The Timing of GLP-1 Receptor Agonists Used After Bariatric Surgery

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Disclosures

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Outlines

Why do we need adjuvant GLP-1 RAs?

When & how long do we use it?

Post-MBS:

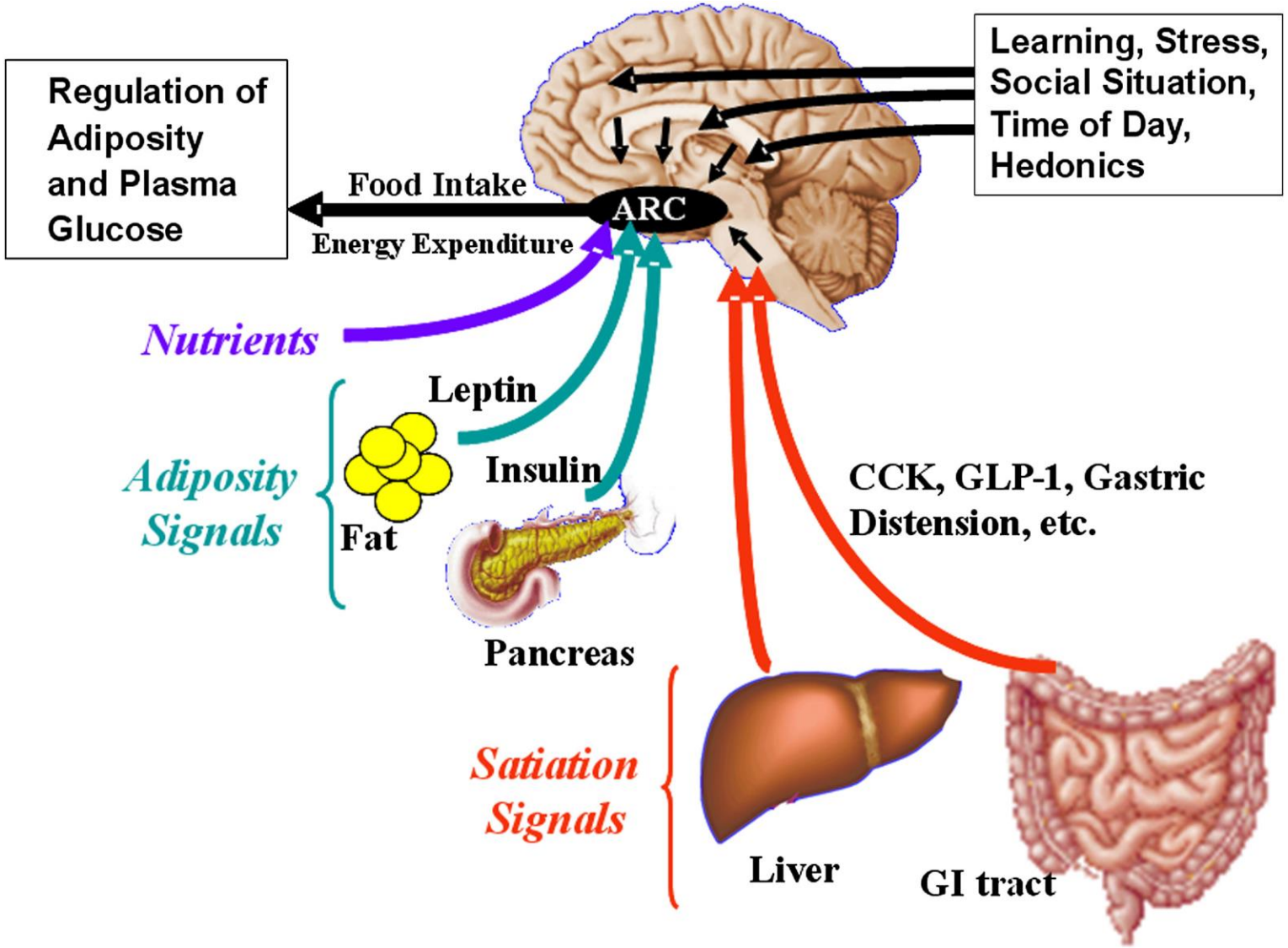
- Suboptimal clinical response
  - Inadequate weight loss (Weight loss plateau)
  - no improvement or worsening of any obesity complications
- Recurrent weight gain or Late clinical deterioration (Weight recurrence)

Adjuvant

Why do we need adjuvant GLP-1 RAs?

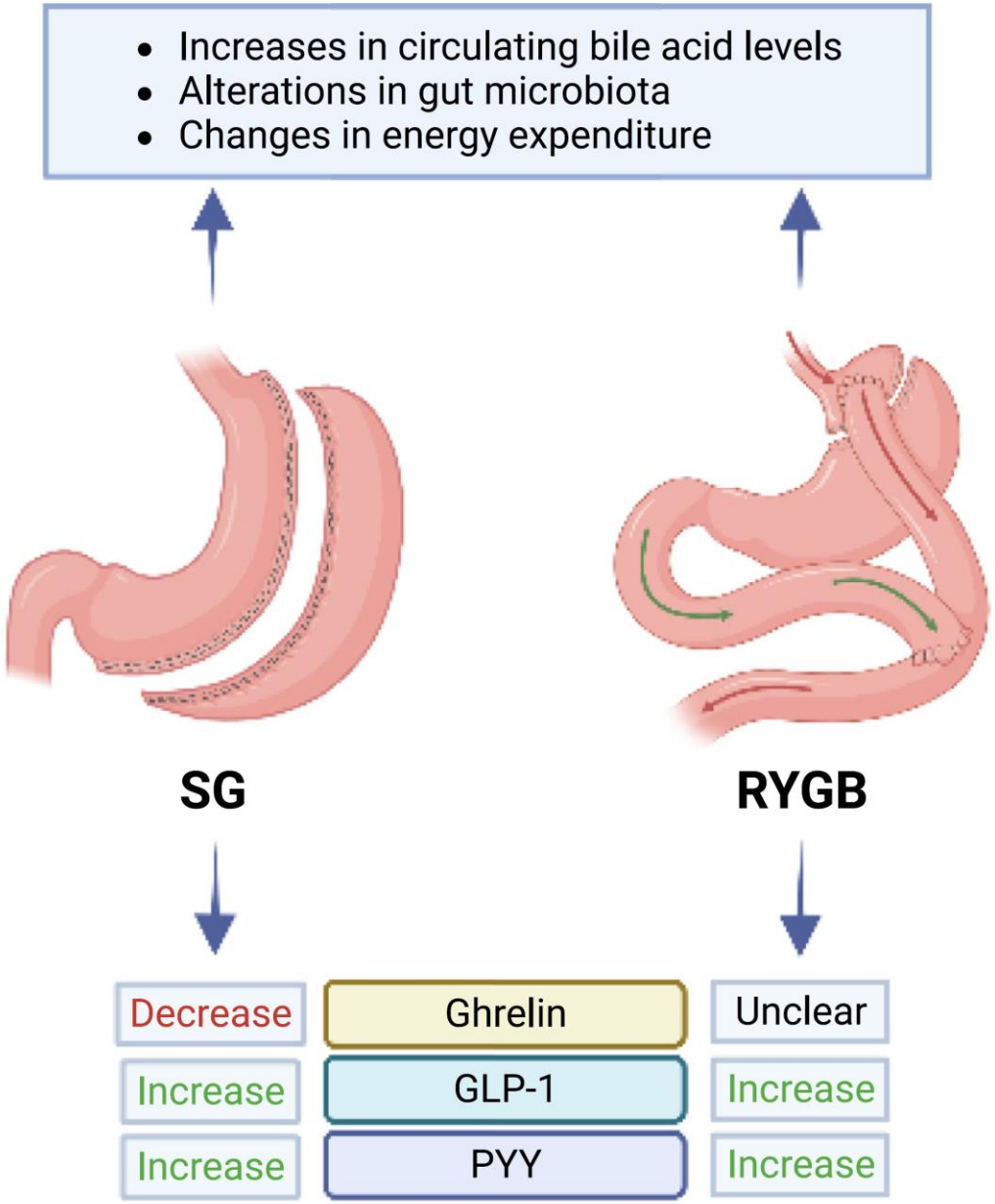
Obesity is a Disease of the Brain and Regulation Pathways

Pathophysiology of eating and weight regulation



*2009 Cell Metabolism Woods et al.

Impact of MBS on Gut Hormones



MBS works through alteration of biochemistry and gut hormones.

Different procedures impact hormones differently and can have different mechanisms of action.

