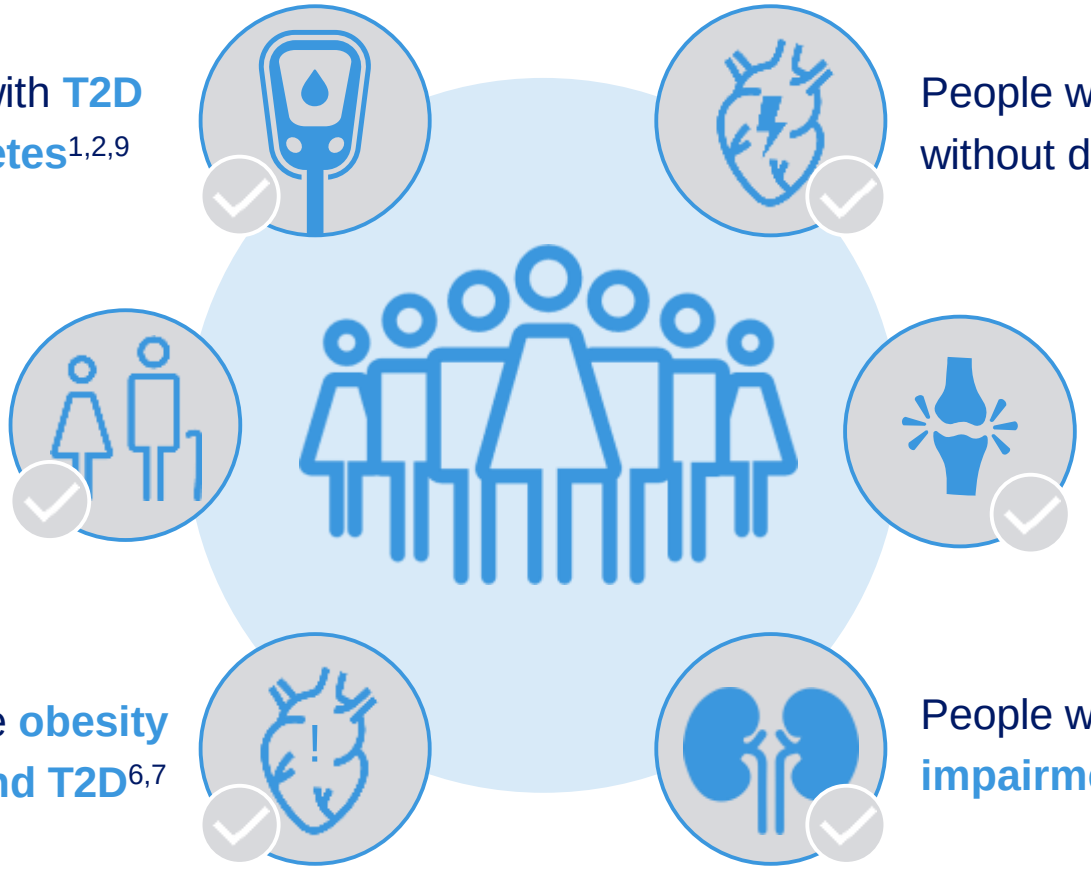
No increased risk of DR in PwO without T2D (STEP 2: few episodes in T2D 6.9% vs 4.2%)

No increased risk of CV events

Note: AE, adverse event; CV, cardiovascular; DR, diabetic retinopathy; GI, gastrointestinal; GLP-1RA, glucagon-like peptide-1 receptor agonist; PwO, people with obesity; T2D; type 2 diabetes.

1. Wilding J et al. N Engl J Med 2021;384:989–1002; 2. Davies MJ et al. Lancet 2021;397:971–84; 3. Wadden T et al. JAMA 2021;325:1403–13; 4. Rubino D et al. JAMA 2021;325:1414–25.

The safety profile of semaglutide 2.4 mg has been established in diverse populations of people with overweight or obesity



People with **T2D or prediabetes**[1,2,9]

People with **CVD**, without diabetes[3]

Adolescents and the **elderly**[3,8]

People with **knee osteoarthritis**[4]

People with the **obesity phenotype of HFpEF and T2D**[6,7]

People with **renal impairment**[1,5*]

**The STEP 2 trial included patients with mild to severe renal impairment, and with eGFR levels ranging from 15 to 90 mL/min per 1.73 m².*
CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HFpEF, heart failure with preserved ejection fraction; STEP, semaglutide treatment effect in people with obesity; T2D, type 2 diabetes.
1. Davies M, et al. Lancet. *2021;397:971-984. 2. Wilding JPH, et al.* N Engl J Med. *2021;384(11):989. 3. Lincoff AM, et al.* N Engl J Med. *2023;DOI:10.1056/NEJMoa2307563. 4. Bliddal H, et al. Obes Facts 2024;17(suppl 1):72.*
5. Lingvay I, et al. Obesity (Silver Spring). 2023 Jan;31(1):111-122. 6. Kosiborod MN, et al. N Eng J Med. 2023; DOI: 10.1056/NEJMoa2306963. *7. Kosiborod MN, et al.* N Engl J Med. *2024;DOI: 10.1056/NEJMoa2313917. 8. Weghuber D, et al.* N Engl J Med. *2022;387(24):2245-2257. 9. McGowan, B et al. Obes Facts 2024;17(suppl 1):7*

