Obesity Medicine and Cardiac Care

St. Mike's Cardiology – April 11, 2026

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Disclosures

Dr. Wharton has received an honorarium for this presentation.

Dr. Wharton discloses honoraria and ad boards for the following companies: Novo Nordisk, Bausch Health Canada, Eli Lilly, Boehringer Ingelheim, Amgen, Metsera, Astra Zeneca

Objectives

1. Discuss the pathophysiology of obesity and association with cardiac disease
2. Discuss current and emerging pharmacotherapy for obesity and cardiac disease

I have permission from these people to share their photo

My 2 babies (Baby James and The Canadian Obesity Guidelines – Sept 2020)

GUIDELINE CPD

Obesity in adults: a clinical practice guideline

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This article is available in French at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.191707/-/DC1

CMAJ Podcasts: author interview at https://www.cmaj.ca/lookup/doi/10.1503/cmaj.191707/tab-related-content

besity is a complex chronic disease in which abnormal or excess body fat (adiposity) impairs health

mplex, progressive and relapsing
rized by abnormal or excessive body
irs health.

y face substantial bias and stigma,
ased morbidity and mortality
body mass index.

ects substantial advances in the
nts, pathophysiology, assessment,
t of obesity, and shifts the focus of
ard improving patient-centred health
ight loss alone.

care should be based on evidence-based principles of
disease management, must validate patients' lived
ces, move beyond simplistic approaches of "eat less,
move more," and address the root drivers of obesity.

- People living with obesity should have access to evidence-informed interventions, including medical nutrition therapy, physical activity, psychological interventions, pharmacotherapy and surgery.

increased throughout the world,[12] and in Canada, it has increased threefold since 1985.[13] Importantly, severe obesity has increased more than fourfold and, in 2016, affected an estimated 1.9 million Canadian adults.[13]

Wharton Medical Clinic est. 2008
Canada

Government funded – free for patients

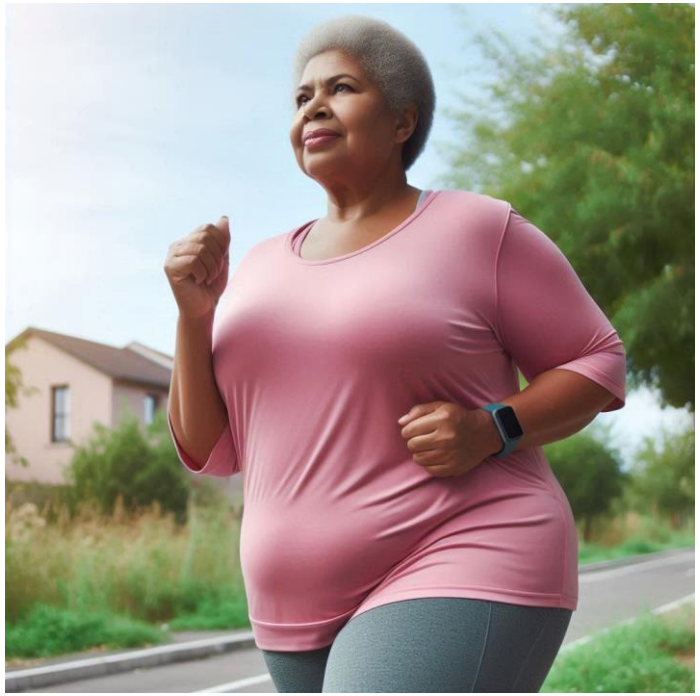
90% - Virtual 10% - In person

Adult Clinic
Paediatric Clinic
Pre-post Bariatric Sx

- Referred by specialist or family doctor
- Most pts consent to research

750,000 pts
(76% women)

