Anti Obesity Medications Mainstay for Recurrent Weight Gain after Metabolic Bariatric Surgery

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CONFLICT OF INTEREST DISCLOSURE

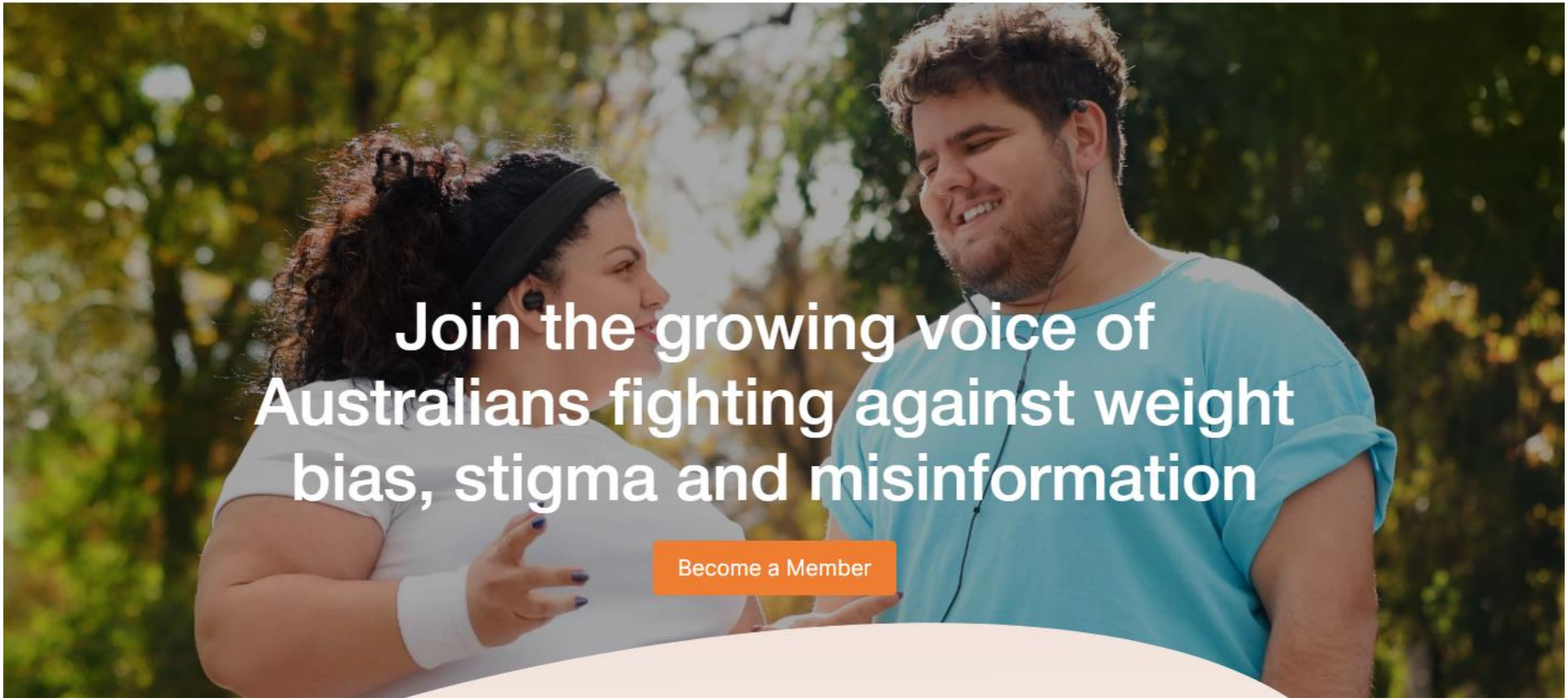
Honoraria for Johnson & Johnson Mentoring Program for Early Career Surgeons intereted in MBSx 2022 & 2023

All Honoraria then donated to Australian Aboriginal Charities

No Pharma Company Honoraria or Consultation Fees for > 5 years

Weight Issues Network

We are WIN | Weight stigma | WIN at Work | Contact WIN | Donate | Free membership



Journal of
Clinical Medicine

MDPI

Article

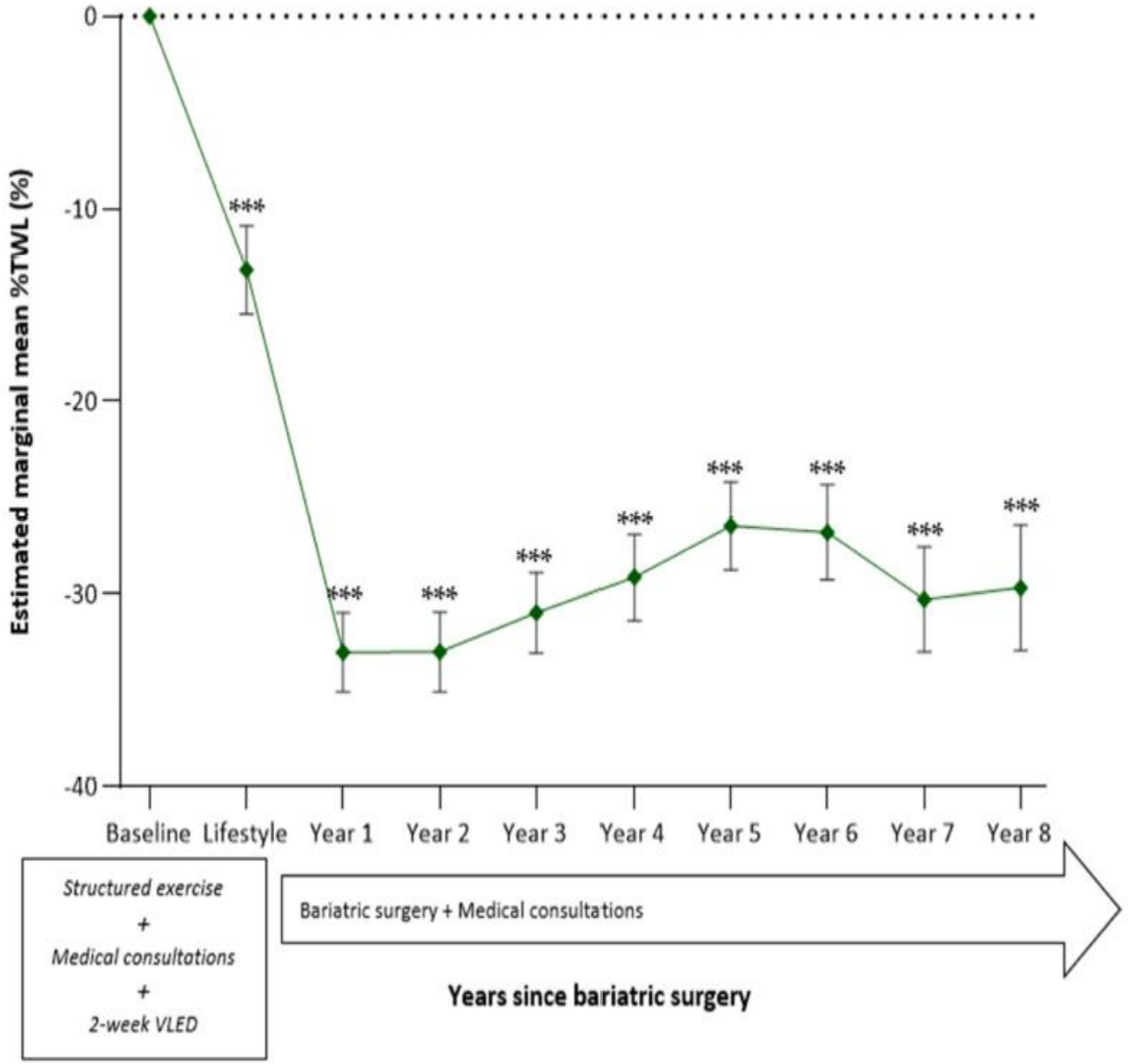
Long-Term Trajectories in Weight and Health Outcomes Following Multidisciplinary Publicly Funded Bariatric Surgery in Patients with Clinically Severe Obesity ($\geq$ 3 Associated Comorbidities): A Nine-Year Prospective Cohort Study in Australia