Semglutide 2.4mg (Wegovy®) - Tried, Tested and Trusted globally

Semaglutide has been studied in

~60,000 people across STEP, SUSTAIN and PIONEER clinical trial programs across

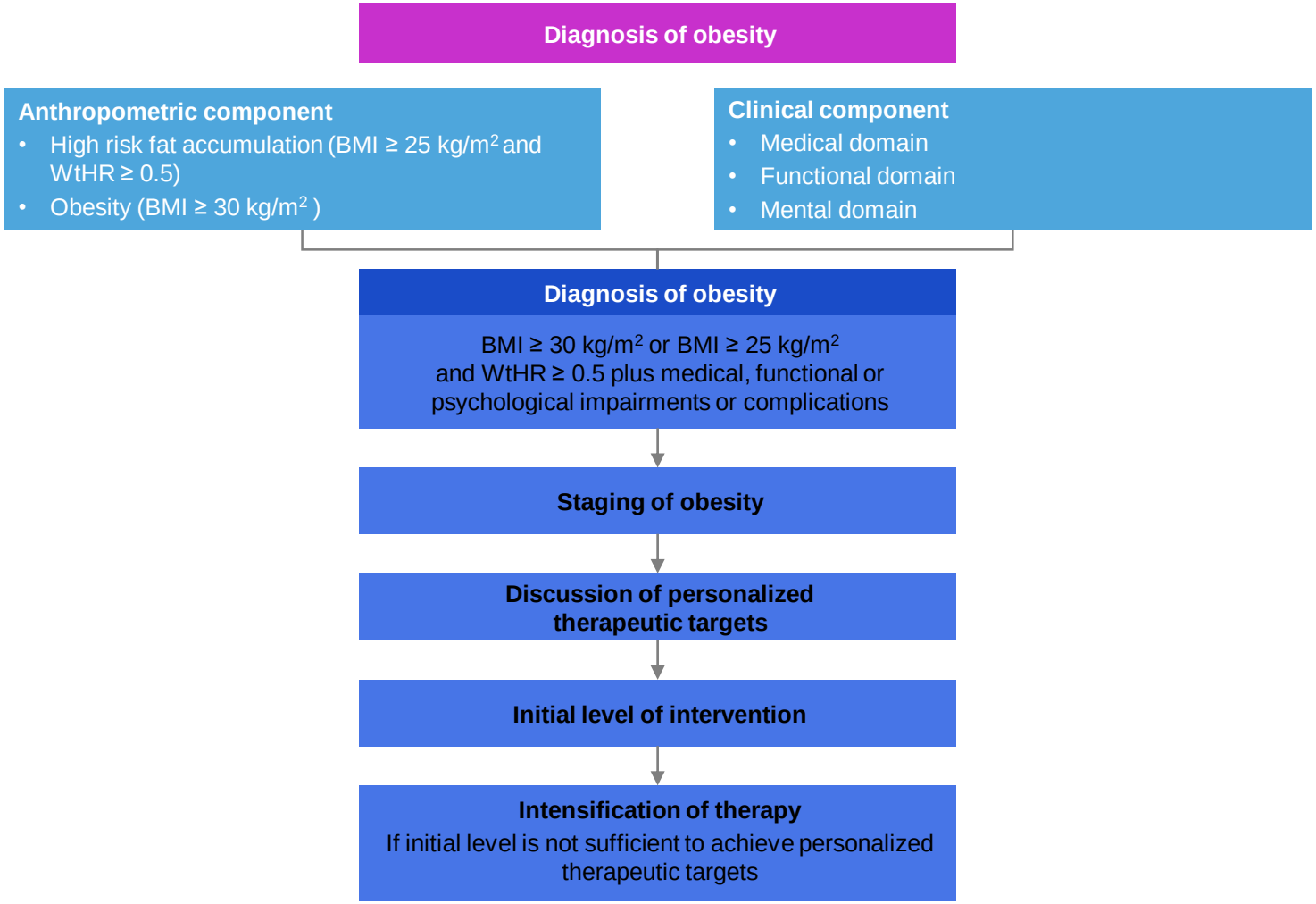
Semaglutide has a worldwide cumulative exposure of more than **49 million patient-years** across indications since 2018

Note: LP-1 RA, glucagon-like peptide-1 receptor agonist; STEP, semaglutide treatment effect in people with obesity.
1. Wilding JPH, et al. N Engl J Med. 2021;384:989–1002. 2. Davies M, et al. Lancet. 2021;397:971–84. 3. Wadden TA, et al. JAMA. 2021;325:1403–13. 4. Rubino D, et al. JAMA. 2021;325:1414–25. 5. Kosiborod MN, et al. N Engl J Med. 2023;21:1069–84. 6. Weghuber D, et al. N Engl J Med. 2022;387:2245–57. 7. Kadowaki T, et al. Lancet Diabetes Endocrinol. 2022;10:193–206. 8. Mu Y, et al. Lancet Diabetes Endocrinol. 2024;12:184–195. 9. Garvey WT, et al. Nat Med. 2022;28:2083–91. 10. Rubino DM, et al. JAMA. 2022;327:138–50. 11. Kosiborod MN, et al. N Engl J Med. 2024;DOI: 10.1056/NEJMoa2313917. 12. McGowan BM, et al. Lancet Diabetes Endocrinol. 2024;12:631-642. 13. Lincoff AM, et al. N Engl J Med. 2023;DOI:10.1056/NEJMoa2307563. 14. ClinicalTrials.gov. NCT04998136. 15. Bliddal H, et al. Obes Facts. 2024;17(suppl 1):72. 16. Novo Nordisk A/S, STEP UP CA. https://www.novonordisk.com/content/nncorp/global/en/news-and-media/news-and-ir-materials/news-details.html?id=915087. 17. Aroda VR et al. Diabetes Care 2019;42:1724–32; 18. Rodbard HW et al. Diabetes Care. 2019;42(12):2272–2281; 19. Rosenstock J et al. JAMA 2019;321:1466–80; 20. Pratley R et al. Lancet 2019;394:39–50; 21. Mosenzon O et al. Lancet Diabetes Endocrinol 2019;7:515–27; 22. Husain M et al. N Engl J Med 2019. 381:841–51; 23. Pieber TR et al. Lancet Diabetes Endocrinol 2019;7:528–39; 24. Zinman B et al. Diabetes Care. 2019;42(12):2262–2271. 25.Yamada et al. Lancet Diabetes Endocrinol 2020;8:377–91; 26. Yabe et al. Lancet Diabetes Endocrinol 2020;8:392–6; 27.Aroda V, Lancet 2023; doi.10.1016/S0140-6736(23)01127-3; 28. Sorli C et al. Lancet Diabetes Endocrinol 2017;5:251–60; 29. Ahrén B et al. Lancet Diabetes Endocrinol 2017;5:341–54; 30. Ahmann AJ et al. Diabetes Care 2018;41:258–66; 31. Aroda VR et al. Lancet Diabetes Endocrinol 2017;5:355–66; 32. Rodbard HW et al. J Clin Endocrinol Metab 2018;103:2291–301; 33. Marso SP et al. N Engl J Med 2016;375:1834–44; 34. Pratley RE et al. Lancet Diabetes Endocrinol 2018;6:275–86; 35. Lingvay I et al. Lancet Diabetes Endocrinol 2019;7:834–44; 36. Zinman B et al. Lancet Diabetes Endocrinol 2019;7:356–67; 37. Capehorn MS et al. Diabetes Metab 2020;46:100–9; 38. Kellerer M et al. Diabetes, obesity and metabolism 2022, https://doi.org/10.1111/dom.14765; 39. Seino Y et al. Diabetes Obes Metab 2018;20:378–88; 40. Ji L et al, Diabetes Obes Metab. 2021 Feb;23(2):404-414; 41. Kaku K et al. Diabetes Obes Metab 2018;20:1202–12; 42. Frías JP et al, Lancet Diabetes Endocrinol. 2021 Sep;9(9):563-574; 43. Perkovic V, et al. N Engl J Med. 2024: DOI: 10.1056/NEJMoa2403347; 44. ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT03811561; 45. https://clinicaltrials.gov/study/NCT05514535. Accessed December 2022;. https://clinicaltrials.gov/ct2/show/NCT04560998; 46. Bergmann NC, et al. Diabetes Obes Metab. 2023;25:18-35; 47. Data of file (IQVIA MIDAS® monthly volume sales data from 2018 to 2024). Novo Nordisk A/S, Bagsværd, Denmark.