- 15 Internists
- Interdisciplinary team



WHARTONMEDICALCLINIC.COM

CLINICAL TRIALS

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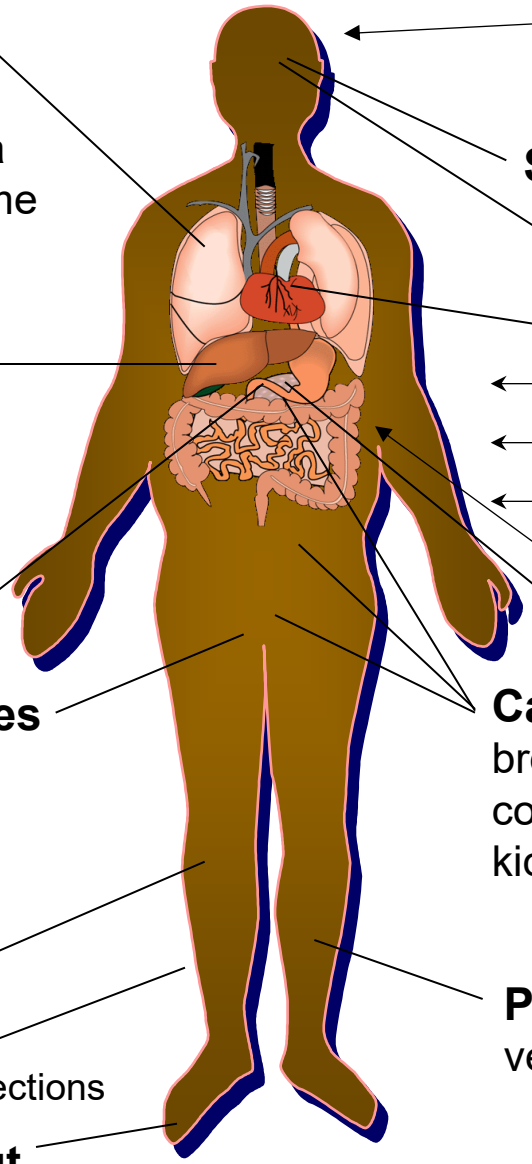
Adipose Tissue Dysfunction

- Inability to store excess calories
- Cellular hypoxia
- Inflammation - adipokines

Obesity is both a disease and a risk factor for disease – Not exclusionary



Pulmonary disease
abnormal function
obstructive sleep apnea
hypoventilation syndrome

Nonalcoholic fatty liver disease
steatosis
steatohepatitis
cirrhosis

Gall bladder disease

Gynecologic abnormalities
abnormal menses
infertility
polycystic ovarian syndrome
urinary incontinence

Osteoarthritis

Skin
fungal/bacterial infections

Gout

Cognitive decline
Mental health conditions

Stroke

Cataracts

Coronary heart disease

Diabetes

Dyslipidemia

Hypertension

Renal Failure

Cancer
breast, uterus, cervix
colon, esophagus, pancreas
kidney, prostate

Phlebitis/DVT (Blood Clots)
venous stasis

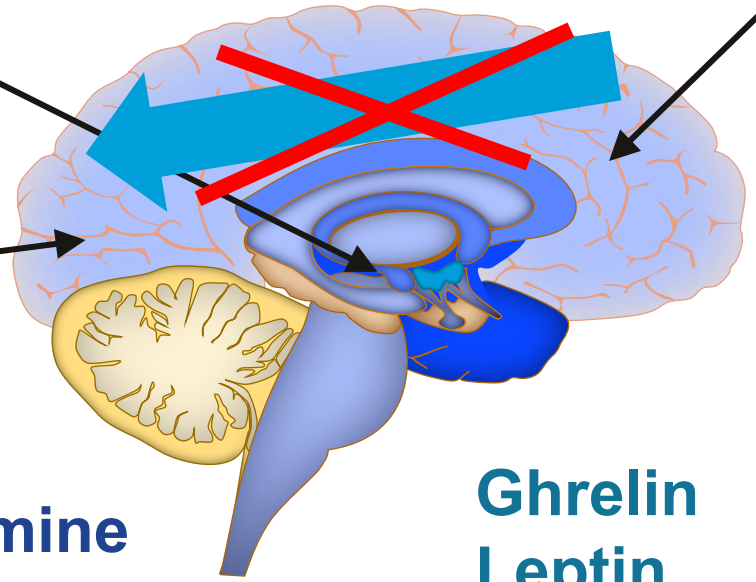
The GBD 2015 Obesity Collaborators. Health Effects of Overweight and Obesity in 195 Countries over 25 Years. NEJM 2017; 2017;377:13-27
https://www.nejm.org/doi/10.1056/NEJMoa1614362

Neuropathology Associated with Obesity

Hypothalamic Hunger System

Frontal Lobe Executive Function

Mesolimbic Reward System



Dopamine
Opioid
Cannabinoid
Receptors

Ghrelin
Leptin
PYY
GLP-1
CCK
Amylin

Lau DCW, Wharton S. Canadian Adult Obesity Clinical Practice Guidelines: The Science of Obesity. Available from: https://obesitycanada.ca/guidelines/science