Michelle M.C. Tan [1,2,3,4,*], Xingzhong Jin [5,6], Craig Taylor [7], Adrian K. Low [8], Philip Le Page [7], David Martin [7,9], Ang Li [1,10], David Joseph [7,9] and Nic Kormas [2,3,*]

J. Clin. Med. **2022**, *11*, 4466. https://doi.org/10.3390/jcm11154466

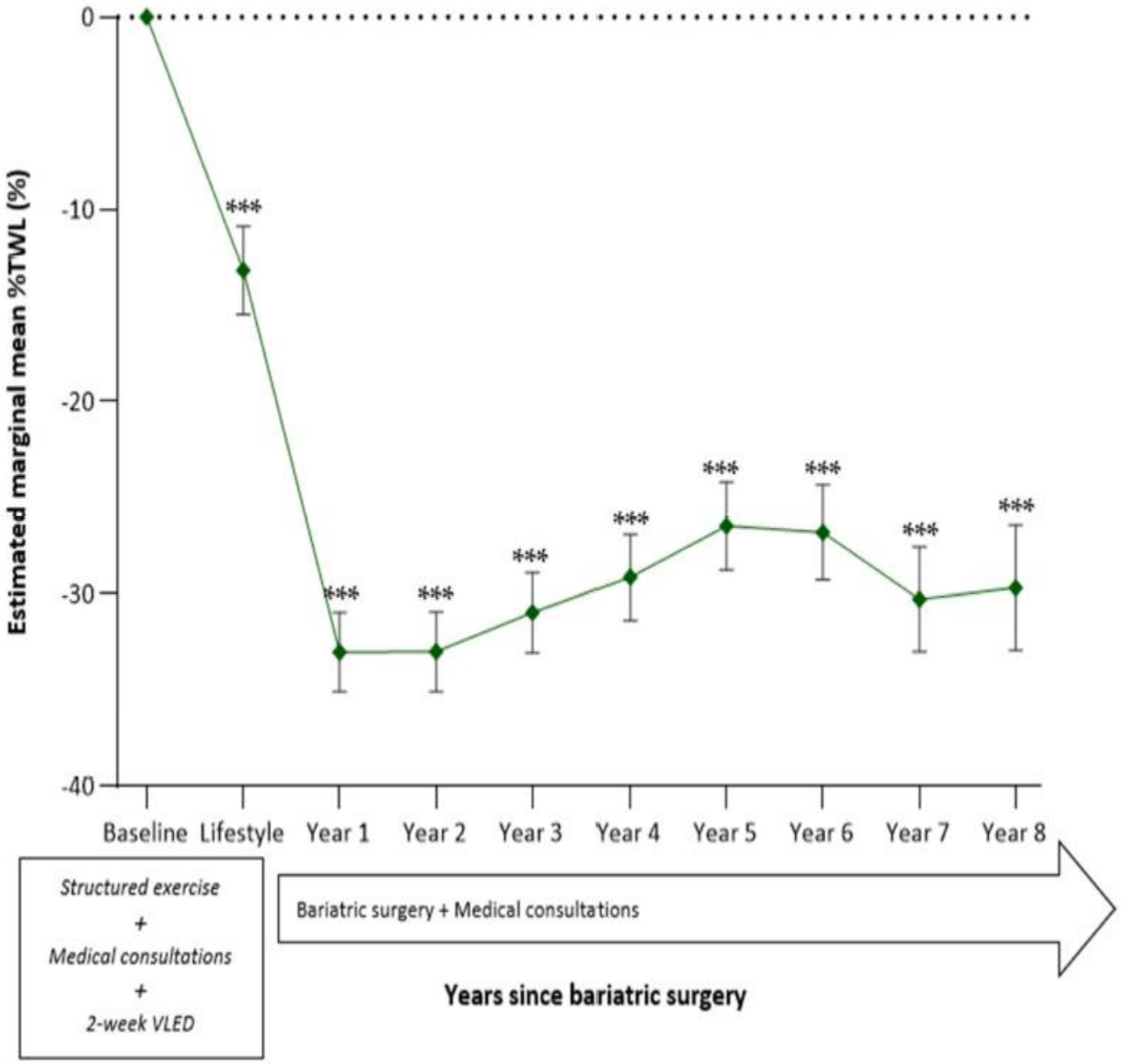
Tan M, Kormas N, et al JCM 2022

- n = 65 Public MBS cases
- Weight 149 ± 45kg
- 7 comorbidities (3-12)
- BMI 52 ± 13 kg/m2
- 54 ± 11 years of age
- 54% female
- 57% on social welfare
- 80% LSG
- 10% LGB
- 10% OAGB
- 8 years follow up



Tan M, Kormas N, et al JCM 2022

- 13% weight loss pre-op
- Diabetes 85% Remission 50%
- OSA CPAP 63% No CPAP 41%
- Severe Osteoarthritis 75%
- Significant Mental Health Issues 55%



Mr AN Weight 468kg (1032 lbs) BMI 146kg/m2 MBSx (LSG) at 378 kg (833 lbs)