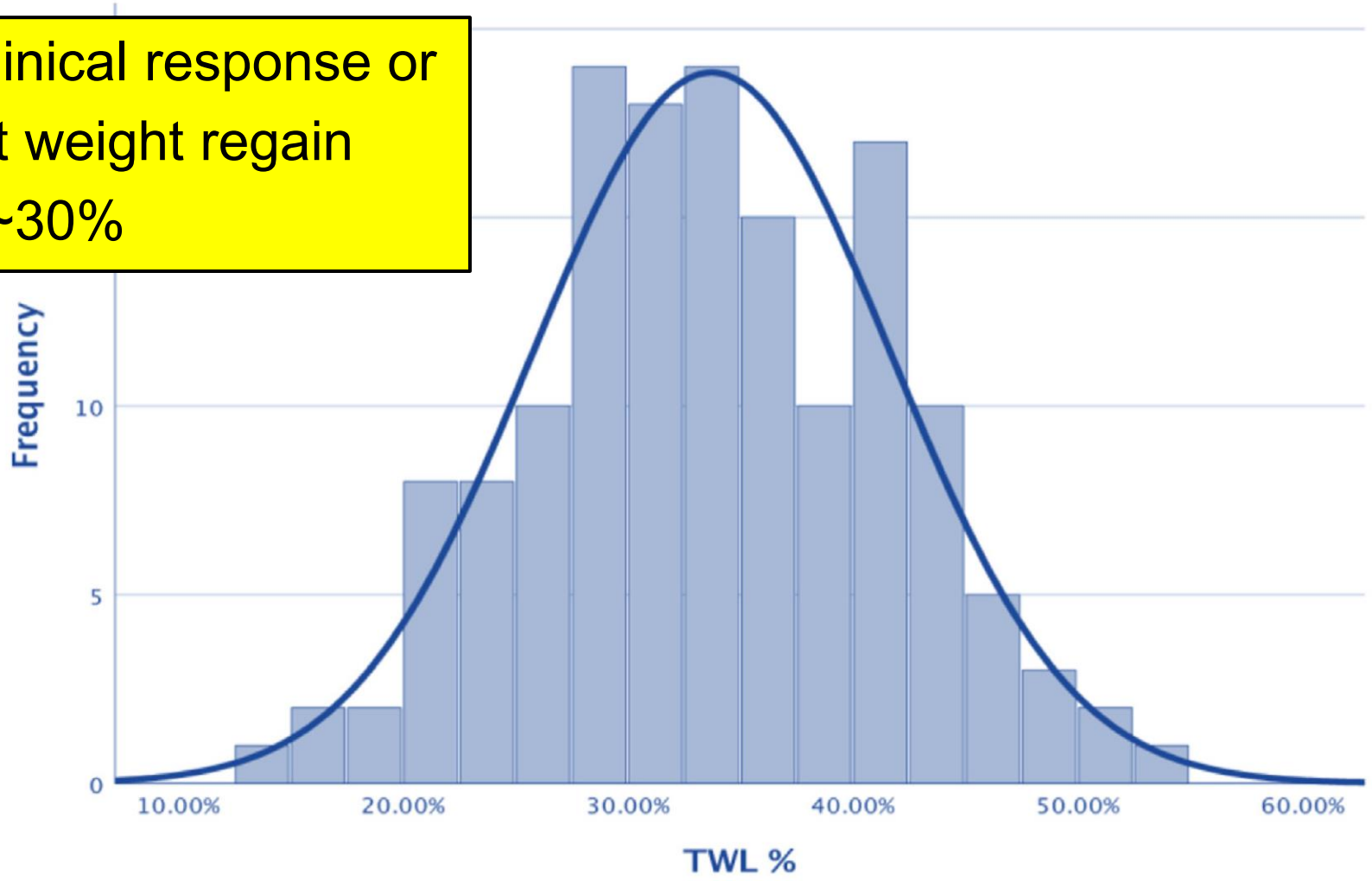
*2023 Gastroenterol Clin North Am Alabduljabbar.et al.

Variable Response

All treatments including MBS have variation of response within individuals.

There is a bell-shaped curve distribution.

Suboptimal clinical response or
Significant weight regain
~30%

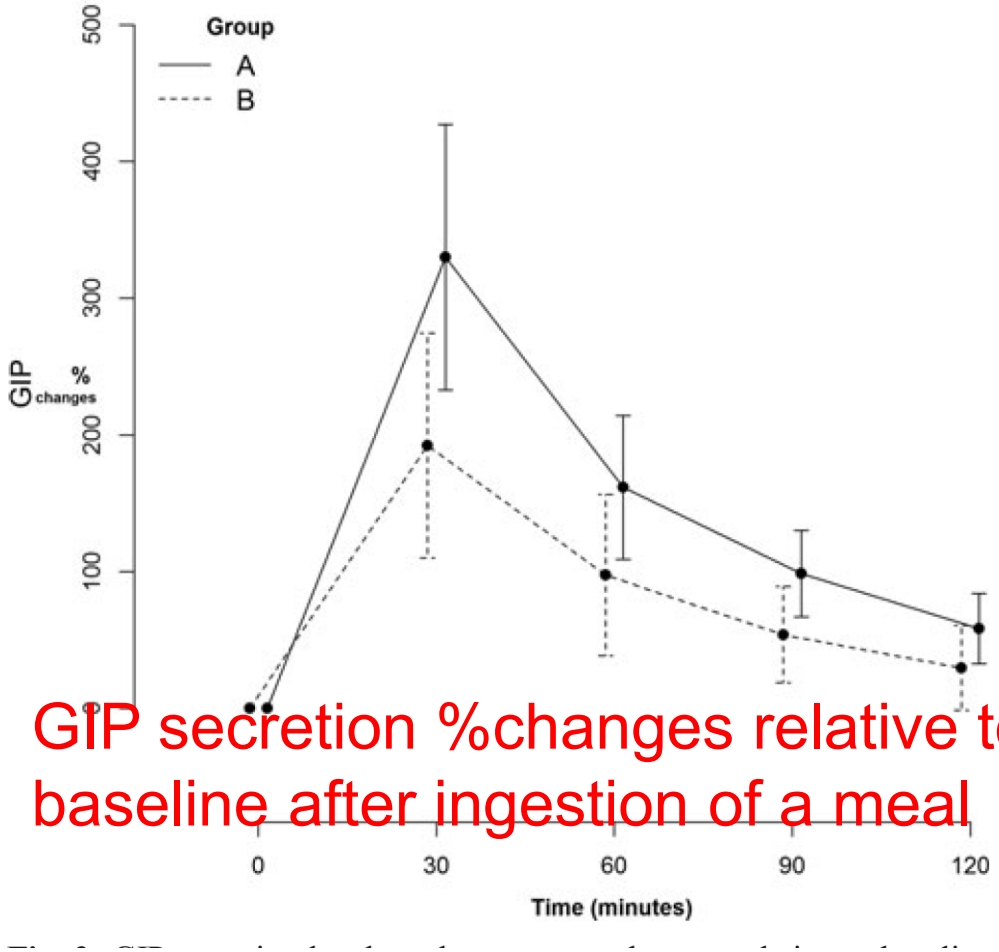


*2024 SOARD Pugin et al.

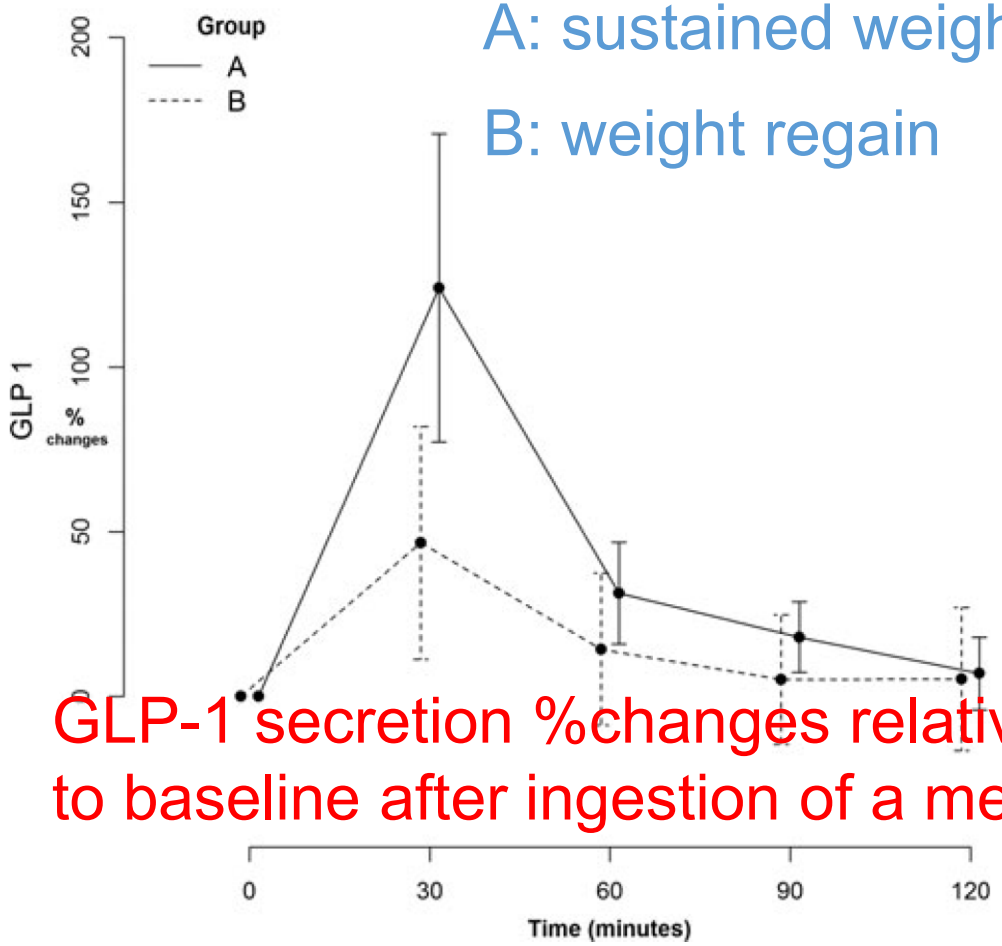
Possible Mechanism of Weight Regain

Hormonal impact is different in those with weight regain.

Less increase in GLP-1 & GIP for weight regain group.



GIP secretion %changes relative to baseline after ingestion of a meal



GLP-1 secretion %changes relative to baseline after ingestion of a meal

A: sustained weight loss

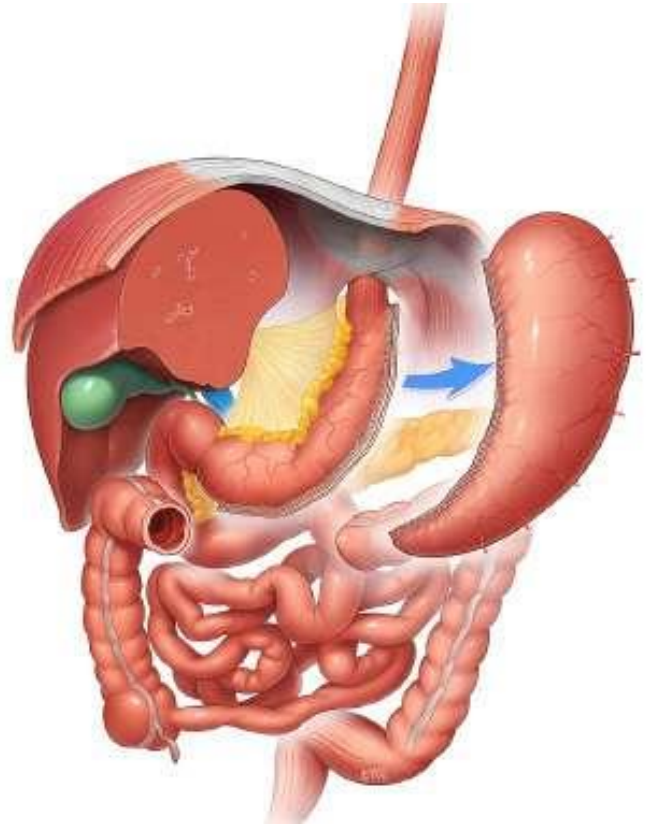
B: weight regain

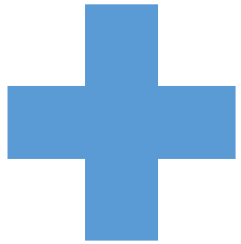
*2016 Obes Surg Santo et al.