3 Generations of Weight Management Medications

Generation I: weight loss (8-10%)	• liraglutide 3.0mg (Approved in Canada 2016) • naltrexone/bupropion (Approved in Canada 2018)
Generation II: weight loss (15%)	• semaglutide 2.4mg (Approved in Canada 2021)
Generation III: weight loss (>20%)	• tirzepatide (Approved in Canada 2025)

SELECT Trial – Heart Disease. Lincoff et al. NEJM 2023

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

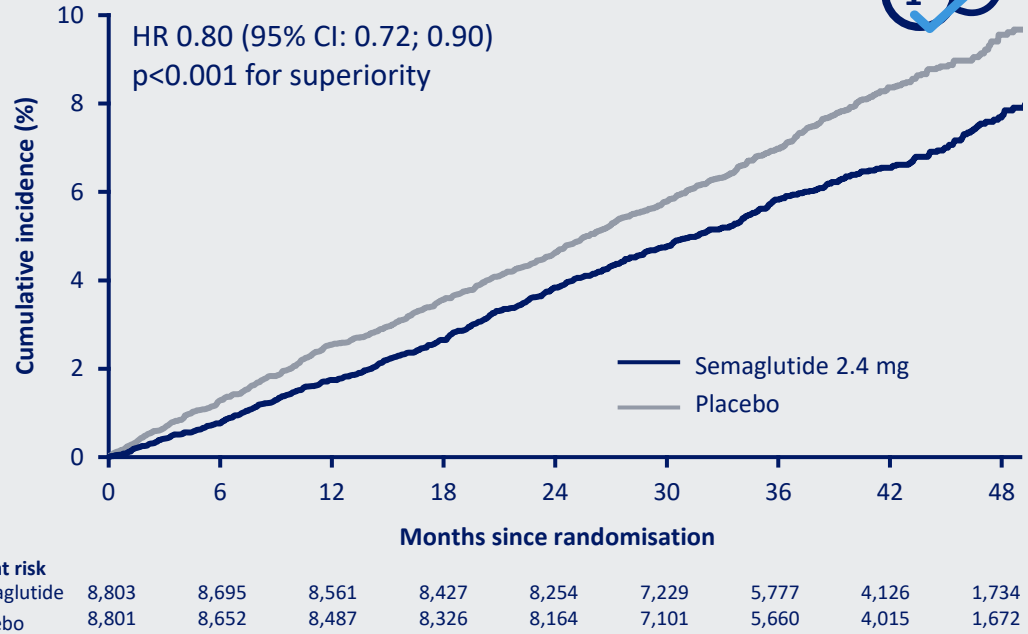
Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes

A. Michael Lincoff, M.D., Kirstine Brown-Frandsen, M.D., Helen M. Colhoun, M.D., John Deanfield, M.D., Scott S. Emerson, M.D., Ph.D., Sille Esbjerg, M.Sc., Søren Hardt-Lindberg, M.D., Ph.D., G. Kees Hovingh, M.D., Ph.D., Steven E. Kahn, M.B., Ch.B., Robert F. Kushner, M.D., Ildiko Lingvay, M.D., M.P.H., Tugce K. Oral, M.D., Marie M. Michelsen, M.D., Ph.D., Jorge Plutzky, M.D., Christoffer W. Tornøe, Ph.D., and Donna H. Ryan, M.D., for the SELECT Trial Investigators*

SELECT: Key trial results

Primary endpoint

Semaglutide 2.4 mg **reduced the risk of MACE by 20%** vs placebo[1,2]



No. at risk									
Semaglutide	8,803	8,695	8,561	8,427	8,254	7,229	5,777	4,126	1,734
Placebo	8,801	8,652	8,487	8,326	8,164	7,101	5,660	4,015	1,672

Confirmatory secondary endpoints

HRs (95% CI) for the confirmatory secondary endpoints were[1]:

- Death from CV causes: 0.85 (0.71; 1.01); p=0.07*
- HF composite†: 0.82 (0.71; 0.96)
- Death from any cause: 0.81 (0.71; 0.93)