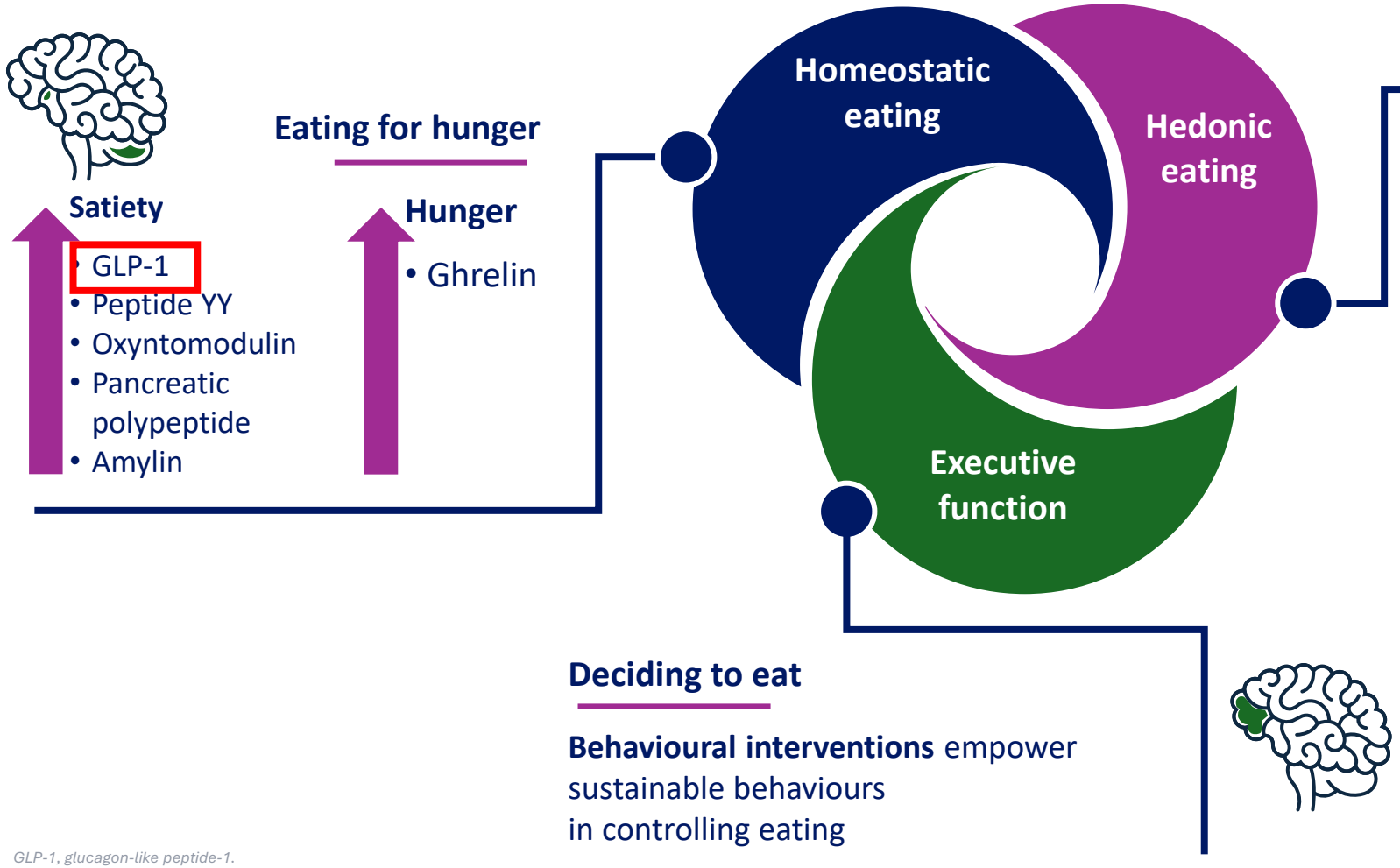
Initial Thoughts

- Where is psychological reassessment in our program today?

- Why would you recommend revisional Metabolic Bariatric Surgery (MBSx) given lower response rates and increased complications, when newer incretin based anti-obesity medications can achieve 15% weight loss compared with previous anti-obesity medications achieving 5-10% weight loss at 1 year in surgical naïve patients?

- Metabolic Surgery still most effective treatment in adults with severe obesity and diabetes achieving 25% weight loss at 2 years post operatively

Appetite Driven Energy Consumption



GLP-1, glucagon-like peptide-1.

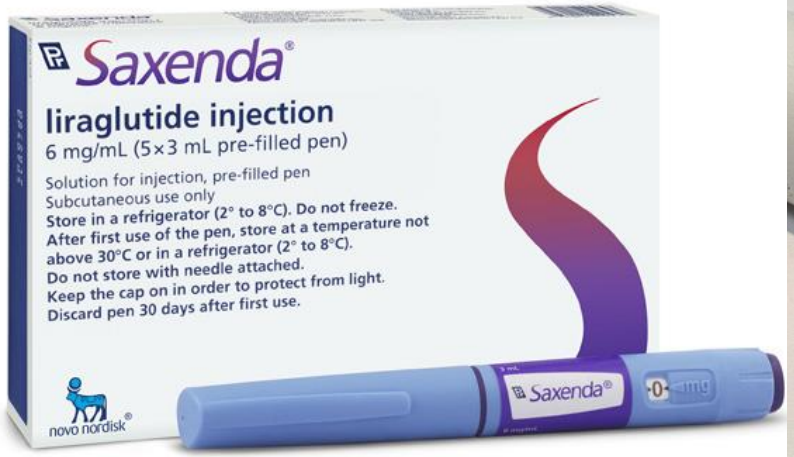
Non-Appetite Driven Energy Consumption

- Enjoyment
- Escape (Hunger vs Unwanted/Painful Feeling)
- Entrenched Behaviour

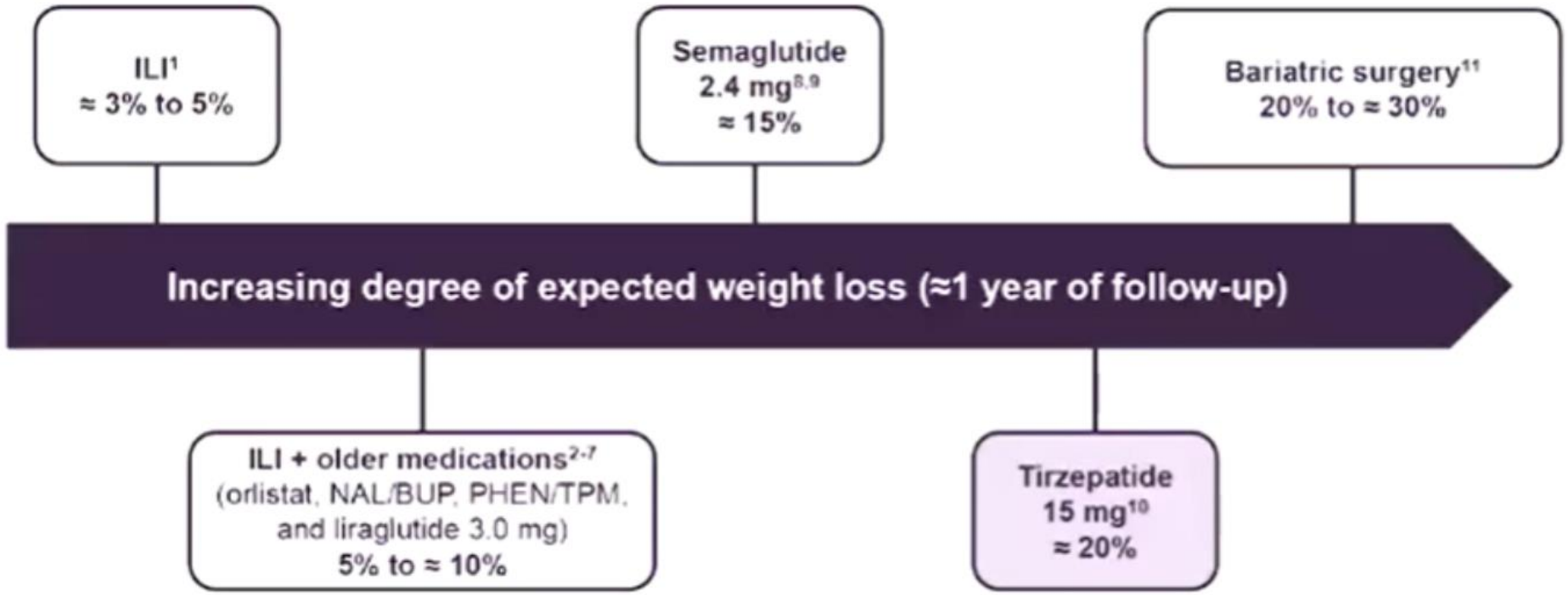

THARAWAL ABORIGINAL CORPORATION
A.M.S.
"Your Health, Our Commitment"
NO SMOKING
STRONG SPIRITS
STRONG MINDS

So what should we do now that we don’t believe Psychologically Driven Eating is Leading to RWG?