Adjuvant Therapy

Enhance or prolong effects of surgery

Treat persistent disease





When & how long do we use it?

Combination of OMM and MBS

Neoadjuvant

Post-MBS:

- Suboptimal clinical response

  Inadequate weight loss (*Weight loss plateau*)

  no improvement or worsening of any obesity complications

- Recurrent weight gain or Late clinical deterioration (*Weight recurrence*)

Adjuvant

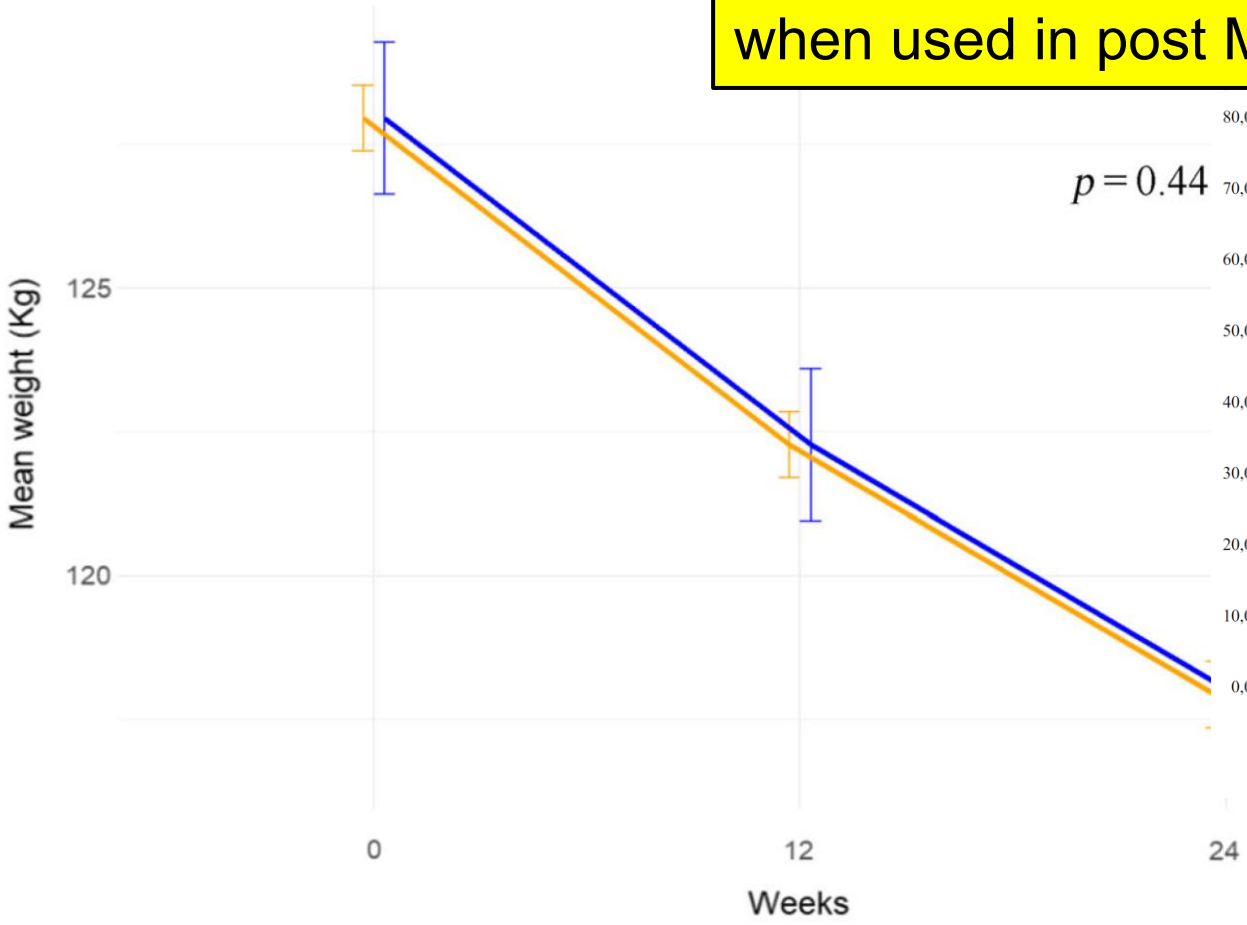
Similar Effect with or without MBS (Observational Study)

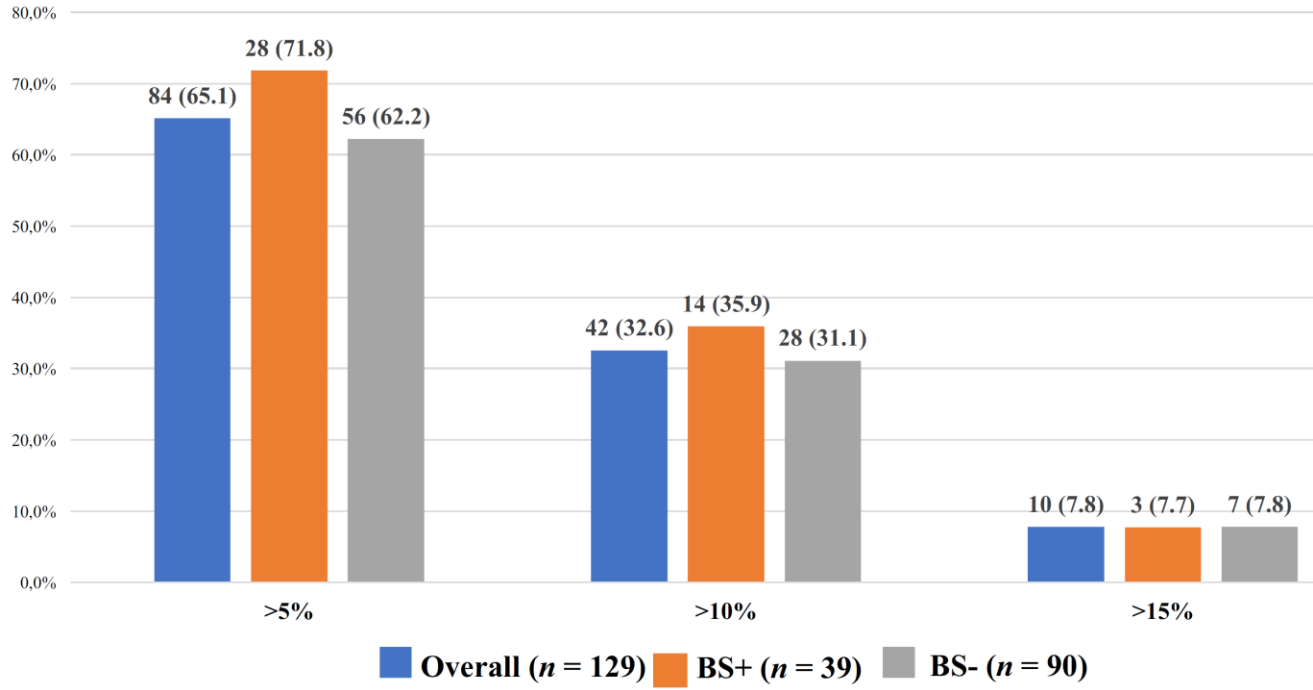
BMI ≥ 40 kg/m^2, 39 pts with MBS (IWL or WR) and 90 without MBS.

Semaglutide 2.4mg for 24 weeks

TWL -9.8% vs. -8.8%

Weight loss with GLP-1 RAs appears to be similar when used in post MBS and in non-surgical weight loss.





*2023 JAMA Surgery Mok et al.

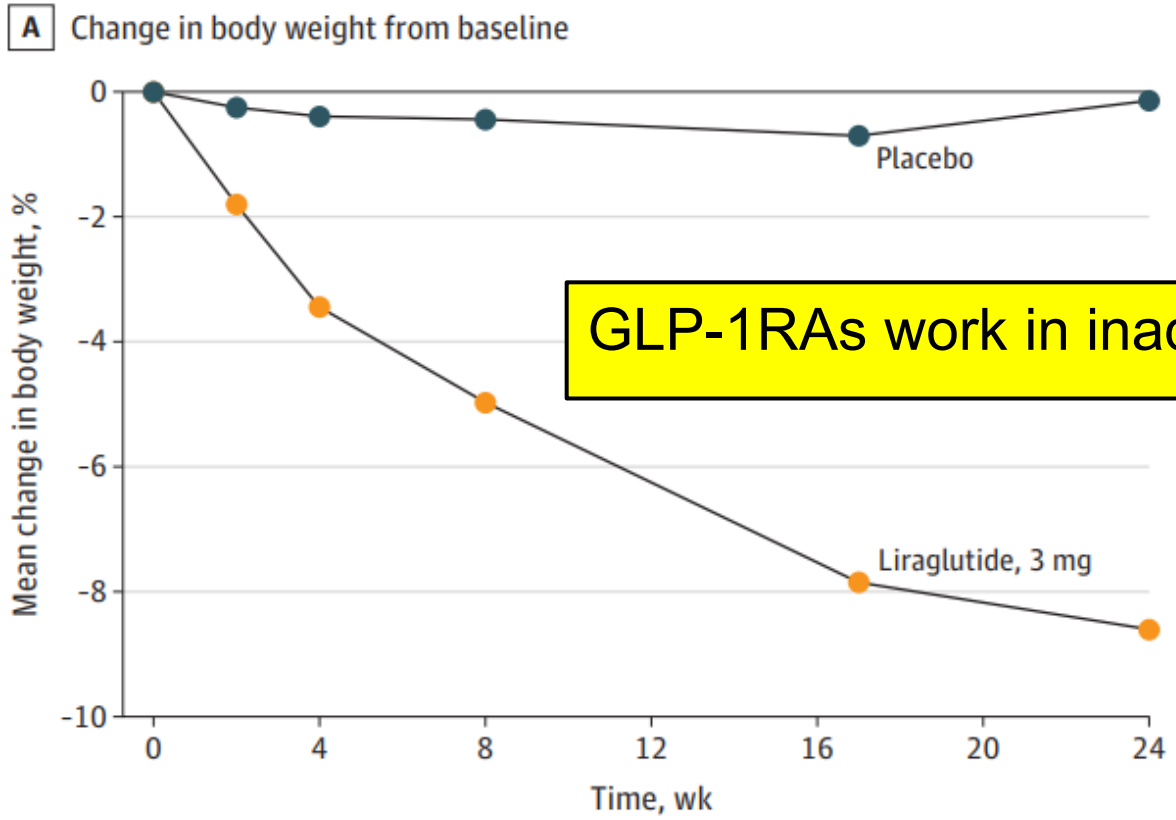
BARI-OPTIMISE Trial (Evidence from RCT in Inadequate WL)

20% or less TWL and suboptimal GLP-1 response, at least 1yr post-op, 70pts

Liraglutide 3.0mg daily vs placebo adjunct to lifestyle intervention for 24 weeks

TWL -8.3% vs. -0.5%

Figure 2. Effect of Liraglutide, 3.0 mg, Once Daily vs Placebo Over Time



GLP-1RAs work in inadequate weight loss.