Safety and tolerability

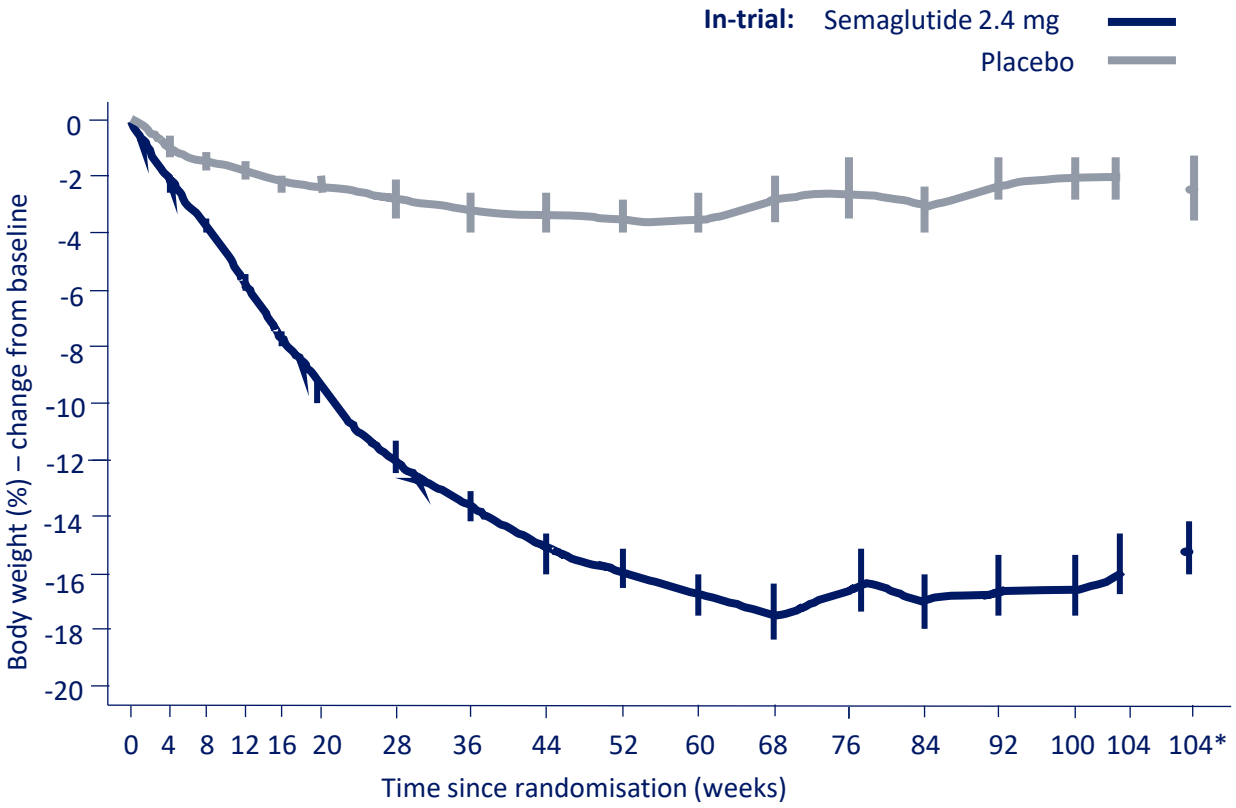
The safety and tolerability profile of semaglutide 2.4 mg in people with established CVD and overweight or obesity was consistent with previous semaglutide 2.4 mg trials[1]

**p-value did not meet statistical significance required for hierarchical testing and so superiority testing was not performed for the remaining confirmatory secondary endpoints. †HF hospitalisation, urgent HF visit or CV-related death.*
CI, confidence interval; CV, cardiovascular; CVD, cardiovascular disease; GI, gastrointestinal; HF, heart failure; HR, hazard ratio; MACE, major adverse cardiovascular event.
1. Lincoff AM et al. N Engl J Med 2023;DOI:10.1056/NEJMoa2307563; 2. Novo Nordisk A/S. Company announcement, 8 August 2023. Available at: https://www.novonordisk.com/content/nncorp/global/en/news-and-media/news-and-ir-materials/news-details.html?id=166301. Accessed October 2023.