Pharmacotherapy

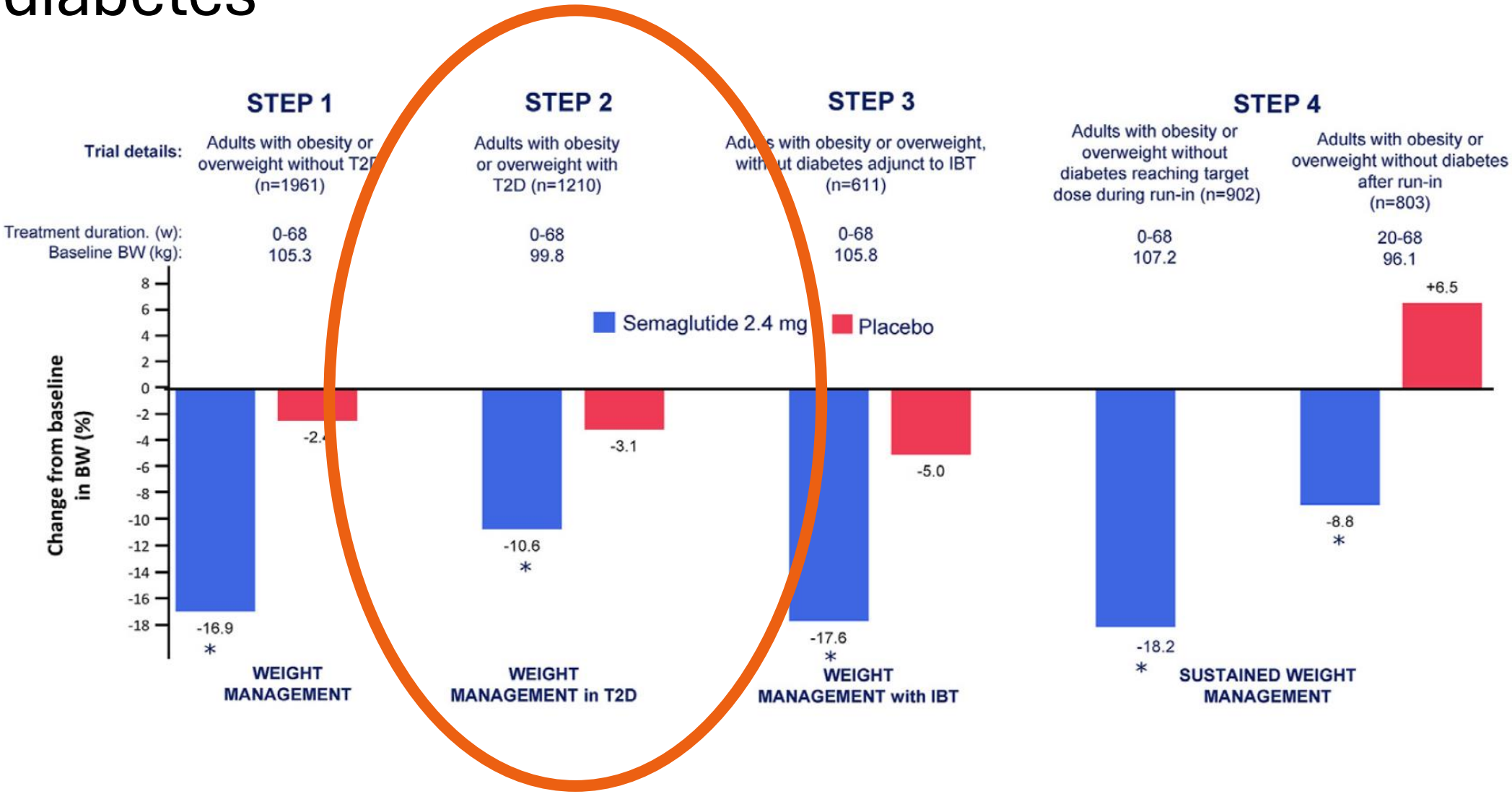


Efficacy of current obesity management options



The Obesity Society – Obesity fellowship course (2024)

Efficacy of Semaglutide for Obesity in patients with diabetes



Drucker, D. J. (2022). GLP-1 physiology informs the pharmacotherapy of obesity. *Molecular Metabolism (Germany)*, *57*, 101351–101351.

Real world data

Amount weight loss is not as large in real world setting

Average weight loss:

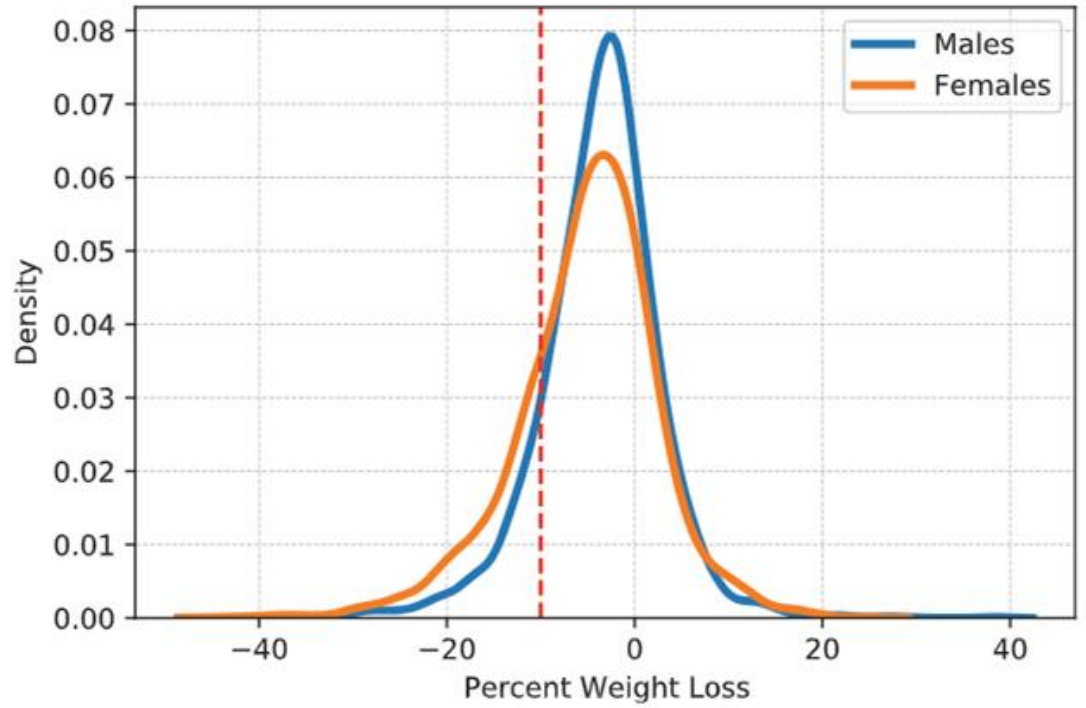
10% in clinical trials

Vs. 5% in real world setting

>10% weight loss responders:

25% in clinical trials

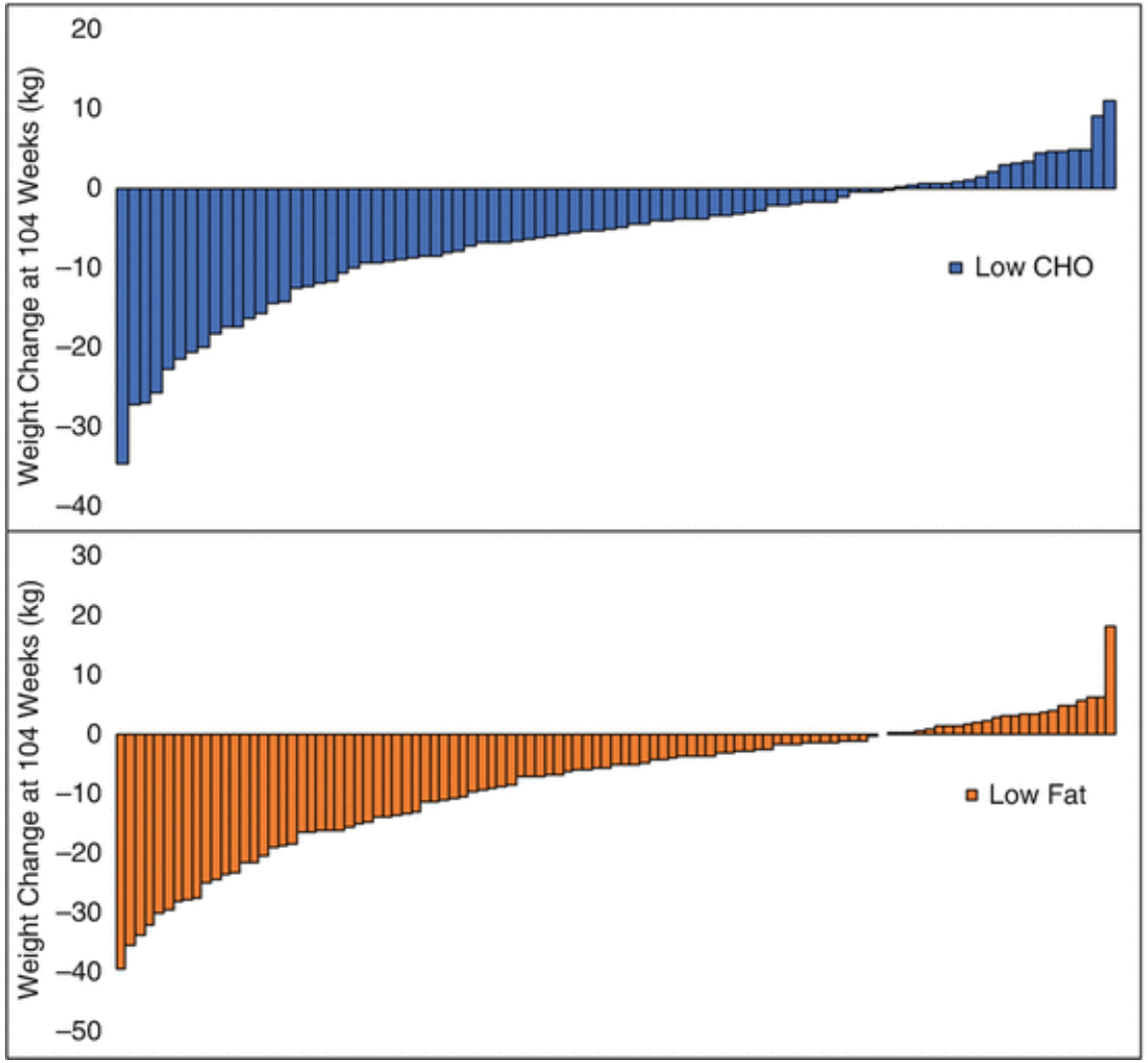
vs 18% in real world data



E 3 Density plots for percent weight loss for the 3555 total trackable individuals on semaglutide, stratified by male and female The threshold of 10% weight loss is shown by the vertical red line. Female individuals had a greater proportion of the population lo rcent of weight than male individuals.

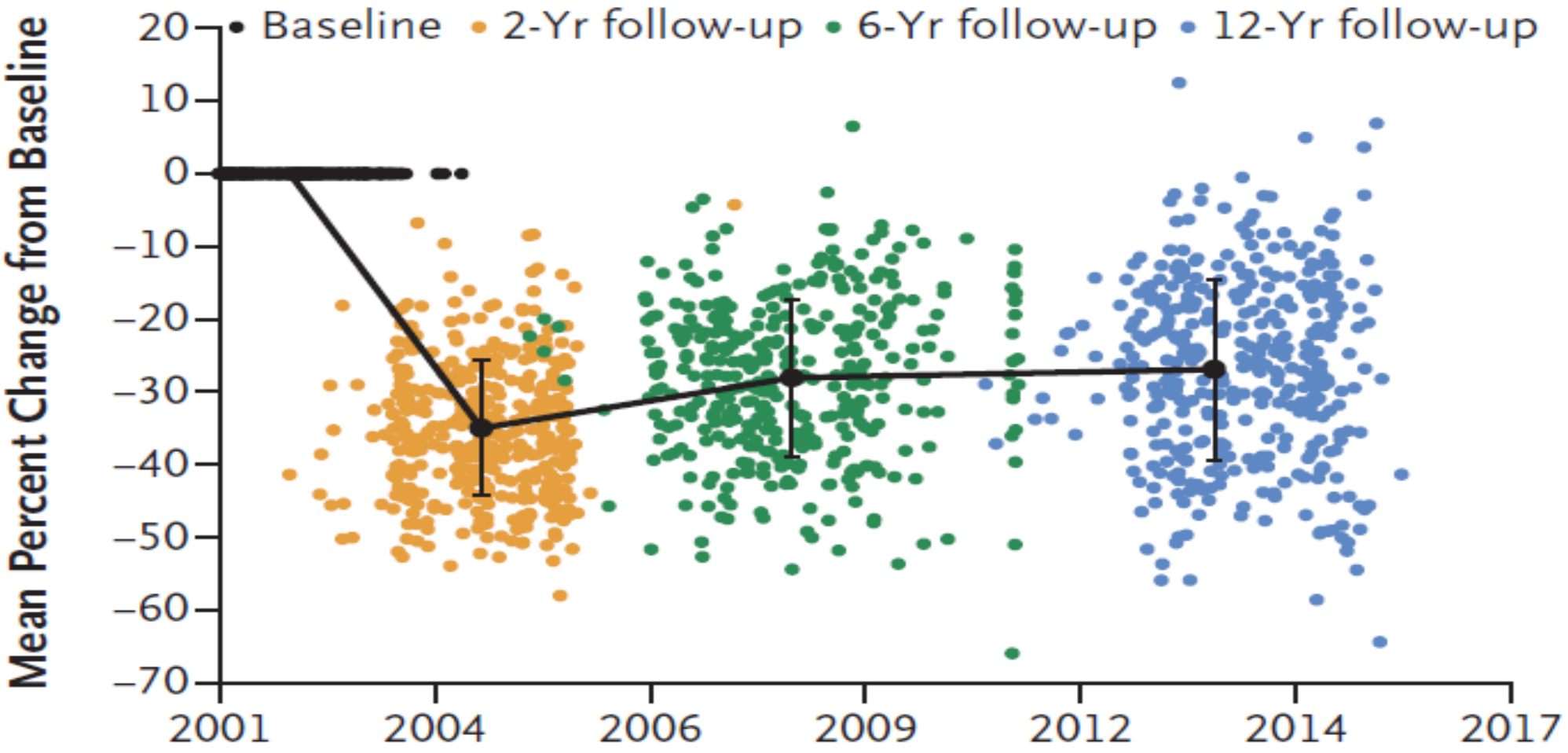
Powell et al. (2023). Medications and conditions associated with weight loss in patients prescribed semaglutide based on real-world data. *Obesity (Silver Spring, Md.)*, *31*(10), 2482–2492.