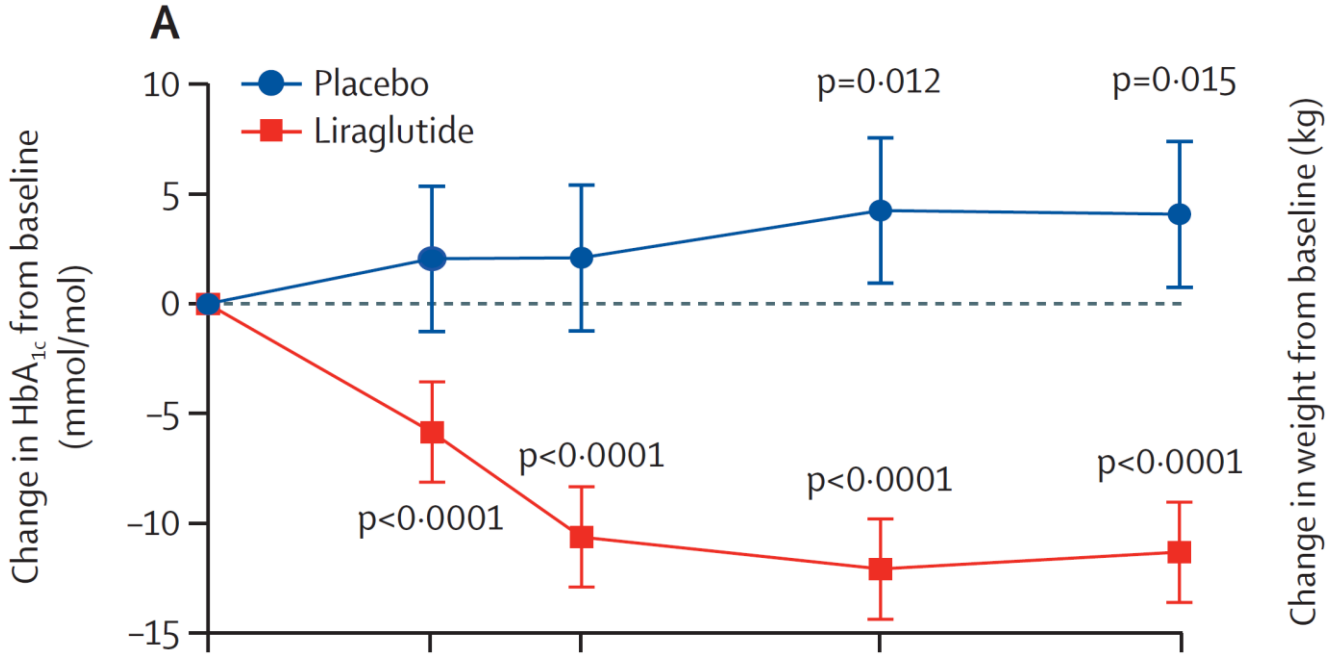
*2023 JAMA Surgery Mok et al.

GRAVITAS trial (Evidence from RCT in T2DM)

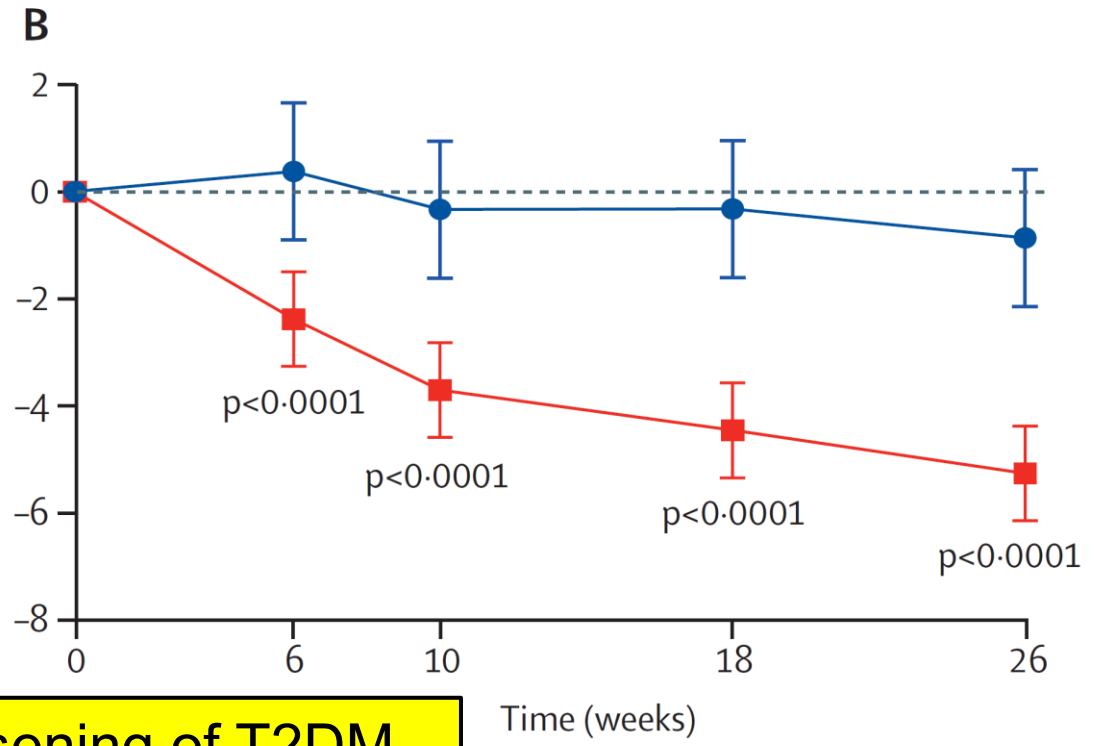
Persistent or recurrent T2DM at least 1-year after RYGB or SG

Liraglutide 1.8mg for 26 weeks (N=53) vs. placebo (N=23)

HbA1c change difference –13.3 mmol/mol (p=0·0001)



Weight change Difference 4.23kg (p=0·0001)



GLP-1RAs work in no improvement or worsening of T2DM.

*2019 Lancet Diabetes Endocrinol Miras et al.

Post-MBS GLP-1 Effect from Meta-analysis in IWL or WR

10 studies included meta-analysis involving 769 patients (392 treated with GLP-1 RAs)

Mean age 44.1 years, Male 30.5%

Time interval from surgery to the initiation of GLP-1RAs: 1.5 to 86.7 months

Treatment durations: 4 to 12 months

Result

1. Significantly greater WL in the GLP-1RAs group compared to placebo (SMD = 0.82, 95% CI 0.23 to 1.42). Subgroup
2. Treatment durations ≤ 6 months indicated a higher WL in the GLP-1RAs group (SMD = 0.79, 95% CI 0.25 to 1.34).
3. Adverse events were primarily gastrointestinal, with nausea significantly more frequently in the GLP-1RAs group (OR = 2.01, 95% CI 1.24 to 3.27).

*2025 Eat Weight Disord Mousavi et al.

Treatment Duration from Meta-analysis in IWL or WR

A total of 19 articles using 3 mg of Liraglutide and 1mg of Semaglutide

Result

Treatment duration	≤ 6 months	6–12 months	>12 months
Weight loss (Kg)	7.02	8.65	6.99
BMI loss (kg/m2)	3.07	5.22	3.09

Semaglutide showed significantly greater weight loss compared to Liraglutide, with a mean difference of 4.15 kg.

Common complications

nausea (19.1%), constipation (8.6%), abdominal pain (3.7%), and vomiting (2.4%)

*2024 Obes Rev Esparham et al.

Adverse Event According to Duration of Medication

Single center retrospective cohort with 559 patients

Female 89% and mean age 47.8 years

Median duration of surgery to AOM exposure: 30 months

Result

GLP-1RAs use was not associated with higher odds of AEs:

GLP-1RAs adjusted odds ratio (aOR) 1.1 (95% CI 0.5–2.6)

FDA-approved and off-label AOM aOR 1.1 (95% CI 0.6–2.3)

AOM initiation ≥12 months after surgery was associated with lower risk of AEs compared to <12 months (aOR 0.01 [95% CI 0.0–0.01]; $p < 0.001$).

*2024 Diabetes Obes Metab Samuels et al.

Adjuvant GLP-1 RA (RCT)

BMI > 30 kg/m^2 undergoing LSG

Liraglutide (L-L group, 12) vs. placebo (L-P group, 11) from 6 weeks post-operative until 6 months

Parameters	Follow-up	L-L group ($n = 12$)	L-P group ($n = 11$)	p value
TWL (%)	6 weeks	12.7 ± 4.1	10.7 ± 3.9	0.198
	12 weeks	20.6 ± 6.3	17.7 ± 6.1	0.188
	24 weeks	28.2 ± 5.7	23.2 ± 6.2	0.116
BMI loss (kg/m^2)	6 weeks	6.2 ± 2.4	4.6 ± 2.6	0.267
	12 weeks	8.6 ± 3.0	7.1 ± 3.3	0.381
	24 weeks	11.7 ± 3.5	9.5 ± 4.0	0.287
EWL (%)	6 weeks	27.2 ± 10.1	20.4 ± 6.8	0.168
	12 weeks	42.6 ± 10.3	34.1 ± 8.1	0.112
	24 weeks	58.7 ± 14.3	44.5 ± 8.6	0.043*

Liraglutide Augments Weight Loss after LSG

*2021 Obes Surg Thakur et al.