Transition from conventional treatments (Lifestyle, Diet, OADs, insulin) to GLP-1

A new framework for the diagnosis, staging and management of obesity in adults

A new framework For the diagnosis, staging and management of obesity in adults. This flowchart of the diagnostic and therapeutic pathways results from the statements in Table 1. WtHR, waist-to-height ratio



Busetto L et al. Nat Med 2024;30:2395

Stepped approach to obesity management

	BMI 25–26.9 kg/m²	BMI 27–29.9 kg/m²	BMI 30–34.9 kg/m²	BMI 35–39.9 kg/m²	BMI ≥40 kg/m²
Surgery			When optimal medical and behavioral management has been insufficient	With adiposity-related complications	+
Pharmacotherapy		With adiposity-related complications	+	+	+
Behavioral modification	+	+	+	+	+

All individuals, regardless of body size or composition, benefit from a healthy, well-balanced eating pattern and regular physical activity

BMI, body mass index.

Wharton et al. CMAJ 2020;192:E875-91.

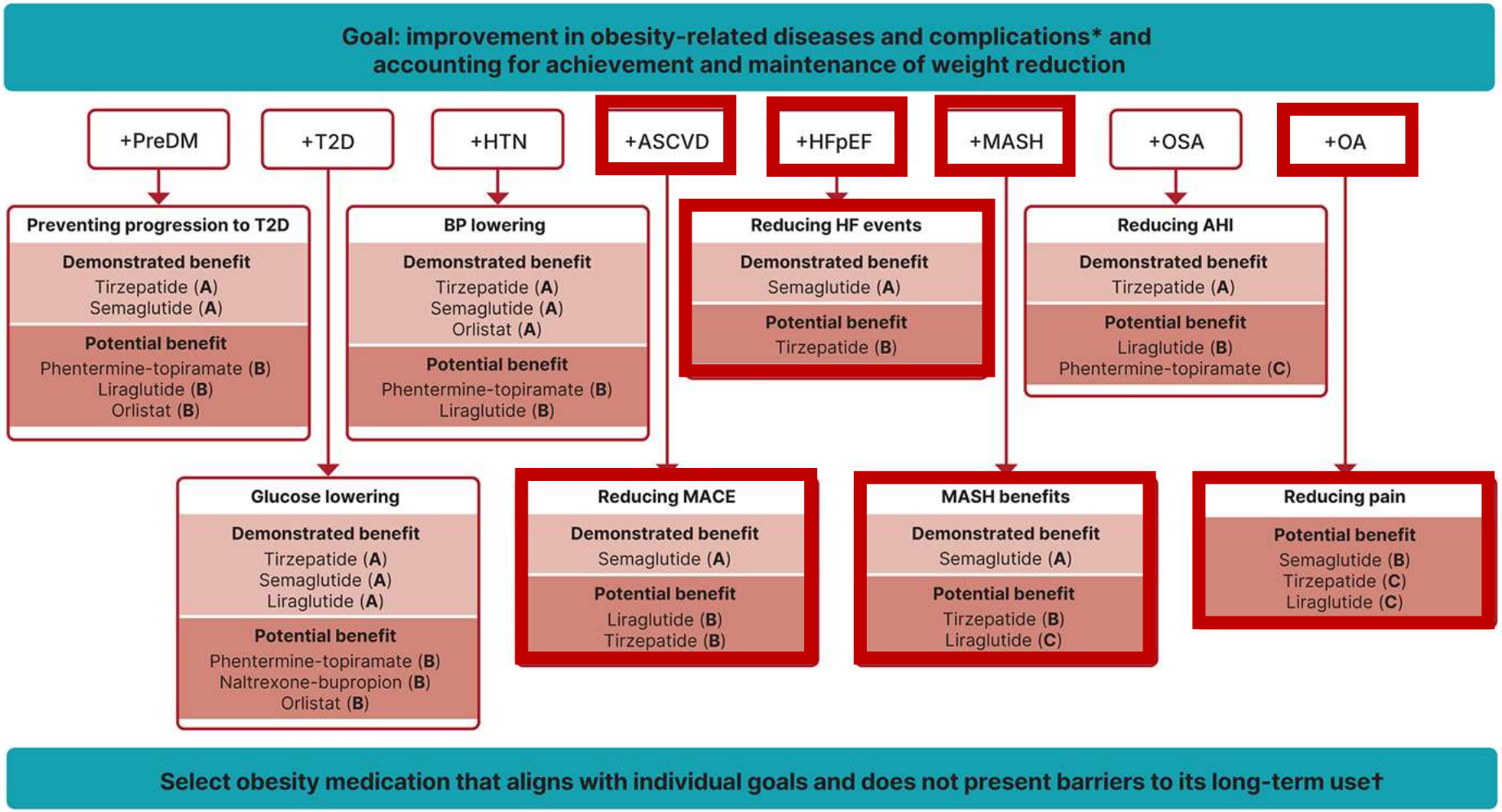
Semaglutide
is endorsed by
ADA as a
‘very high efficacy’
drug for both
glucose-lowering and
weight-lowering
effects

American Diabetes Association®

Standards of Care in Diabetes - 2025: Diabetes Care, January 2025, Vol.48

Semglutide 2.4mg (Wegovy®) Preferred over Tirzepatide across multiple patient profiles

ADA Standards of Care for Obesity 2026



ASCVD, atherosclerotic cardiovascular disease; HFpEF, heart failure with preserved ejection fraction; HTN, hypertension; MASH, metabolic dysfunction–associated steatohepatitis; OA, osteoarthritis; ORC, obesity-related complication; OSA, obstructive sleep apnoea; PreDM, prediabetes; T2D, type 2 diabetes

American Diabetes Association Professional Practice Committee for Obesity. BMJ Open Diabetes Res Care 2026;13:e005729. Note - Wegovy is not approved for MASH in INDIA

novo nordisk®

ONCE-WEEKLY wegovy® semaglutide injection 2.4 mg

Integrating GLP-1 with nutrition for sustainable outcomes and as key for long term success and relapse prevention