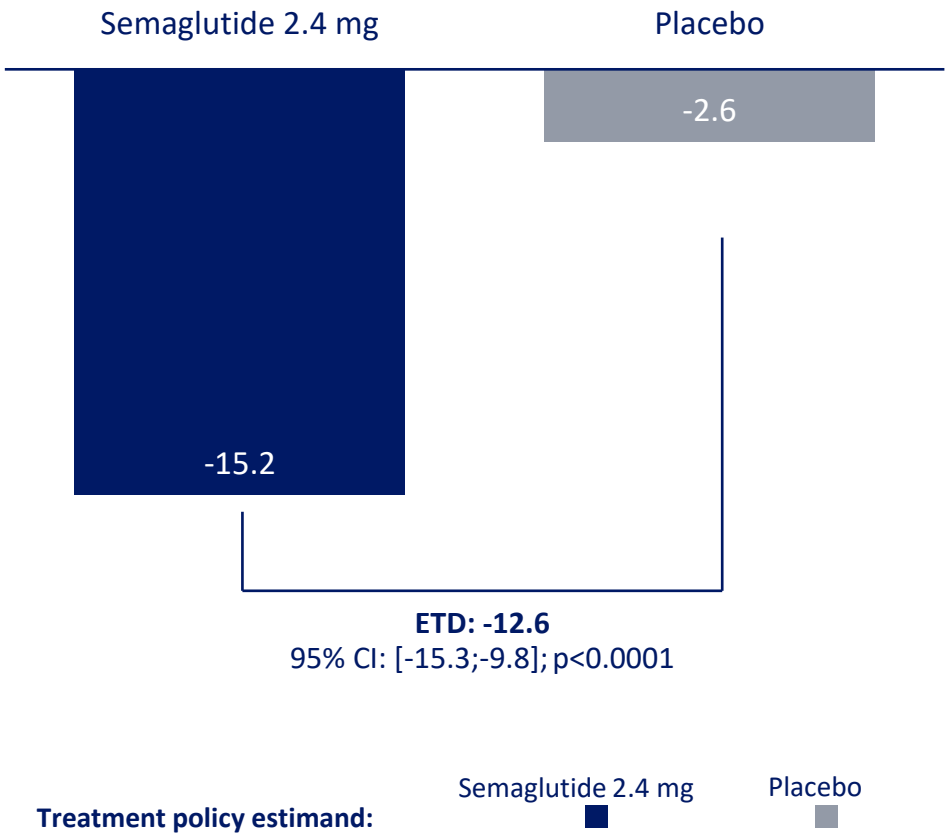
Semaglutide 2.4mg over 2 years
Change in body weight (%): primary endpoint

Observed mean change

Mean at baseline body weight: 106.0 kg



Estimated change from baseline to week 104



Estimated means – treatment policy.104, Estimated means. Error bars are +/- standard error of the mean. Numbers shown in the lower panel are numbers of subjects contributing to the mean. ETD, estimated treatment difference; CI, confidence interval. Novo Nordisk. Data on file. NCT0369343.*

Adult Obesity Pharmacotherapy Decision Table

		Liraglutide 3 mg daily	Naltrexone/ Bupropion 16/180 mg BID	Orlistat 120 mg TID	Semaglutide 2.4 mg weekly	Tirzepatide 5/10/15 mg weekly
Cardio-Metabolic Complications	Prediabetes	✓		✓	✓	✓
	T2D	✓	✓	✓	✓	✓**
	MASH	✓		∅	✓	✓
	ASCVD		🔍		✓	🔍
	HFpEF				✓	✓*
Mechanical Complications	OSA	✓				✓**
	OA	∅			✓	🔍
Patient Reported Outcome Measures (PROMS)	QoL	+	+		+	+
	Physical Function	+	+		+	+
	Cravings		+		+	
Average weight loss (placebo subtracted)		5.4%	4.8%	2.9%	12.4%	11.9/16.4/17.8%