Timing of Starting OMM: Earlier rather than Later

Retrospective single center study with 197 bariatric surgery patients

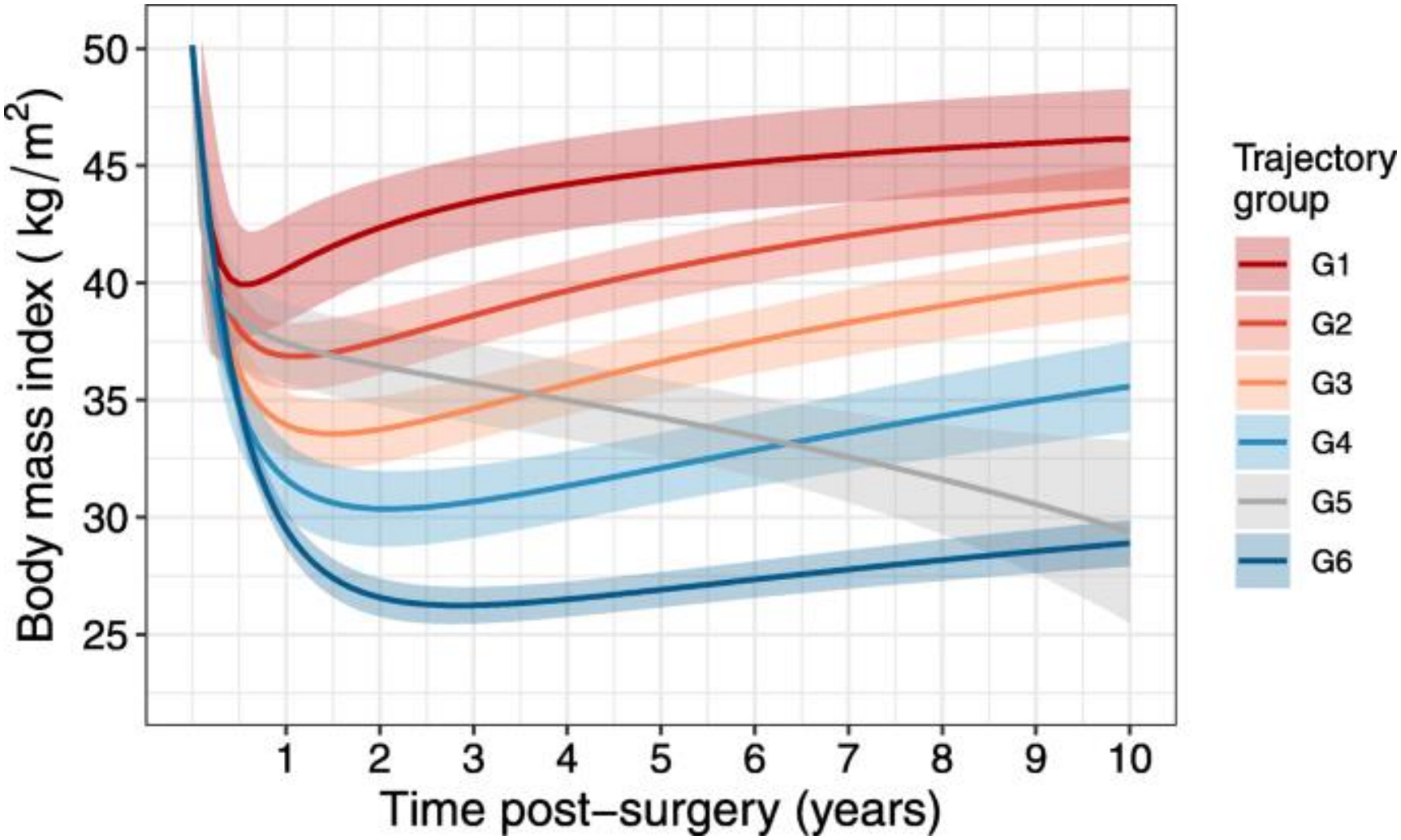
All kinds of OMM including GLP-1 RAs

	All patients	WR	AWL	NR	*p* values		
					WR vs. AWL	WR vs. NR	AWL vs. NR
Weight at start of medication (kg)	101.5 (± 19.4)	101.7 (± 18.8)	97.2 (± 23.5)	107.9 (± 14.4)	0.25	0.18	0.09
BMI at start of medication (kg/m^2)	38.0 (± 5.8)	38.0 (± 5.9)	36.6 (± 5.9)	40.2 (± 4.3)	0.18	0.12	*0.02*
%TBWL at post-op nadir	29.4 (± 10.5)	32.1 (± 10.1)	25.1 (± 7.1)	17.1 (± 7.0)	*< 0.01*	*< 0.01*	*< 0.01*
%TBWL on meds from initiation	7.5 (± 5.9)	7.7 (± 5.9)	6.7 (± 5.9)	7.6 (± 6.7)	0.34	0.91	0.50
%TBWL on meds from post-op nadir	− 11.3 (± 23.3)	− 16.5 (± 24.7)	4.0 (± 10.7)	− 2.3 (± 10.7)	*< 0.01*	*0.02*	*0.04*
%TBWL on meds from pre-op weight	22.9 (± 10.0)	22.5 (± 9.3)	28.1 (± 10.4)	15.4 (± 9.1)	*< 0.01*	*< 0.01*	*< 0.01*
Time (months) from surgery to medications							
Mean (±SD)	65.6 (± 106.5)	67.3 (± 51.7)	32.6 (± 22.1)	47.2 (± 33.8)	*< 0.01*	0.17	*0.03*
Median (IQR)	44.0 (26.4)	47.8 (31.0)	25.9 (17.5)	42.8 (24.8)			

AWL group initiated OMM earlier and experienced more weight loss when compared to their pre-operative weight or post-operative nadir.

*2021 J Gastrointest Surg Edgerton et al.

Initial Weight Loss is Important



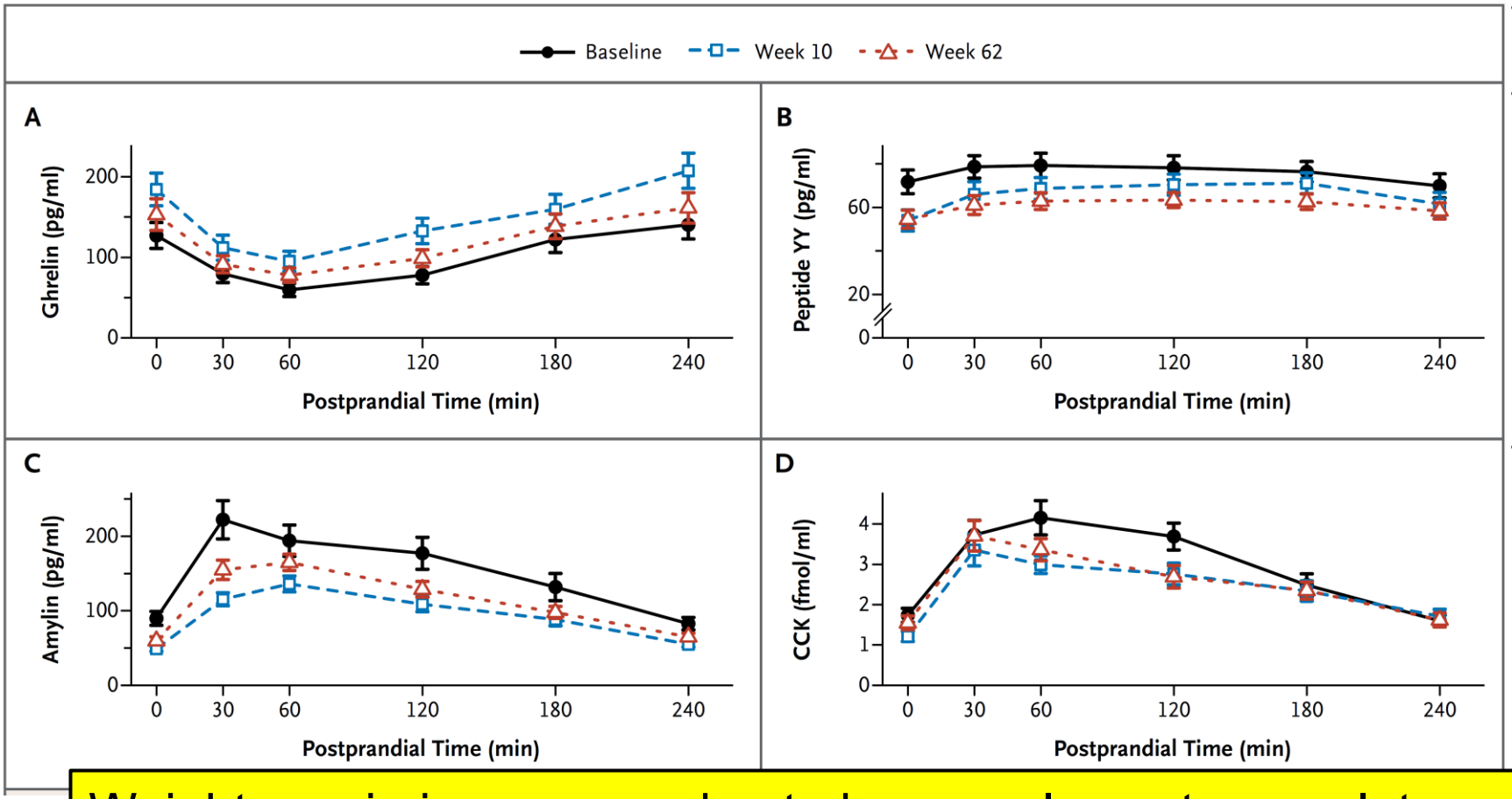
The difference in initial weight loss can lead to differences in long-term weight loss.