Lifestyle modifications

Focus required on multidisciplinary aspects[1]

Medical nutrition therapy

High-quality hypocaloric diet

Physical activity

150-300 minutes of moderate-intensity activity per week

Behavioral & Psychological interventions

Behaviour-changing strategies to foster adherence

Lifestyle modifications

To improve adherence and outcomes, interventions should be individualized to each PwO[2]

PwO, people with obesity

1.Papamargaritis et al, Cardiovascular Research (2023) 119, 2825–2842; 2. Cornier MA, Am J Manag Care. 2022;28(suppl 15):S288-S296

Nutritional recommendations when on GLP-1 therapies

Physical activity recommendation:

Resistance exercise
To maintain and build muscle strength

Physical activity
Weekly 150 minutes of moderate intensity

Nutritional recommendation:

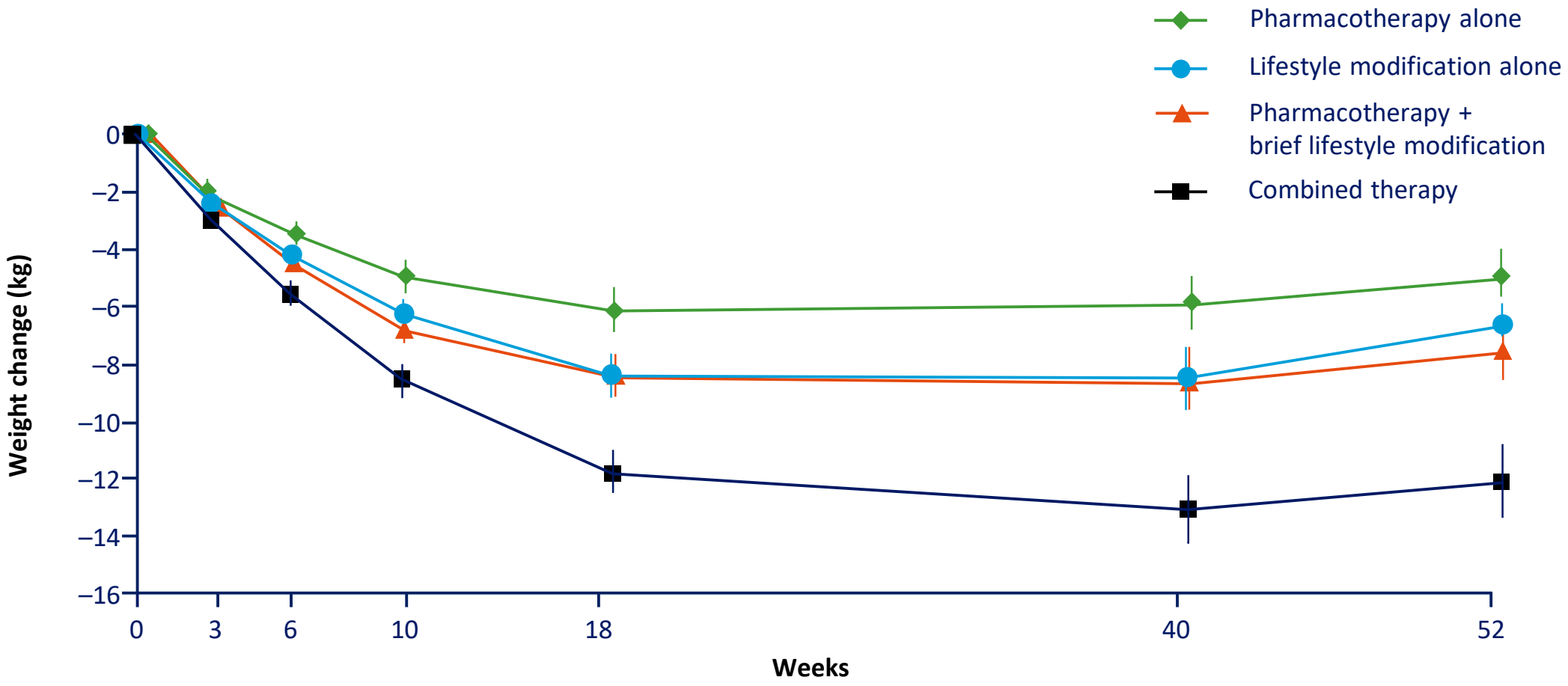
Protein
~1.5g/kg/day

Fibre
>21g/day (women), >30g/day (men)

Hydration
>2-3L/day

McCrimmon RJ, Catarig AM, Frias JP, Lausvig NL, le Roux CW, Thielke D, Lingvay I. Effects of once-weekly semaglutide vs once-daily canagliflozin on body composition in type 2 diabetes: a substudy of the SUSTAIN 8 randomised controlled clinical trial. Diabetologia. 2020 Mar;63(3):473-485.

Pharmacotherapy in Addition to Diet and Exercise Can Help Patients Achieve Clinically-Relevant Weight Loss



Data are mean ± standard error
Pharmacotherapy: sibutramine; Pharmacotherapy alone: Patients received a daily dose of 15 mg/day; Lifestyle modification alone: Patients attended 30 lifestyle counseling sessions; Pharmacotherapy + brief therapy: Patients were given sibutramine and received brief lifestyle counseling; Combined therapy: Patients received sibutramine and attended 30 lifestyle counseling sessions

Wadden TA, *et al.N Engl J Med*. 2005;353:2111–2120.

Semaglutide is not approved for MASH/PAD management in

GLP 1RA -Semaglutide: A wide range of benefits for our patients

Weight loss

Up to 21%

Weight reduction[8]

STEP UP

Glycemic control

Up to 2.8%

A1C reduction[7]