Weight loss variability



Weight 12 years after Roex-en-Y Gastric Bypass

Adams T NEJM Sept 2017



The utility of weight loss medications after BSx for weight regain or inadequate weight loss: A multi-center study

WLM

Evaluated 15 medications that were prescribed by obesity medicine physicians within the centers:

Phentermine **37.9%**	Metformin* **38.6%**
Topiramate* **60.8%**	Bupropion* **23.5%**
Zonisamide* **20.4%**	Orlistat **1.3%**
Sibutramine** **0.94%**	Liraglutide **11.9%**
Exenatide* **2.2%**	Pramlinitide*
Naltrexone* **4.1%**	Lorcaserin** **12.2%**
Phentermine/topiramate* **5.3%**	Canagliflozin* **0.94%**
Naltrexone/bupropion **2.8%**	

*Not indicated or registered for weight management in Australia. Please refer to respective PI's
**Withdrawn from the market

Stanford FC, Rubino F et al Surg Obes Relat Dis. 2017 Mar;13(3):491-500

The utility of weight loss medications after BSx for weight regain or inadequate weight loss: A multi-center study

Results

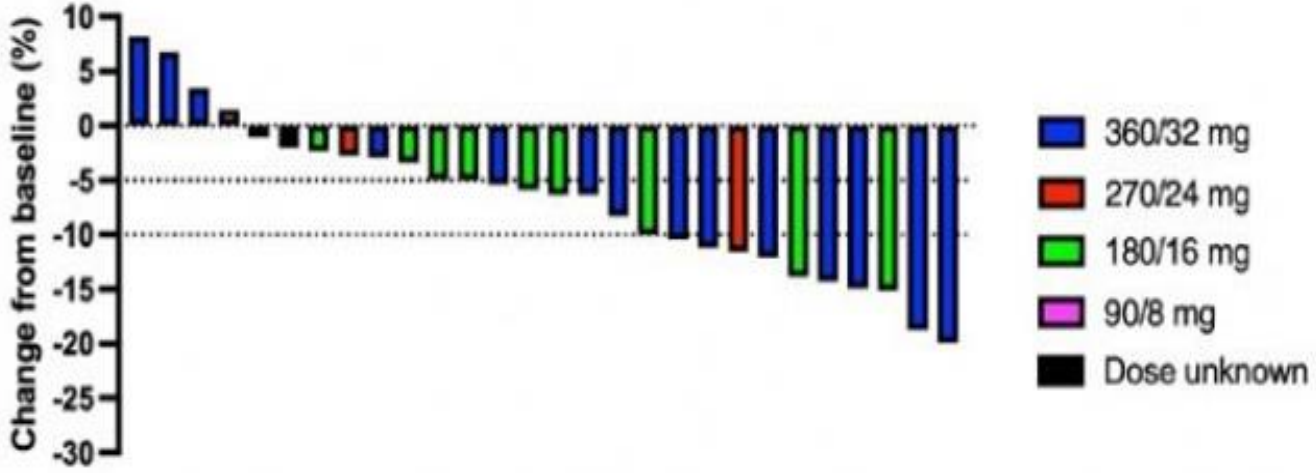
- Patients who had undergone RYGB were more likely to achieve greater weight loss compared with patients who had undergone an SG
- Topiramate only medication statistically shown to lead to weight loss (P = .02)
- 15% had > 15% weight loss with > 12 months follow up
- Patients with a history of psychiatric co-morbidity - more likely to lose ≥ 15% of their postsurgical total weight (P = .002)

Stanford FC, Rubino F et al Surg Obes Relat Dis. 2017 Mar;13(3):491-500

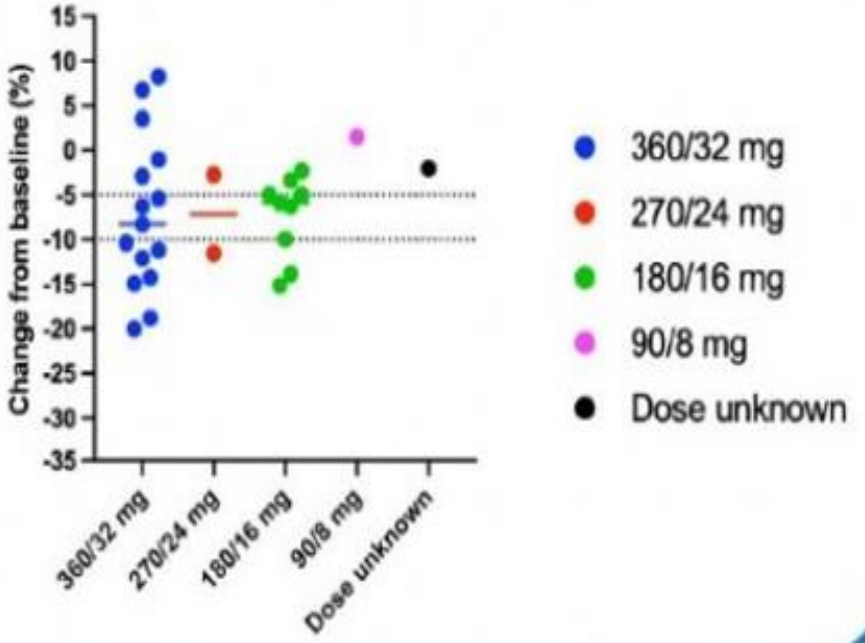
Contrave (Bupropion/Naltrexone) Post MBSx 2024

Outcomes

Body weight change from baseline to 4 months per individual



Similar weight loss even if maximal dose is not used§



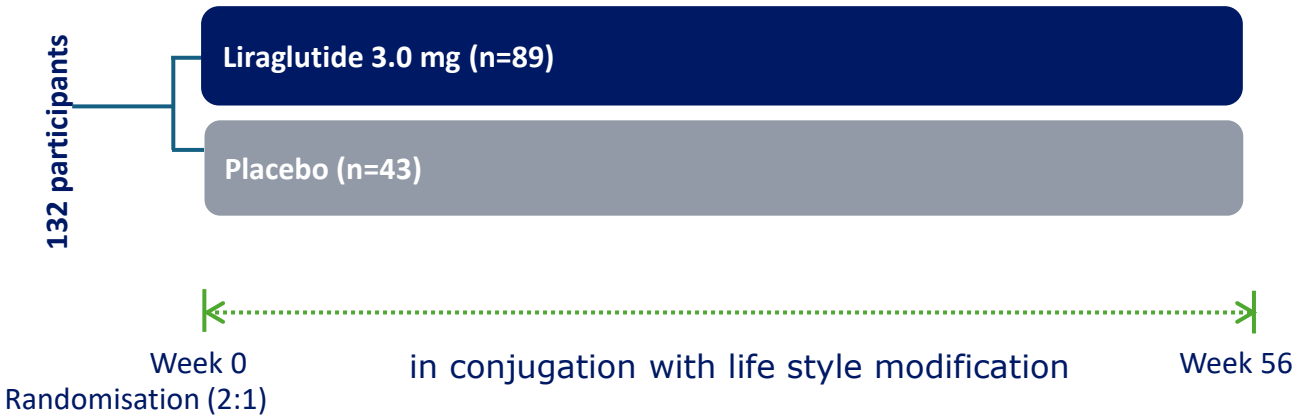
Yskout M et al Abstract presented at ECO Poster Presentation 2024, Italy