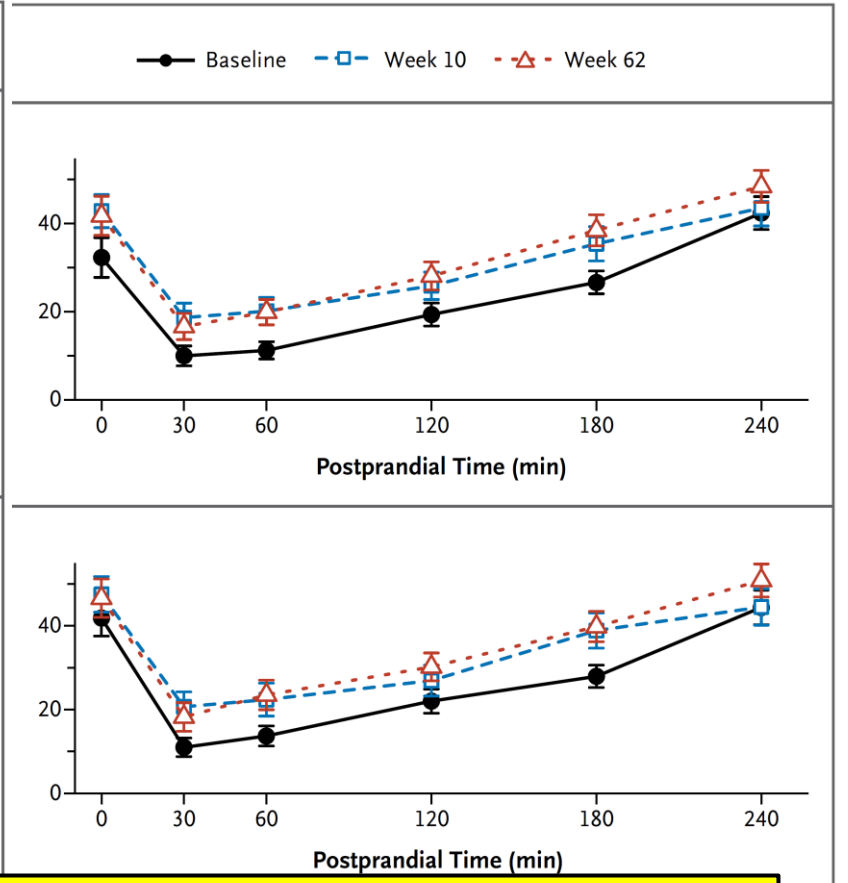
*2018 JAMA Surgery Courcoulas et al.

Long-term Hormonal Adaptations to Weight Loss

10-week of weight loss program & 1-year f/u

Check GI hormone (Ghrelin, Peptide YY, Amylin, CCK,& appetite (hunger, desire to eat)





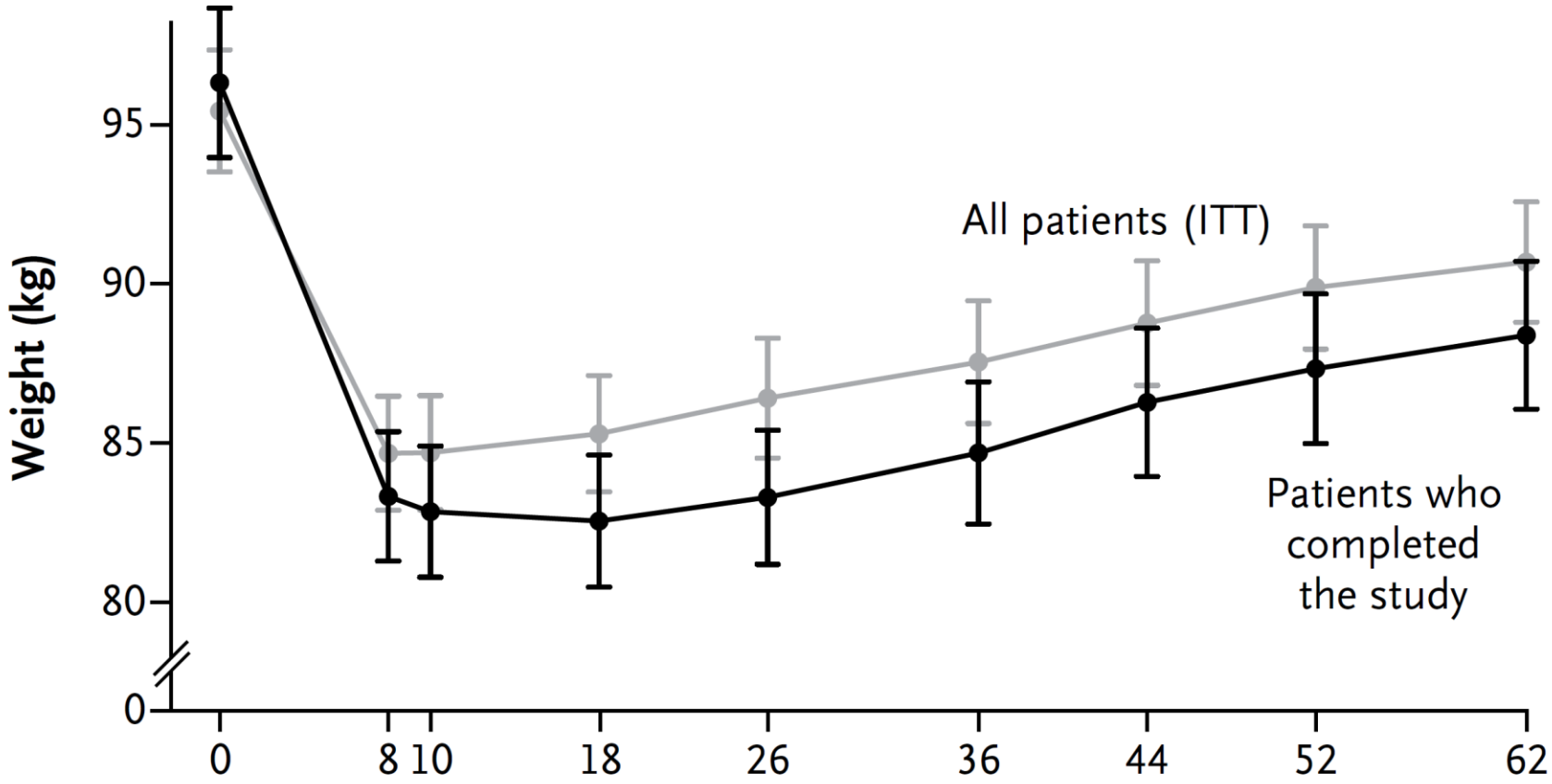
Weight regain is common due to hormonal counter regulatory adaptations for a long period

*2011 NEJM Sumithran et al.

Long-term Strategies is Needed

10-week of weight loss program & 1-year f/u

Patients with completed program vs. without completion

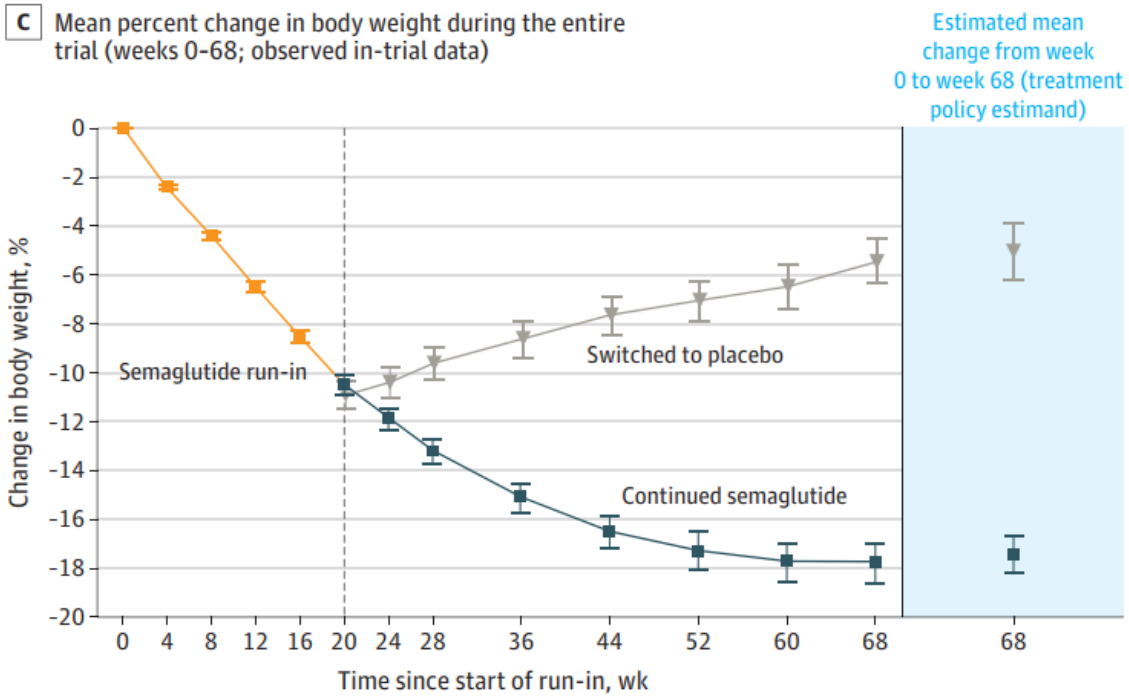


Long-term strategies to counteract this change may be needed to prevent obesity relapse.

*2011 NEJM Sumithran et al.

Sustained Weight Loss is Difficult

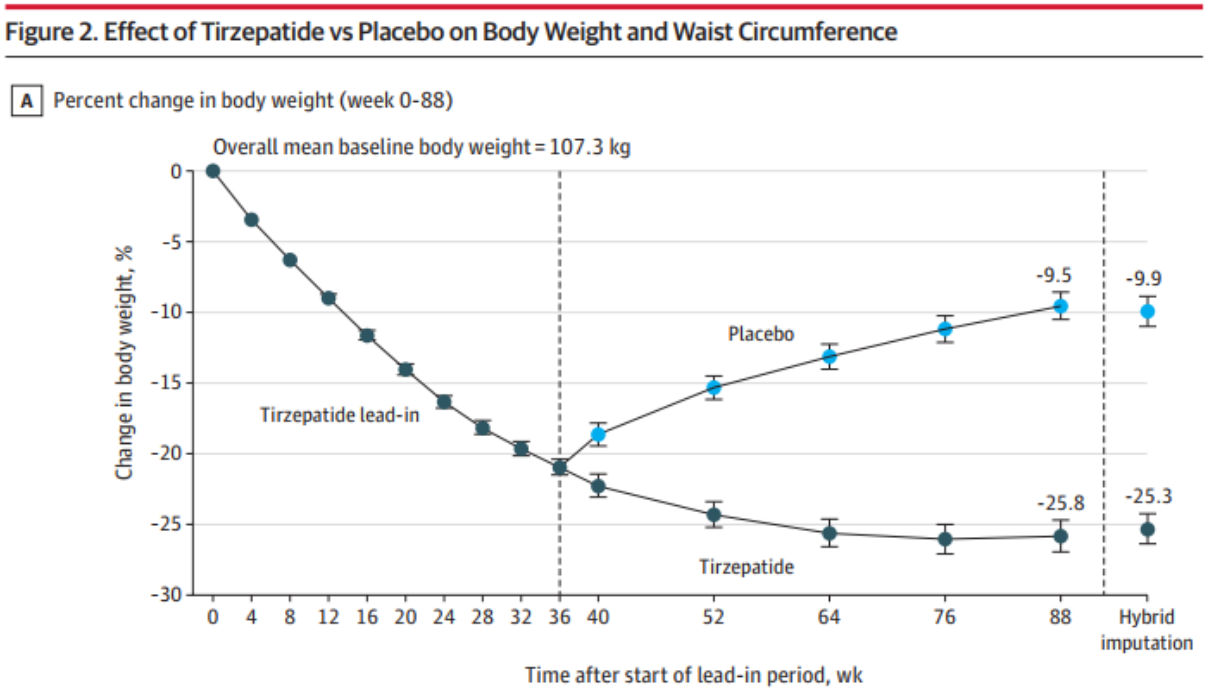
Step 4 Trial: Semaglutide



No. of participants

Semaglutide run-in	803 803 803 802 801							
Continued semaglutide	535 527 531	525	523	521	516	520		535
Switched to placebo	268 267 265	258	260	254	246	250		268