SUSTAIN

Primary prevention

CDSCO approved

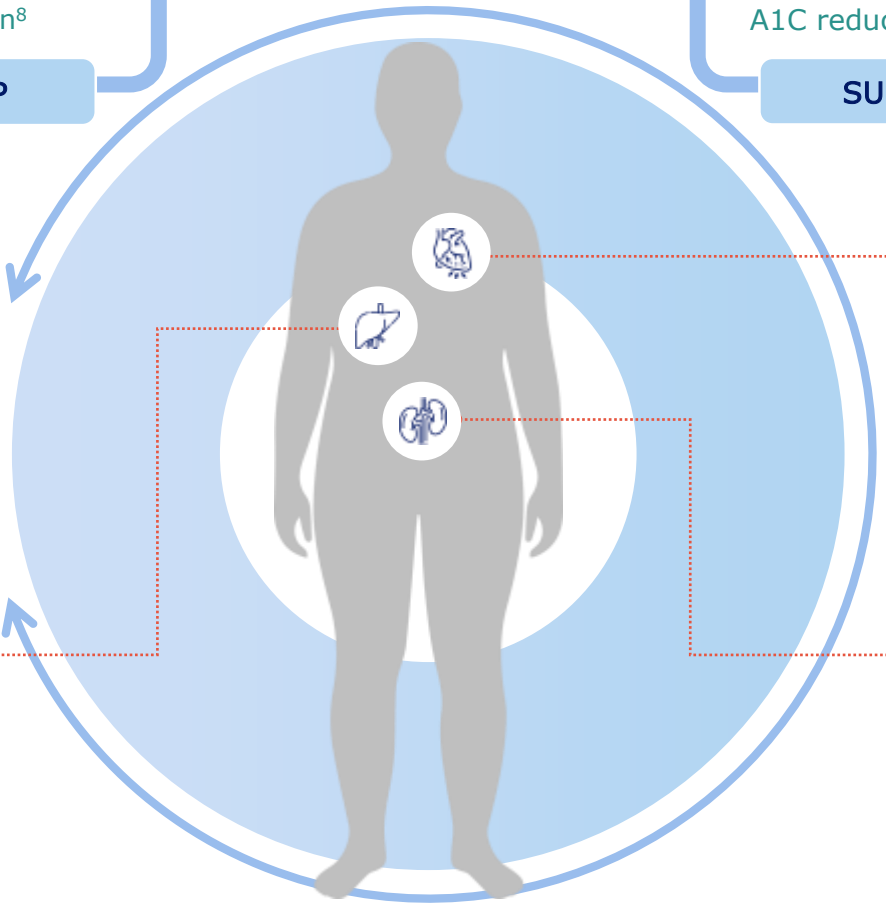
SOUL

All-cause mortality

19%-20%

Reduced risk of all-cause death[1,2]

SELECT & FLOW



CV Outcomes

MACE outcomes

26%

Reduction in MACE[2,4]

SUSTAIN-6

HF outcomes

69%

Reduction in heart failure events or cardiovascular death[5]

STEP-HFpEF

Liver benefits

37%

Improved fibrosis and 63% MASH resolution[6]

ESSENCE

Kidney outcomes

24%

Reduction in Major Kidney Disease Events[10]

FLOW & REMODEL

PAD outcomes

13%

improvement in max. walking distance[9]

STRIDE

CV, cardiovascular; CV, cardiovascular disease; HF, heart failure; MACE, major adverse cardiovascular events; MAKE, major adverse kidney events *; MASH, metabolic dysfunction-associated steatohepatitis; PwO, people with obesity; T2D, type 2 diabetes; WL, weight loss.*

1. Perkovic V. et al. N Engl J Med 2024;391(2):109-121. 2. Lincoff AM, et al. N Engl J Med. 2023; ;389:2221-2232 . 3. Husain M, et al. Diabetes Obes Metab. 2020;22:442-451. 4. Marso S, et al. N Engl J Med. 2016;375:1834-1844;. 5.Butler J et al., Lancet. 2024; 403(10437):1635-1648. 6. Newsome PN et al. Oral Presentation at American Association for the Study of the Liver The Liver Meeting;2024.

Tirzepatide MTD vs Semaglutide MTD for PwO

Head-to-Head Trial

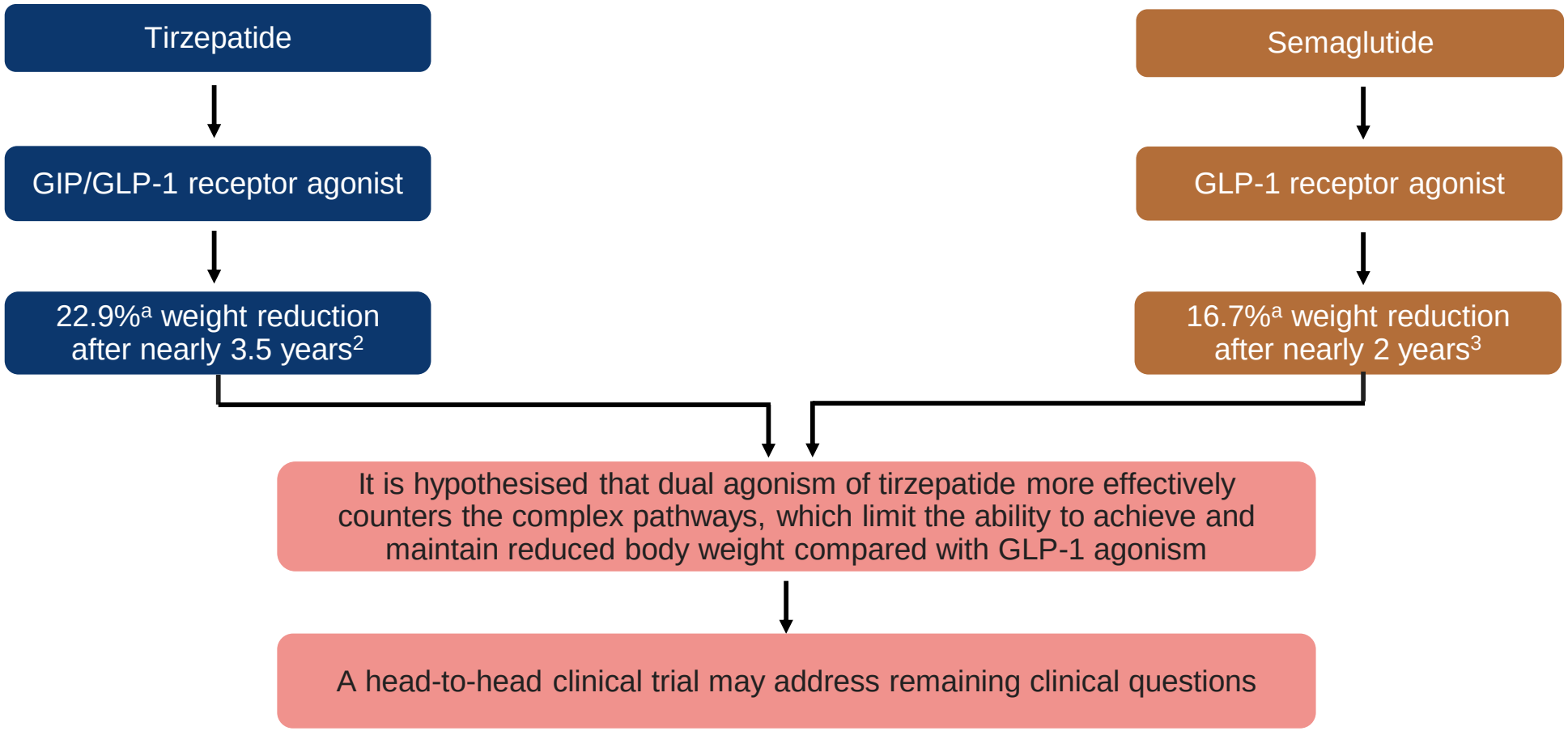
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tirzepatide as Compared with Semaglutide for the Treatment of Obesity

