WHEN SHOULD OBESITY MANAGEMENT MEDICATIONS BE CONSIDERED AFTER MBS?

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Disclosures

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SCOPE OF DISCUSSION with relation to Obesity Management Medication (OMM) Use after MBS

- **Indications for Use**
- **Existing Data and Reports**
- **Practical Considerations**

Use of Obesity Management Medications (OMM) After MBS: Common Indications

- **Insufficient/Inadequate weight loss (Suboptimal initial clinical response, SoCR)**
  - Total weight loss (TWL) < 20%

    OR
  - Inadequate/suboptimal improvement in the obesity complication that was a significant indication for MBS
- **Weight Regain / Recurrent weight gain (RWG)**
  - Weight gain > 30% of nadir weight

    OR
  - Worsening (relapse) of obesity complication that was a significant indication for surgery.
- **Control of Obesity Complications (or Comorbidities)**

Obesity Management Medication Use after MBS

- **Indications for Use of OMM post-MBS**
- **Existing Data and Reports:**
  - **~20 studies: retrospective/prospective**
  - **6 RCTs: 4 for RWG/IWL & 2 for T2D**
- **Practical Considerations**

https://www.bariatricnews.net/post/the-role-of-obesity-management-medications-and-metabolic-and-bariatric-surgery-an-ifso-consensus-m

Retrospective Analyses of OMM Regimen with Phentermine, Topiramate, Phentermine-Topiramate

Author	OMM analyzed	Types of MBS	Weight Loss	
Zilberstein 2004[1] N=16 90 days	• Topiramte (Top), mostly at 25mg daily	AGB (pts with binge eating & difficulty losing wt)	- Mean WL: 7.1kg - Mean EWL 13.2% (3-19%)	
Ard 2019[2] N=13 2 years post-SG	• Phentermine-Topiramate (PHN-Top) BMI > 50 started at 3 months pre-op and continued for 2 years	SG	**PHN-Top**	**No PHN-Top**
			38.2kg	27.0kg
Schwartz 2016[3] N=65 90 days	• PHN • PHN-Top	RYGB 51 AGB 14	• PHN 12.8% excess weight loss or **6.35kg** • PHN-Top 12.9% excess weight loss **3.81kg** - No diff between RYGB & AGB	
Elhag 2019[4] N=129 (MBS46) 3 mths	• Lorcaserin • PHN	SG 40 RYGB 4 AGB 2	• PHN WL 7.65% in both MBS and non-MBS pts • Lorcaserin 1.86% & 2.99% in MBS and non-MBS pts [no comparisons among ops]	
Istan 2020[5] N=350	• PHN-Top (44%) • PHN (34%) • Top (21%) • Lorcaserin (0.9%)	RYGB	OMM esp PHN-Top alters trajectory of WR and reduces rapid WR No data on WL on individual OMM	

Duration refers to follow-up after initiation of OMM; Actual duration of OMM treatment unknown in most studies. Side effects mostly NOT reported.

OMM after bariatric surgery: Experience from 2 Centres

- Patients (N=319) who had RYGB (80%) or SG, from 2000-2014 at MGH, Boston or Weill-Cornell, NY.
- Received weight loss medications, with at least 12 months follow-up after OMM started
- Average 52 months post-op (23 SG vs 59 RYGB)
- OMM studied (pts on average 2 meds)

FDA approved for long-term use	Diabetes medications	Other medications
• Phentermine/topiramate • Bupropion/naltrexone • Lorcaserin • Orlistat • Liraglutide	• Metformin • Canagliflozin • Exenatide • Pramlinitide	• Phentermine • Topiramate • Bupropion • Naltrexone • Sibutramine • Zonisamide

OMM after MBS Augmented Weight Loss after RWG/IWL: Some Differences between SG and RYGB

Parameter (mean)	All (n=319)	SG (19.1%)	RYGB (80.9%)
BMI (pre-op)	48.3	45.0	49.1
%TWL (post-op)	31%	22%	33%
%weight regain	12%	4.8%	14%
Time btw surgery → med (months)	52.4	23.2	59.3
BMI (nadir after med)	34.5	35.2	34.3
%TWL (post-med)	7.8%	4.3%	8.5%