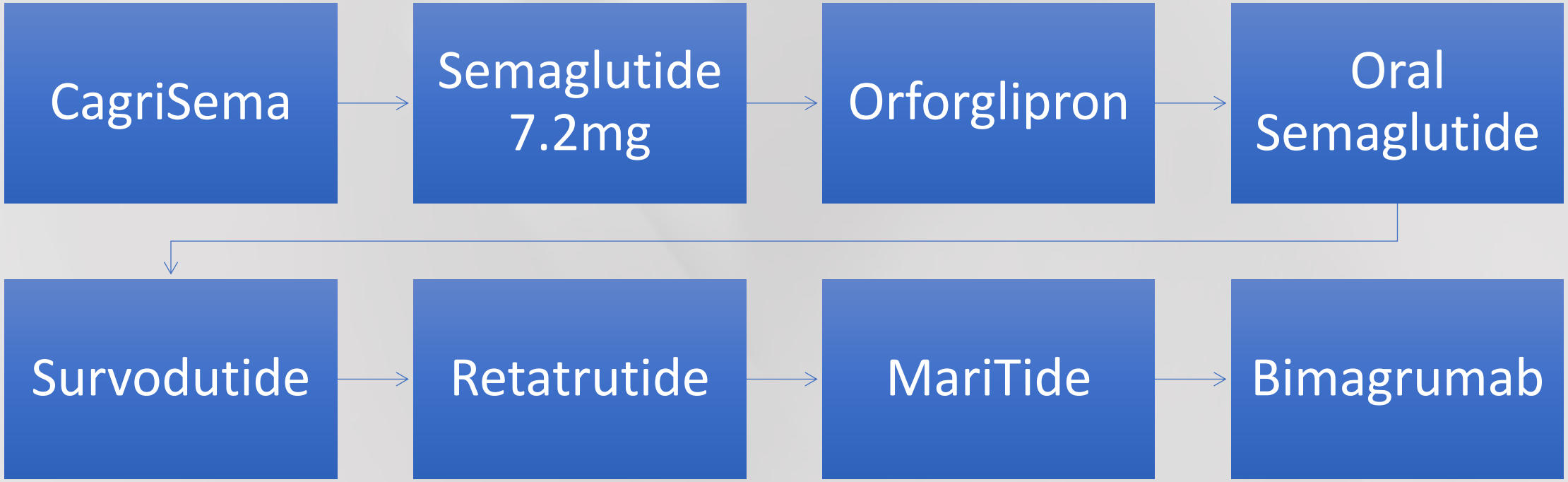
✓ Level 1a Very High Certainty | ✓ Level 2a Moderate Certainty | ✓ Level 3 Low Certainty | ∅ No Benefit | + Benefit | 🔍 In study as identified on www.clinicaltrials.gov

*15 mg, **10 mg or 15 mg . T2D - type 2 diabetes, MASH - metabolic dysfunction-associated steatohepatitis; ASCVD - atherosclerotic cardiovascular disease; HFpEF - heart failure with preserved ejection fraction; OSA - obstructive sleep apnoea; OA - osteoarthritis; QoL - quality of life

Pedersen SD, Manjoo P, Dash S et al. Pharmacotherapy for Obesity Medicine in Adults. https://obesitycanada.ca/guidelines

Pedersen et al. – CMAJ August 11. 2025. 197.

In Development Weight Management Medications



Disparity in Care – costly injectable obesity medications highlights this disparity