Louis J. Aronne, M.D.,[1] Deborah Bade Horn, D.O.,[2]
Carel W. le Roux, M.D., Ph.D.,[3,4] Wayne Ho, M.D.,[5,6] Beverly L. Falcon, Ph.D.,[7]
Elisa Gomez Valderas, M.Sc.,[7] Sagar Das, M.Sc.,[7] Clare J. Lee, M.D., M.H.S.,[7]
Leonard C. Glass, M.D.,[7] Cagri Senyucel, M.D., Ph.D.,[7] and Julia P. Dunn, M.D.,[7]
for the SURMOUNT-5 Trial Investigators*

Background



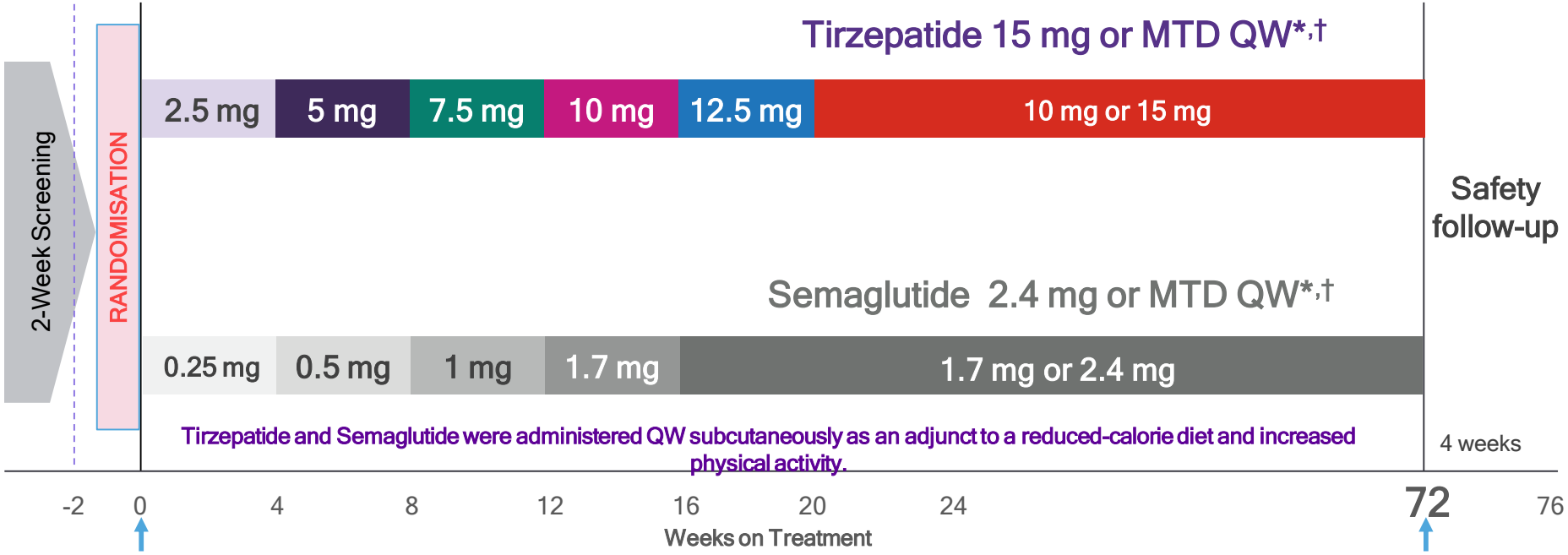
[a]Based on efficacy estimand.

GIP=Glucose-Dependent Insulinotropic Polypeptide; GLP-1=Glucagon-Like Peptide-1.

1. Aronne LJ, et al. *N Engl J Med*. 2025; doi: 10.1056/NEJMoa2416394 (Ahead of print). 2. Jastreboff AM, et al. *N Engl J Med.* 2025;392:958-971. 3. Wilding JPH, et al. *N Engl J Med.* 2021;384:989-1002.

SURMOUNT-5

Tirzepatide MTD vs Semaglutide MTD in Participants With Obesity or Overweight With Obesity-Related Complications, Excluding Diabetes[1]



Phase 3b, multi-center, randomized, parallel arm, open label, active comparator-controlled trial

750 Participants

Primary Endpoint

Percentage change in body weight from baseline to Week 72

*Adjusted for multiplicity. MTD=maximum tolerated dose.