Trial design: Liraglutide 3.0 mg after Roux-en-Y gastric bypass (RYGB)

56 week, double blind, placebo-controlled trial

Inclusion criteria - Patients

- with 18-120 months post RYGB
- who achieved ≥25% TBWL
- who have regained ≥10% TBWL after reaching nadir weight
- who met criteria for weight management pharmacotherapy



Trial information

- Double-blind, placebo controlled, gender stratified, block randomized trial
- Duration: 56 weeks

Trial objective

- To test the efficacy of liraglutide 3.0 mg in conjugation to lifestyle modifications on weight regain after Roux-en-Y gastric bypass

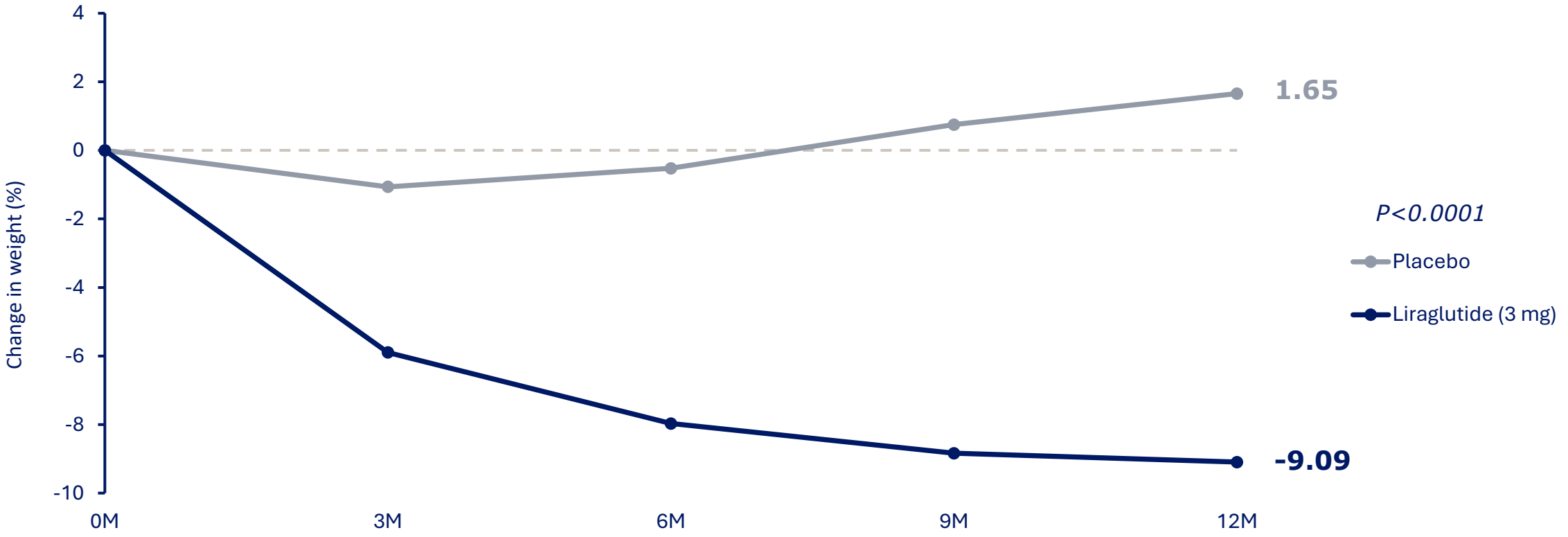
Key endpoints

- Primary: Proportion of patients losing >5% of baseline body weight
- Others: Change in weight (%) from baseline to week 56, proportion with ≥10%, and ≥15% weight loss (week 56 from baseline), change in CVD risk factors

CVD, cardio vascular disease; RYGB, Roux-en-Y gastric bypass; TBWL, total body weight loss

Lofton et al. 2021, Obesity week. Accessed in November 2021. Poster available at: https://tos.planion.com/Web.User/AbstractDet?ACCOUNT=TOS&ABSID=25495&CONF=OW2021&ssoOverride=OFF&CKEY=

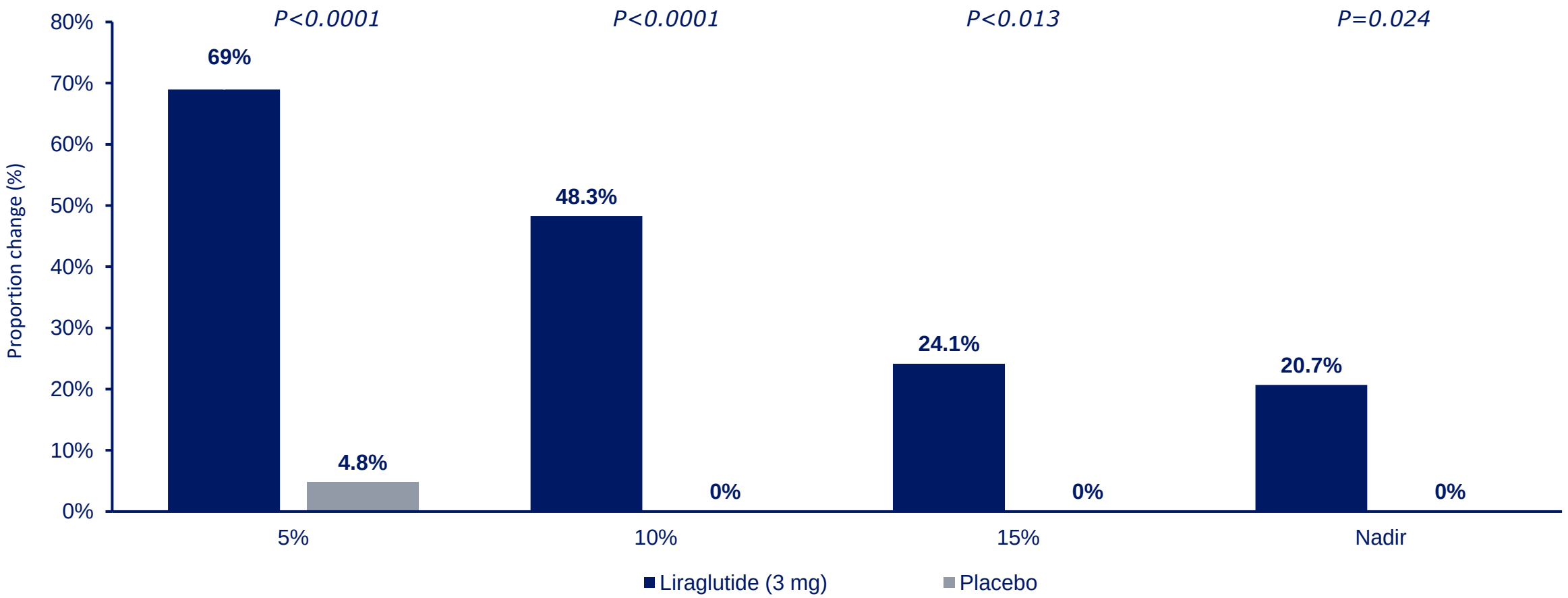
Change in body weight from baseline (%)