The NEW ENGLAND JOURNAL of MEDICINE

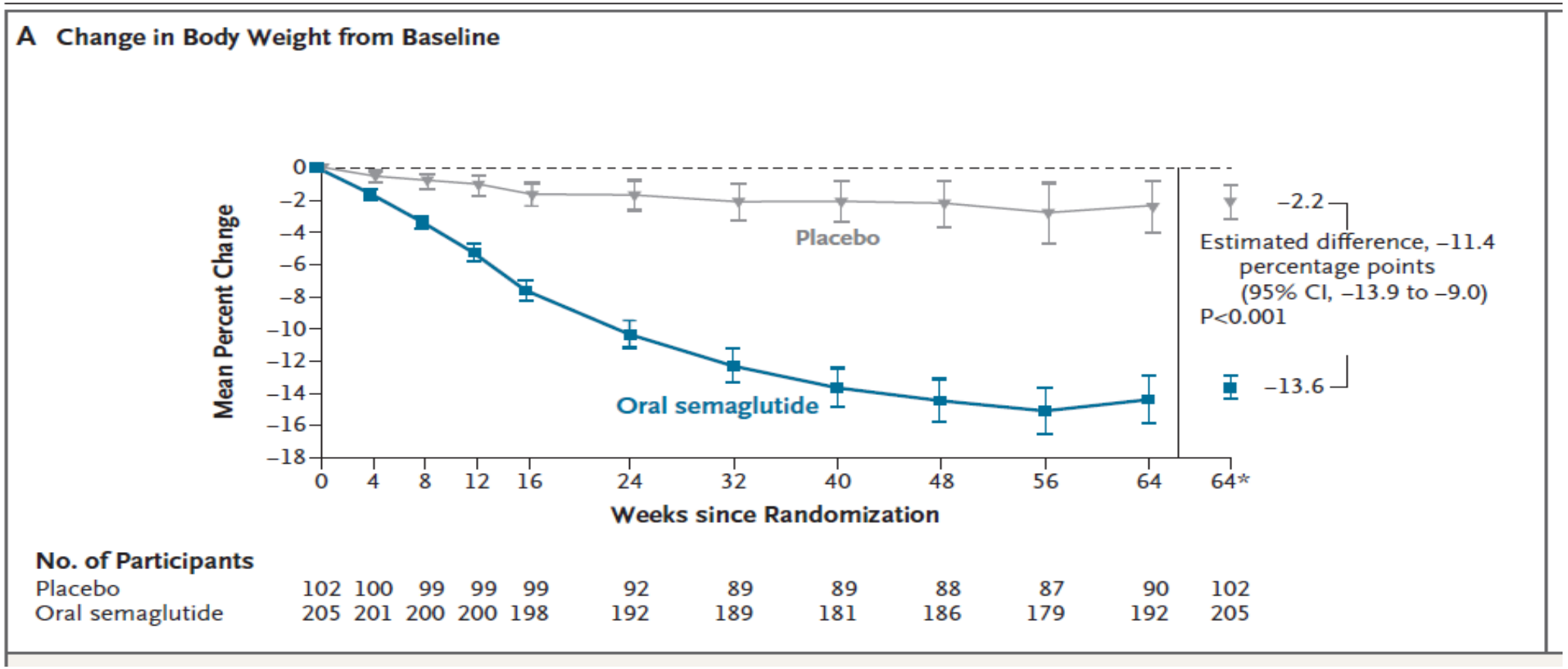
ORIGINAL ARTICLE

Oral Semaglutide at a Dose of 25 mg in Adults with Overweight or Obesity

Sean Wharton, M.D.,[1-4] Ildiko Lingvay, M.D.,[5,6] Pawel Bogdanski, M.D.,[7] Ruben Duque do Vale, M.D.,[8] Stephan Jacob, M.D.,[9] Tobias Karlsson, M.D.,[8] Chaithra Shaji, M.Sc.,[10] Domenica Rubino, M.D.,[11] and W. Timothy Garvey, M.D.,[12] for the OASIS 4 Study Group*

Wharton et al. N Engl J Med 2025;393:1077-87. Published Sept 16, 2025

Oral semaglutide 25mg Percentage Weight Loss



Wharton et al. N Engl J Med 2025;393:1077-87. Published Sept 16, 2025

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Orforglipron, an Oral Small-Molecule GLP-1 Receptor Agonist for Obesity Treatment

Sean Wharton, M.D.,[1-3] Louis J. Aronne, M.D.,[4] Adam Stefanski, M.D., Ph.D.,[5] Nasreen F. Alfaris, M.D., M.P.H.,[6] Andreea Ciudin, M.D., Ph.D.,[7-11] Koutaro Yokote, M.D., Ph.D.,[12] Bruno Halpern, M.D., Ph.D.,[13] Alpana P. Shukla, M.D.,[4] Chunmei Zhou, M.S.,[5] Lisa Macpherson, M.S.P.H.,[5] Sheryl E. Allen, M.D.,[5] Nadia N. Ahmad, M.D., M.P.H.,[5] and Suzanne R. Klise, B.S.,[5] for the ATTAIN-1 Trial Investigators*