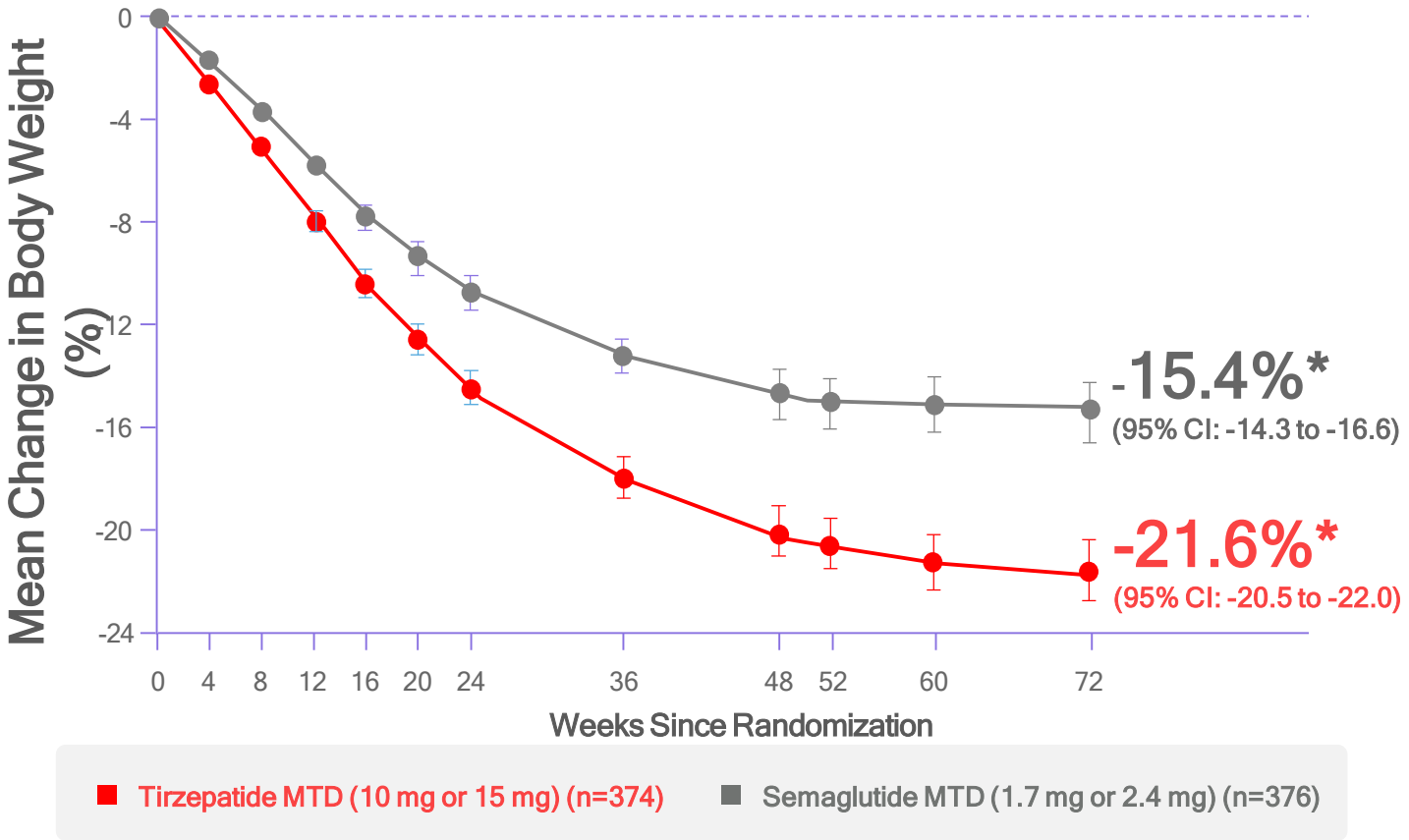
Louis J. Aronne, M.D., et al. Tirzepatide as Compared with Semaglutide for the Treatment of Obesity,N Engl J Med. 2025; doi: 10.1056/NEJMoa2416394

SURMOUNT-5

Tirzepatide MTD Demonstrated Superior Reduction in Body Weight Compared to Semaglutide MTD[1]

Mean Percentage Change in Body Weight From Randomization to Week 72[1]

Overall mean baseline weight=113.2 kg



At 72 weeks, participants taking Tirzepatide MTD (10 mg or 15 mg) experienced a mean percentage **body weight reduction of -21.6%** vs -15.4% in those taking Semaglutide MTD (1.7 mg or 2.4 mg)[1]

Studied in a randomized, open-label, phase 3b trial of adults with obesity (BMI ≥30 kg/m²), or overweight (BMI ≥27 kg/m²) with at least 1 obesity-related complication (eg, hypertension, dyslipidemia), excluding diabetes. The study included a 2-week screening period and a 72-week treatment period.[1]

Participants in both the Tirzepatide and Semaglutide treatment arms received lifestyle intervention, including a reduced-calorie diet and increased physical activity.[1]

Efficacy estimand, mITT population. MMRM analysis.[1]

Limitations of an open-label study may be related to a bias in evaluation of the outcomes, efficacy and/or safety, and analysis was not tested against a placebo-controlled comparison group.

*Data are least-squares mean with 95% confidence intervals or no. (%).[1]

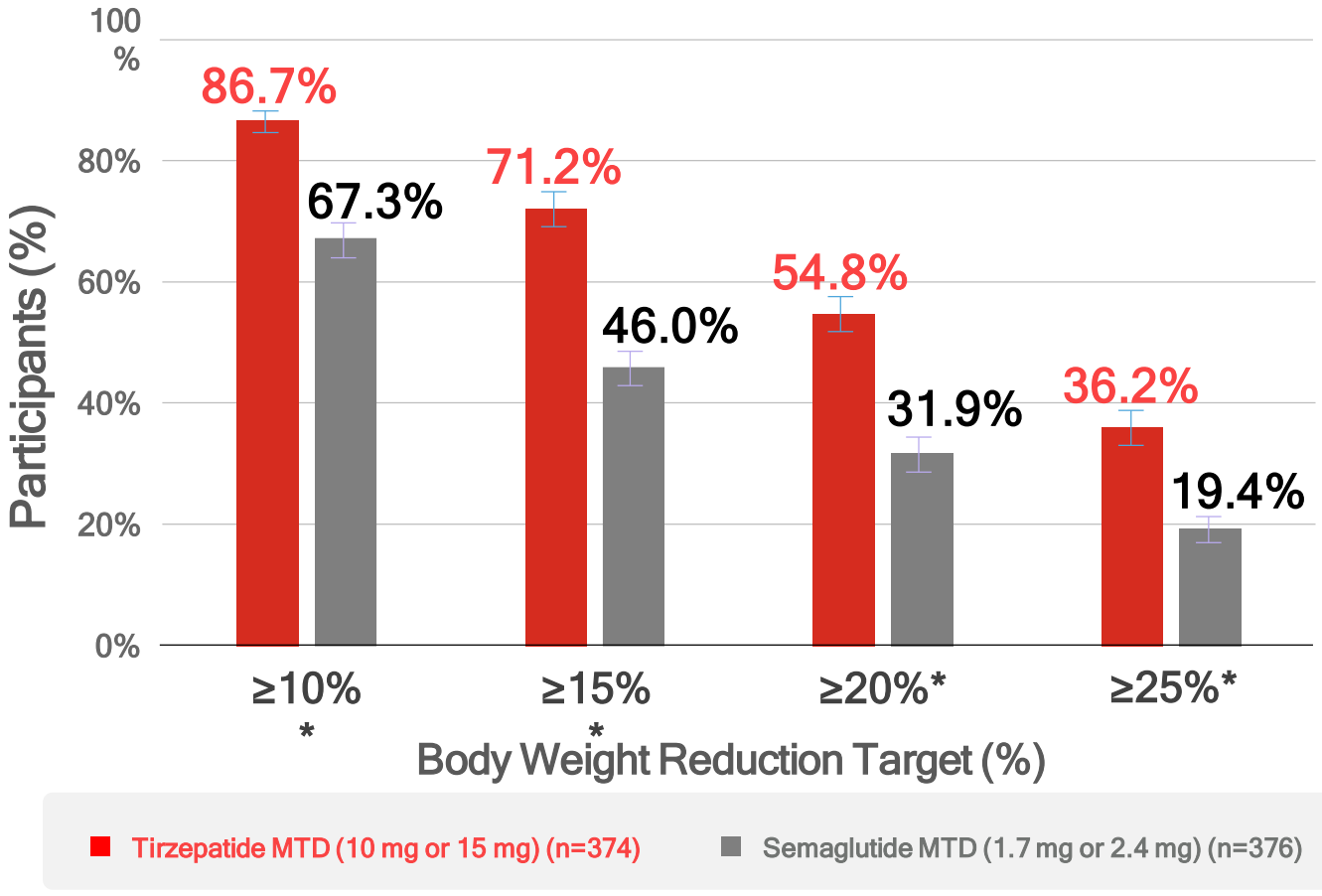
1. Louis J. Aronne, M.D., et al. Tirzepatide as Compared with Semaglutide for the Treatment of Obesity,N Engl J Med. 2025; doi: 10.1056/NEJMoa2416394