Surmount 4 Trial: Tirzepatide



No. at risk

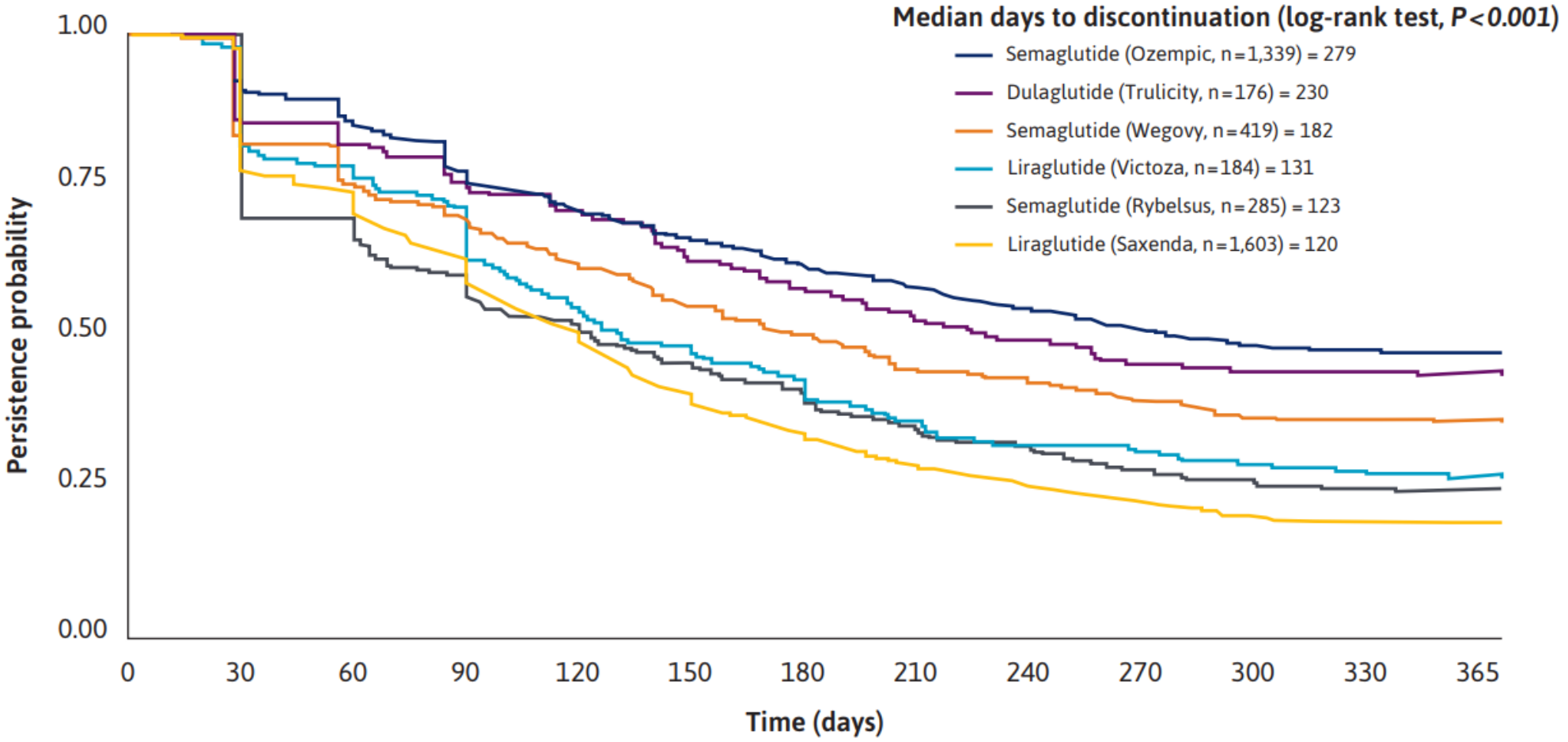
Tirzepatide lead-in	670 666 669 668 667 667 669 663 659 670						
Tirzepatide	335 333	328	317	310	310	335	
Placebo	335 330	317	303	292	289	335	

Real-world Study: Adherence is Low

4,066 commercially insured patients with obesity (no diabetes)

46.3% adherence at 180 days

32.3% adherence at 1 year



- APMBSS 2025 Consensus meeting -

How to manage the patients with suboptimal clinical response after metabolic and bariatric surgery

Korean Society for Metabolic and Bariatric Surgery
Scientific Committee of KSMBS
& Consensus meeting Task Force Team

Courtesy of Prof. Sang-Yong Son.

Statements

Statement 1. *The Asian-Pacific region should adopt **BMI thresholds** of 32.5 irrespective of comorbidities and 27.5 with comorbidities, reflecting the IFSO's recent recommendations*

Statement 2. ***%TWL** along could be sufficient to access weight loss outcomes in Asian bariatric patients*

- *Q1. Appropriateness of %TWL < 20% for defining SoCR in Asian MBS patients*
- *Q2. Necessity of other weight loss evaluation factor than %TWL*
- *Q3. Is %EWL better than %TWL?*

Statement 3. ***Adjunctive pharmacotherapy** should be firstly considered for patients who have suboptimal clinical response after the primary metabolic and bariatric surgery*

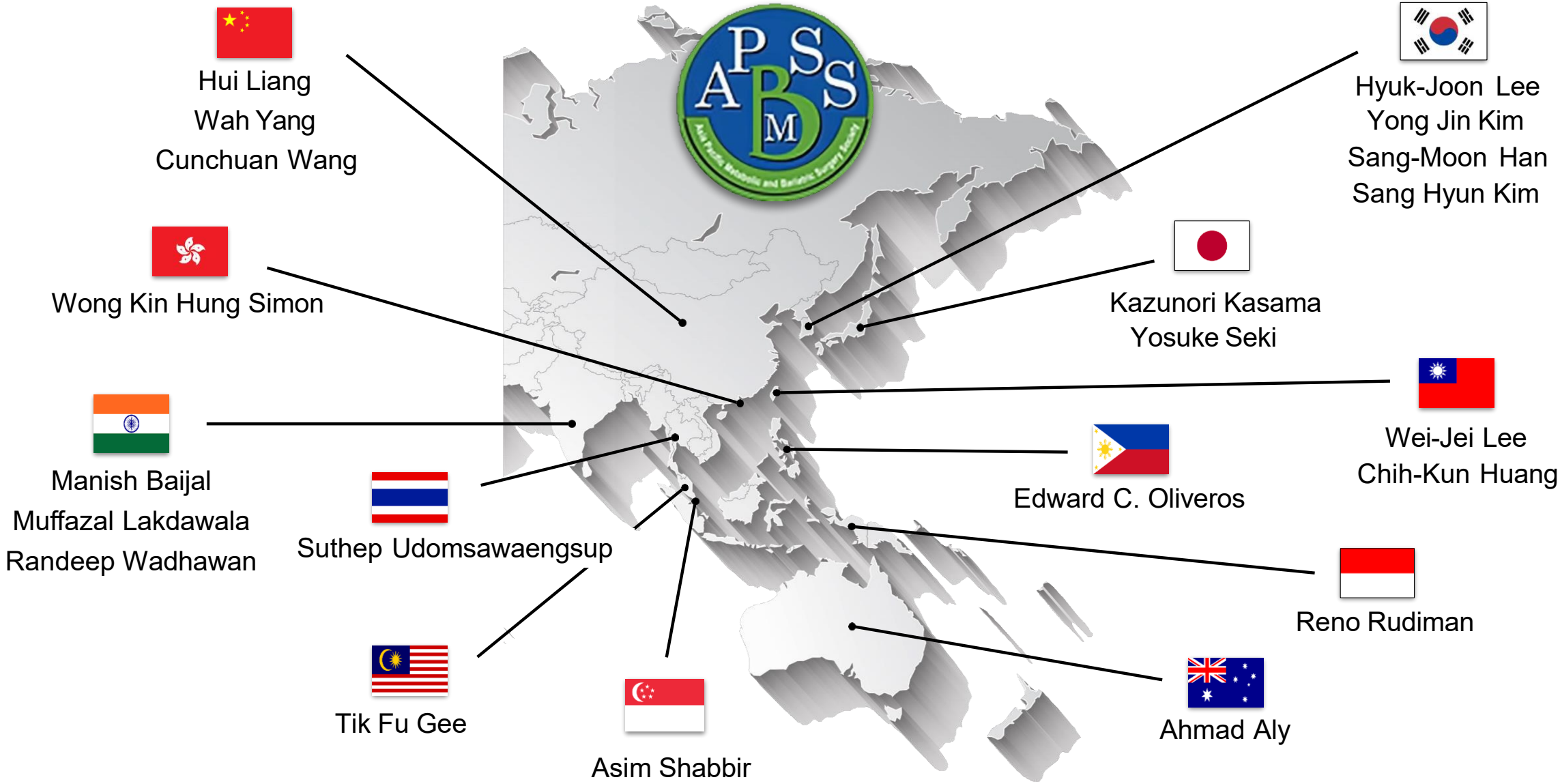
- *Q1. Start time point of adjunctive pharmacotherapy*
- *Q2. First line medications for adjunctive pharmacotherapy*

Statement 4. ***Revision surgery** should be determined for patients who have suboptimal clinical response at least 18 months follow-up after the primary metabolic and bariatric surgery*