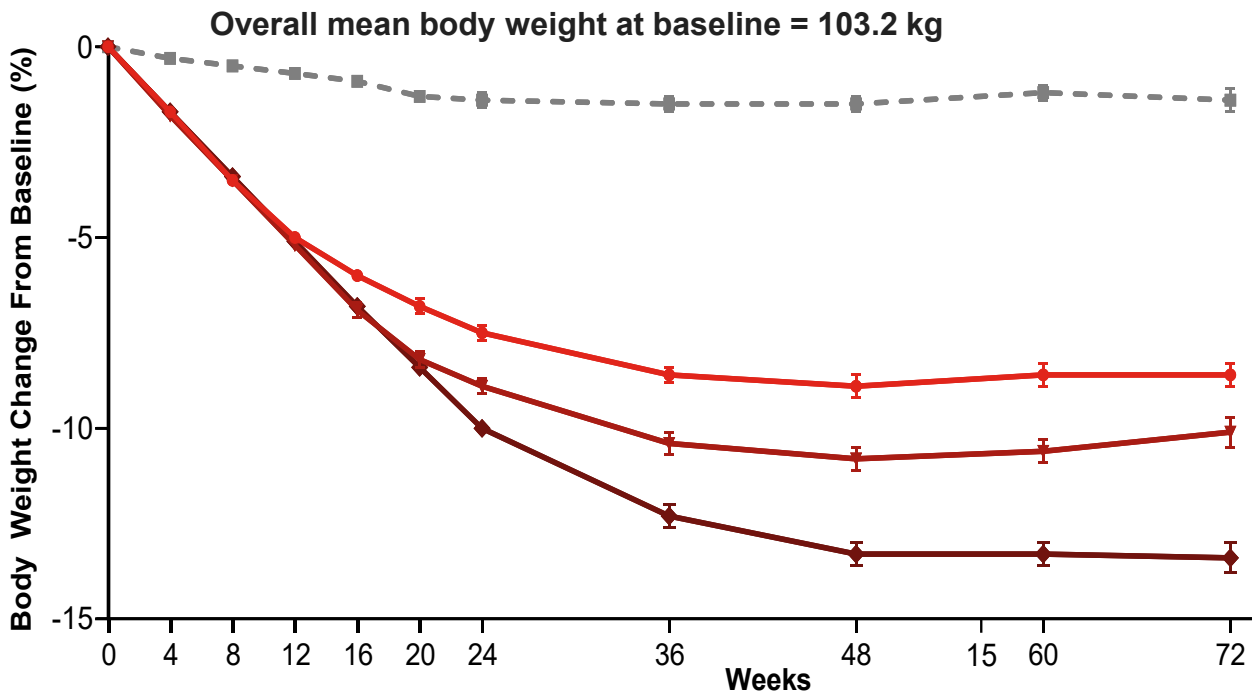
Wharton et al. NEJM, Published September 16, 2025. DOI: 10.1056/NEJMoa2511774

ATTAIN-1 | Orforglipron in Obesity Management Mean Percent Change in Body Weight

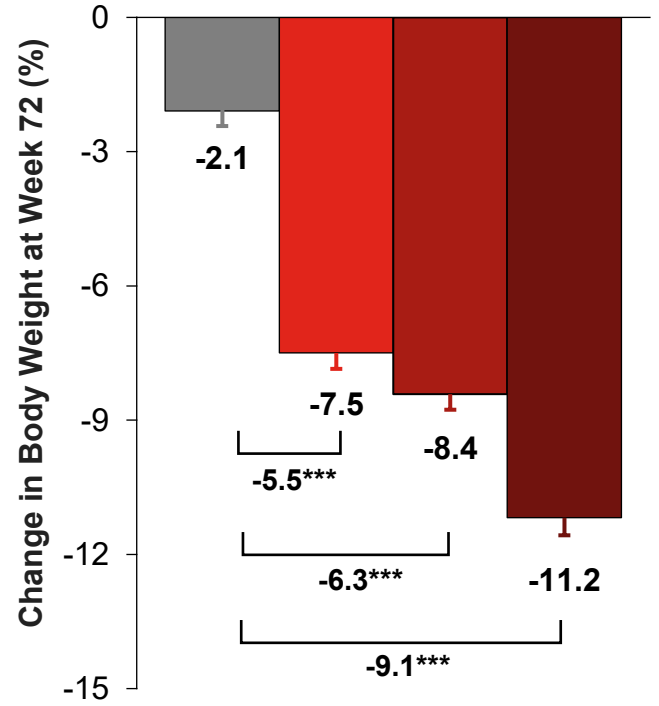
Primary Endpoint

PBO OFG 6 mg OFG 12 mg OFG 36 mg

Observed On-Treatment Curves and Efficacy Estimand (N=3127)



Treatment Regimen Estimand (N=3127)



- OFG vs. PBO: ***p<0.001. p-Values are for MBE change difference vs. PBO. [a]MBE for percent change from baseline to Week 72 and ETD between OFG groups and PBO based on MMRM analysis (efficacy estimand). Notes: Data are mean (SE) unless stated otherwise. The curves shown from Week 0 to Week 72 based on observed mean with SE using efficacy estimand data points set, including all data points obtained during the treatment period and up to the earliest date of discontinuation of study treatment or initiation of prohibited weight management treatments. *ETD=estimated treatment difference; MBE=model-based estimate; MMRM=mixed model for repeated measures; N=total number of participants; OFG=orforglipron; PBO=placebo; SE=standard error.*

Conclusion – Obesity Medicine and Cardiac Care

- Obesity is genetic and drives inflammation
- Semaglutide 2.4mg is effective for weight loss and cardiac protection
- Emerging evidence from the entire GLP1 class for improvement in cardiac risk factors
- Oral medications may be more appealing to cardiologist and non metabolic MDs.

AI generated image

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