SURMOUNT-5

1 in 3 Participants Taking Tirzepatide Achieved ≥25% Mean Reduction in Body Weight vs 1 in 5 Taking Semaglutide MTD[1]

Percentage of Participants Who Achieved Weight Reduction Targets at Week 72[1]

Overall mean baseline weight=113.2 kg



36.2% (vs. 19.4%)
of participants taking
Tirzepatide MTD demonstrated mean
weight reduction of ≥25%
at 72 weeks

Studied in a randomized, open-label, phase 3b trial of adults with obesity (BMI ≥30 kg/m^2), or overweight (BMI ≥27 kg/m^2) with at least 1 obesity-related complication (eg, hypertension, dyslipidemia), excluding diabetes. The study included a 2-week screening period and a 72-week treatment period.[1]

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*Data are least-squares mean with 95% confidence intervals or no. (%).[1]

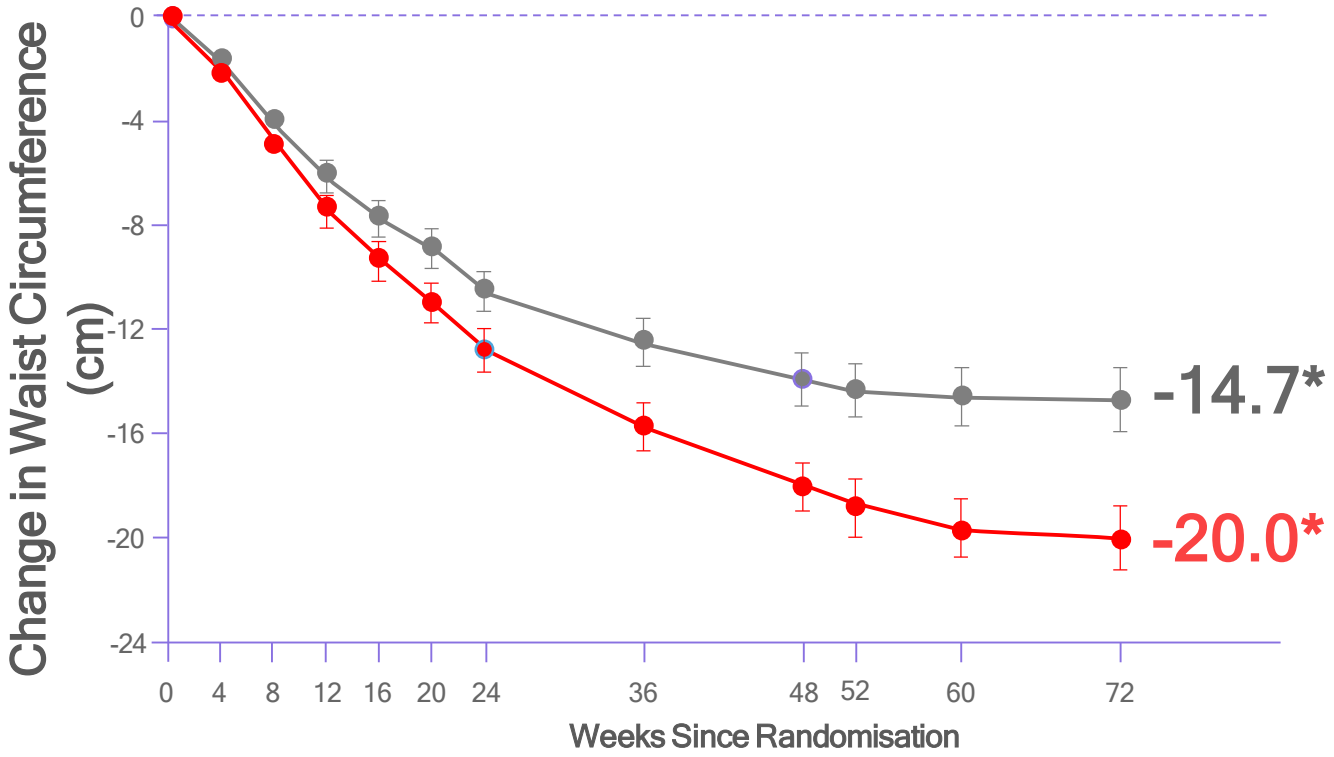
1. Louis J. Aronne, M.D., et al. Tirzepatide as Compared with Semaglutide for the Treatment of Obesity,N Engl J Med. 2025; doi: 10.1056/NEJMoa2416394

SURMOUNT-5

Participants Taking Tirzepatide Experienced Superior Reduction in Waist Circumference vs. Participants Taking Semaglutide at Week 72[1]

Change in Waist Circumference (cm) From Randomisation to Week 72[1]

Overall mean baseline waist circumference=118.3 cm (46.6 inches)



Tirzepatide MTD (10 mg or 15 mg)(n=374)

Semaglutide MTD (1.7 mg or 2.4 mg)(n=376)

*Data are least-squares mean with 95% confidence intervals or no. (%).[1]

Participants taking Tirzepatide MTD experienced a

-20.0 cm (-7.9 inches)

reduction in waist circumference

at 72 weeks*

Studied in a randomized, open-label, phase 3b trial of adults with obesity (BMI ≥30 kg/m^2), or overweight (BMI ≥27 kg/m^2) with at least 1 obesity-related complication (eg, hypertension, dyslipidemia), excluding diabetes. The study included a 2-week screening period and a 72-week treatment period.[1]

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1. Louis J. Aronne, M.D., et al. Tirzepatide as Compared with Semaglutide for the Treatment of Obesity,N Engl J Med. 2025; doi: 10.1056/NEJMoa2416394

Thank You Team PFNDAI (Dr. Bhalkar, Dolly, Samreen), Sheryl, Dr. Banshi sir

Thank you audience for a patient hearing!