- *Q1. Best time point to determine revision time*
- *Q2. Optimal indications for revision surgery*

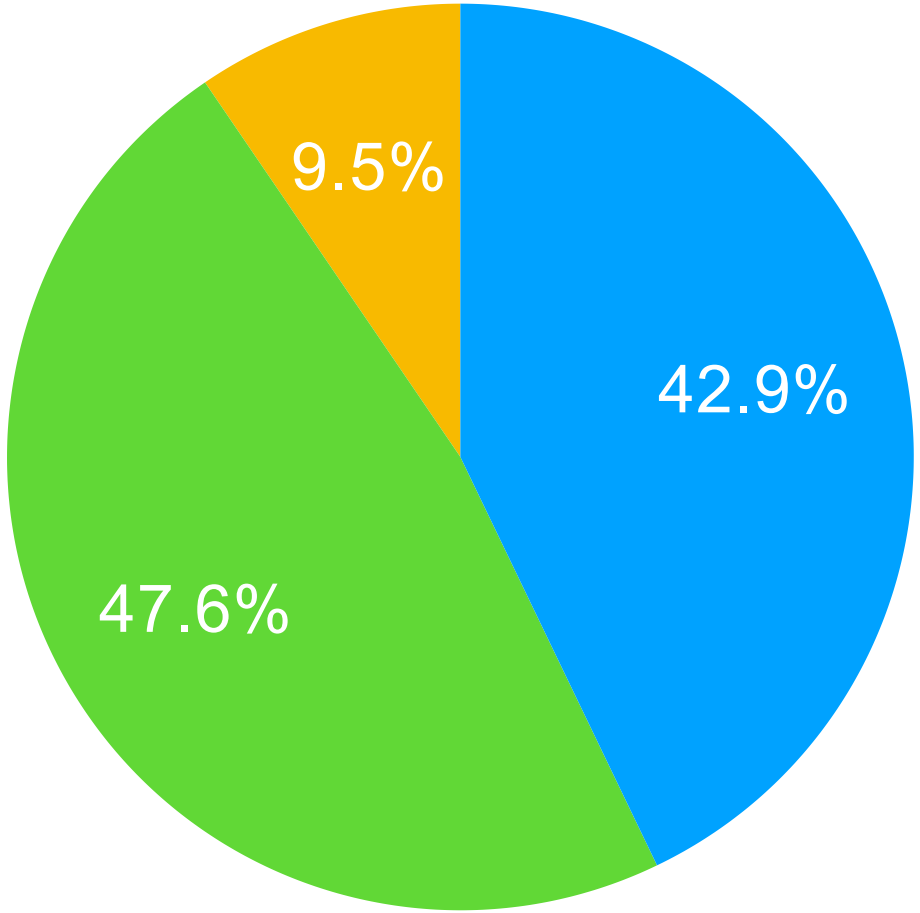
Courtesy of Prof. Sang-Yong Son.

Invited Panels / Survey participants



Courtesy of Prof. Sang-Yong Son.

Statement 3. Adjunctive pharmacotherapy should be firstly considered for patients who have suboptimal clinical response (SoCR) after the primary metabolic and bariatric surgery.



- Strongly agree
- Agree
- Neutral
- Disagree
- Strongly disagree
- Not responded

Consensus rate:

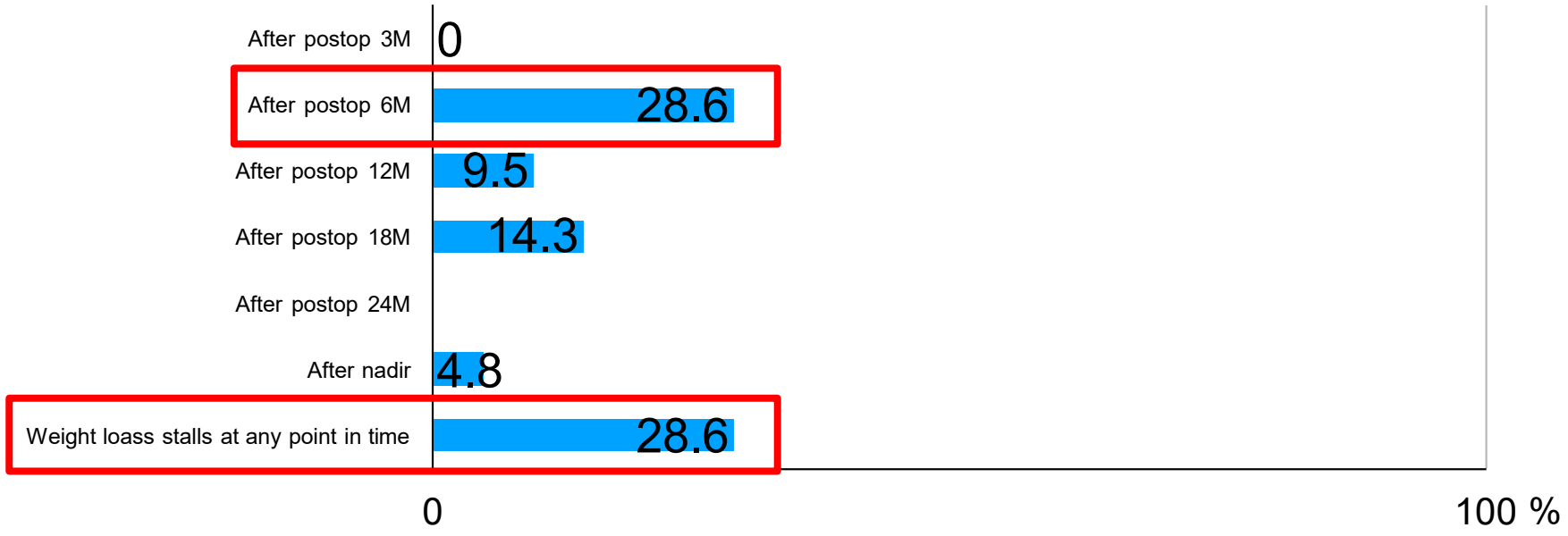
90.5%

N	Mean	Min	Max	SD	CV
21	1.67	1	3	0.642	0.385

CV < 0.5 No further survey
CV 0.5-0.8 Stable, further discussion required
CV > 0.8 Require additional surgery

Statement 3. Adjunctive pharmacotherapy should be firstly considered for patients who have suboptimal clinical response (SoCR) after the primary metabolic and bariatric surgery.

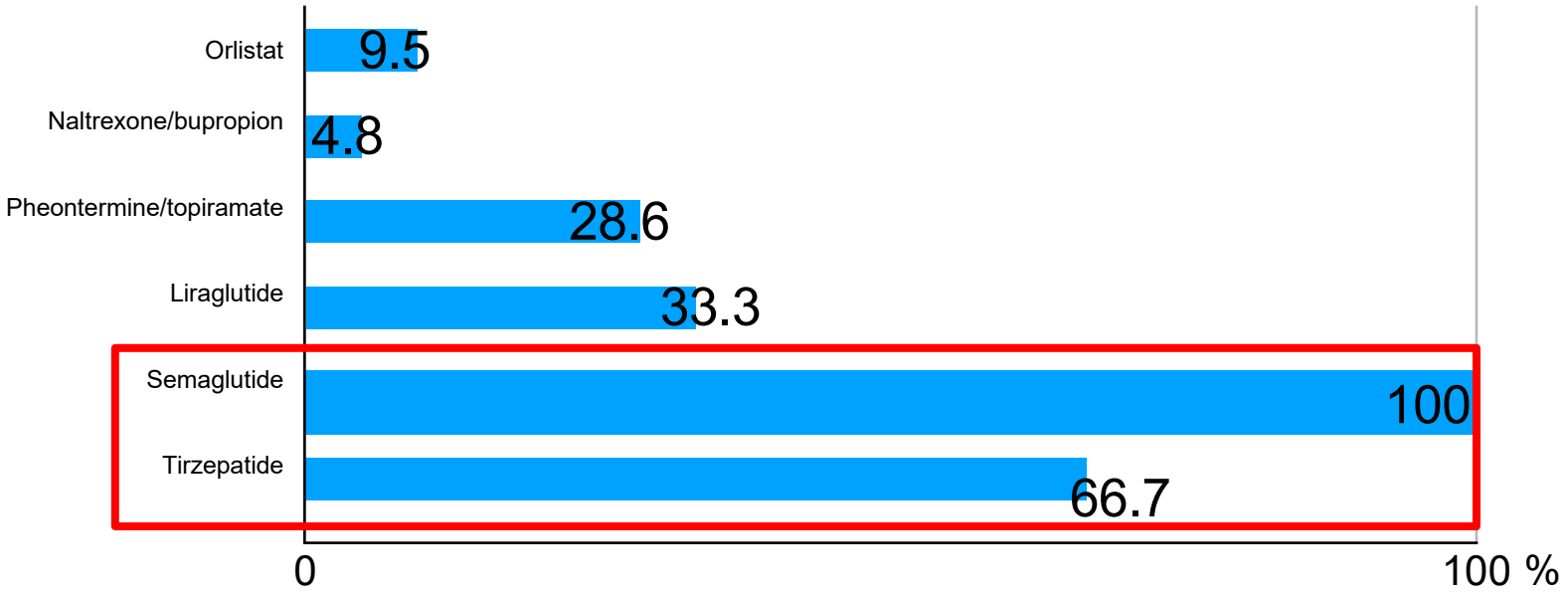
Q1. At what point after metabolic / bariatric surgery could be considered for adjunctive pharmacotherapy?



Courtesy of Prof. Sang-Yong Son.

Statement 3. Adjunctive pharmacotherapy should be firstly considered for patients who have suboptimal clinical response (SoCR) after the primary metabolic and bariatric surgery.

Q2. Which of the following medications could be considered for the first line of adjunctive pharmacotherapy? ***(Multiple choice is possible)***



Courtesy of Prof. Sang-Yong Son.

In Summary

1. Weight loss with GLP-1 RAs appears to be similar when used in post MBS and in non-surgical weight loss (Additive effect)

2. GLP-1 RAs seem to have best effect when started at weight loss plateau before weight gain (Experts opinion & limited retrospective study)

3. GLP-1 RAs may have added GI side effects, but not serious.

4. Adjuvant GLP-1 RAs can be used in several options depending on the severity of the patient's disease, the patient's individual goals, etc. (Early intervention, long-term or intermittent use)

IFSO 2028 in Seoul

28 – 31. August. 2028

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