M, month

Lofton et al. 2021, Obesity week. Accessed in November 2021. Poster available at: https://tos.planion.com/Web.User/AbstractDet?ACCOUNT=TOS&ABSID=25495&CONF=OW2021&ssoOverride=OFF&CKEY=

Proportion with ≥5%, 10% or 15% weight loss or met/exceeded nadir at week 56



BARI-STEP Trial 2022

- Phase III Double Blind RCT
- Poor Weight Loss or Weight Regain post MBSx
- RYGB or LSG
- 68 weeks Semaglutide 2.4mg s/c weekly
- Finish date 2025

Future directions

GLP-1 receptor agonists approved for obesity treatment		
Semaglutide	Weekly SC	STEP trials
Liraglutide	Daily SC	SCALE trials

MONOTHERAPY

ENDO-PANCREATIC receptor agonists				
Cagrilintide	AMY RA	Phase II	Novo Nordisk	NCT03856047
ZP8396	AMY RA	Phase I	Zealand Pharma	NCT05096598
Amylin agonist LA	AMY RA	Phase I	Eli Lilly	Not available
DACRA QW II	AMY/CAL RA	Phase I	Eli Lilly	Not available

ORAL MONOTHERAPY

ORAL GLP-1 receptor agonists				
Semaglutide	GLP-1 RA	Phase III	Novo Nordisk	NCT05035095
Danuglipron	sm GLP-1 RA	Phase II	Pfizer	NCT04707313
LY3502970	GLP-1R NPA	Phase II	Eli Lilly	NCT05051579

DUAL RA combinations

ENTERO-ENDOCRINE receptor agonists/antagonists				
Tirzepatide	GIP/GLP-1 dual RA	Phase III	Eli Lilly	NCT04184622
CT388	GIP/GLP-1 dual RA	Phase I	Carmot Therapeutics	NCT04838405
Dapiglutide	GIP/GLP-2 dual RA	Phase I	Zealand Pharma	NCT04838405
AMG133	GIP Receptor Antagonist/ GLP-1 RA	Phase I	Amgen	NCT04478708

DUAL RA combinations

PANCREATIC-ENTERO-ENDOCRINE receptor agonists				
Cagri-Sema	AMY/GLP-1 dual RA	Phase III	Novo Nordisk	NCT03600480
Pemvidutide	GCG/GLP-1 dual RA	Phase II	Altimmune	NCT05295875
BI456906	GCG/GLP-1 dual RA	Phase II	Boehringer Ingelheim	NCT04667377
NN9277	GCG/GLP-1 dual RA	Phase I	Novo Nordisk	NCT03308721

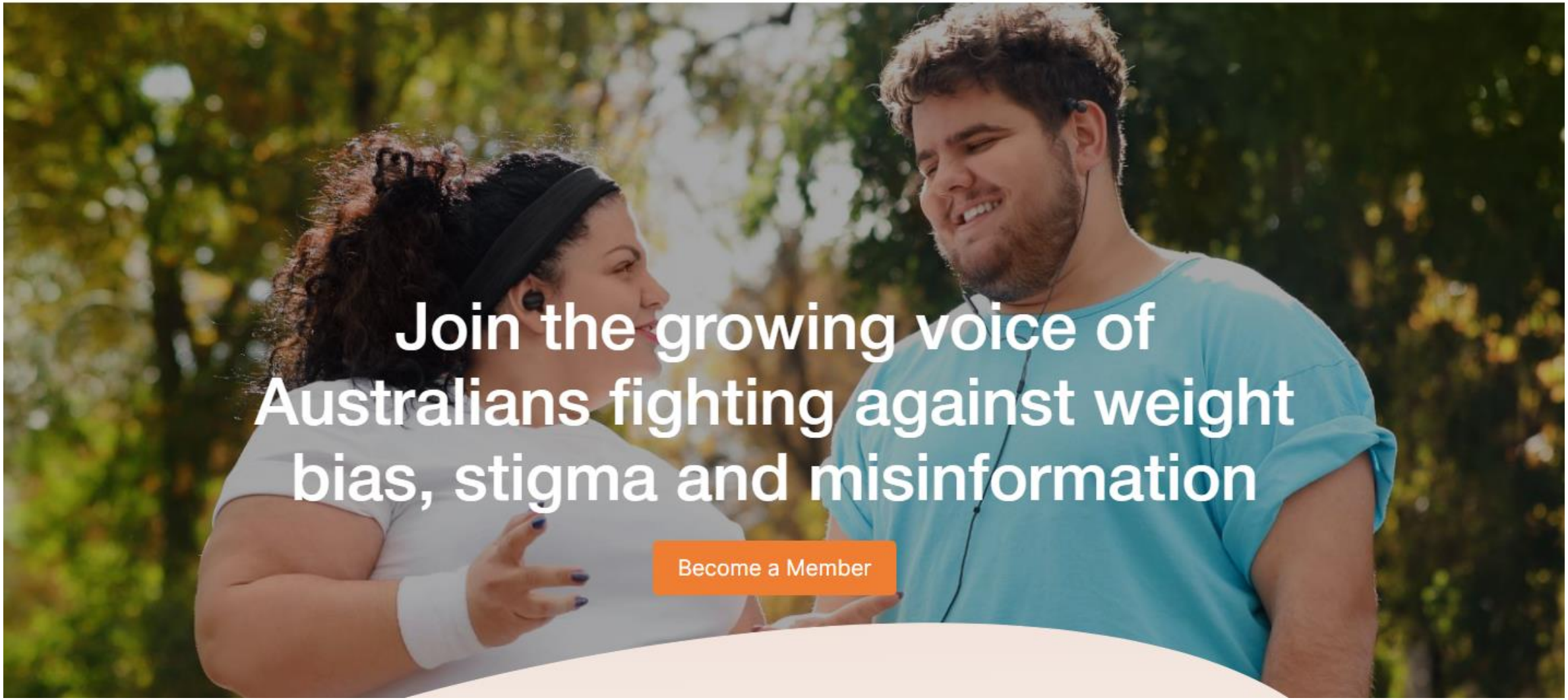
TRIPLE RA combinations

PANCREATIC-ENTERO-ENDOCRINE receptor				
Retatrutide	GIP/GCG/GLP-1 triple RA	Phase II	Eli Lilly	NCT04881760

Jastreboff et al (2023). New Frontiers in Obesity Treatment: GLP-1 and Nascent Nutrient-Stimulated Hormone-Based Therapeutics. *Annual Review of Medicine*, *74*(1), 125–139.

Weight Issues Network

We are WIN | Weight stigma | WIN at Work | Contact WIN | Donate | Free membership



Take Home Points

- Recurrent Weight Gain may occur as result of non-appetite driven factors which need to be excluded before revisional MBSx is considered
- Newer Incretin Based Anti Obesity Medications are significantly more effective in facilitating weight loss than previous AOM's, with no demonstrated significant long term safety issues to date
- Although response cannot be predicted, a trial of AOM's before revisional MBSx seems logical
- Anti Obesity Medications may be as effective at lower doses after MBSx