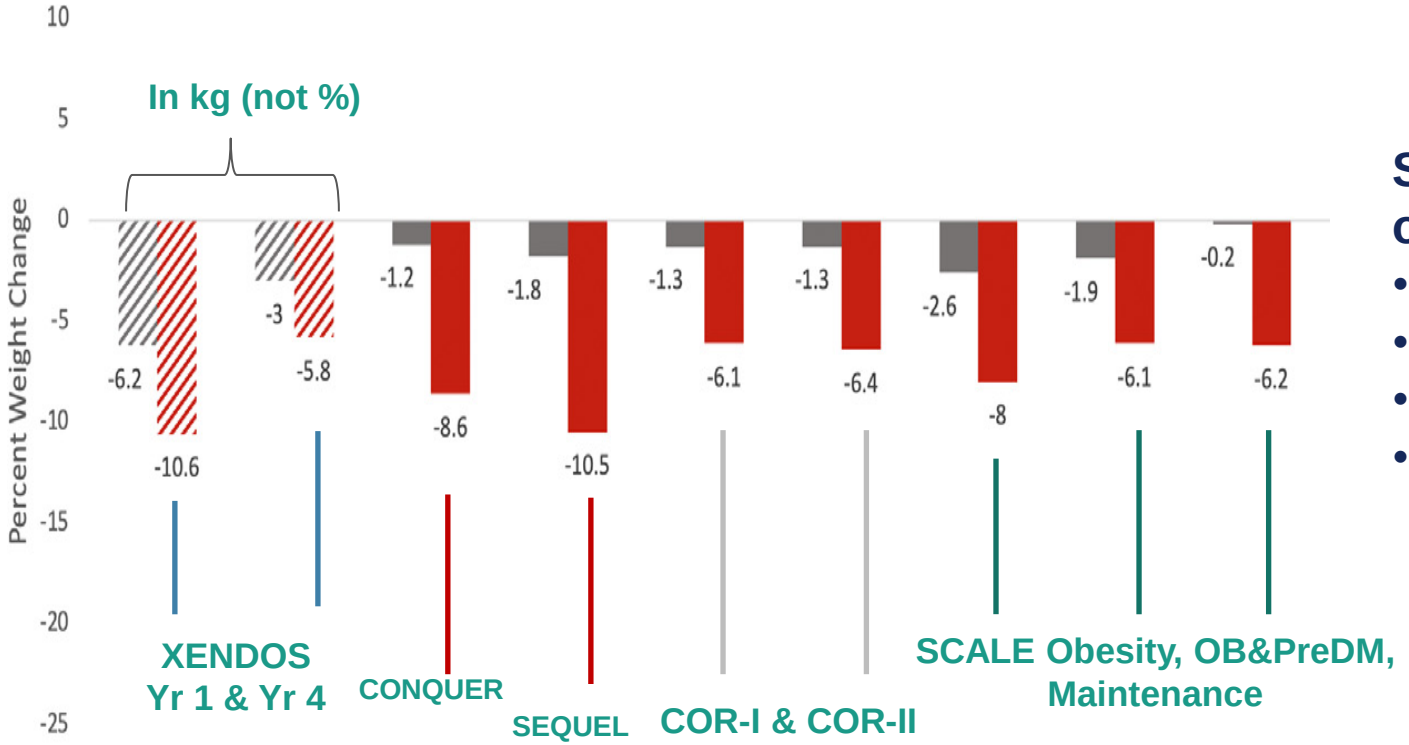
- Topiramate most frequently used and associated with more weight loss.
- Combination pharmacotherapy often used (average number of meds: 2)
- Use for weight "plateau" saw greater cumulative WL greater: 32.3% (plateau) vs 26.8% (RWG)

Use of Liraglutide post-MBS

Author (year)	Size (N)	Dose	Types of MBS	WL
Wharton 2019[11]	117 (1 yr)	3mg	RYGB (53), SG (14), AGB (40)	RYGB 6.6% vs SG 4.9% vs AGB 3.6%; No difference among types of op
Sulim				
Murve				
Elhag				
Gorgo 2016[1]				ed
Vincci				re,
Vincci				g

- Duration of Use: 24 weeks → 24 months
- WL with MBS and without MBS: No difference (compared with SCALE)
- WL after the various types of procedures studied: No sig difference
- Mean WL:
  - At 24-28 weeks: 3.3 - 9.3% (mostly 6-8%)
  - At 12 months: 6.6 – 8.8%
  - At 24 months: 3.4kg
- No predictors of WL for use of Liraglutide post-MBS

Weight Loss Efficacy of OMM: Similar Incremental Effect with and without MBS



Summary of Weight Loss from RCTs of OMM (without MBS)

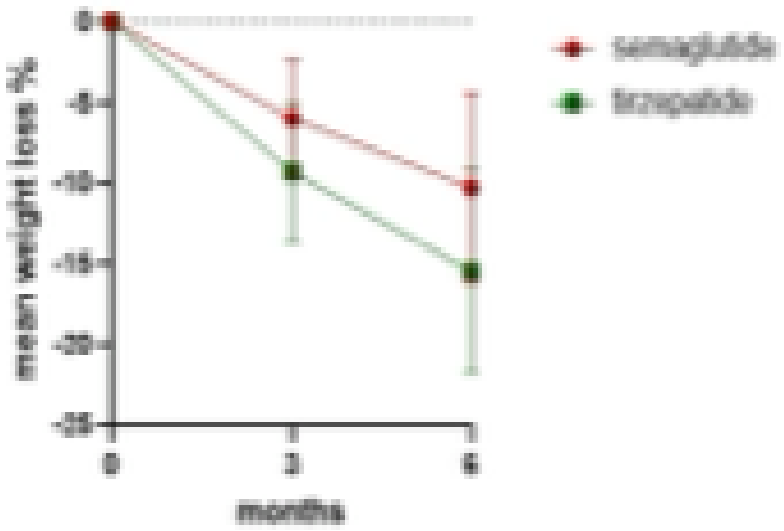
- Phentermine: 4-6kg
- Phentermine-Topiramate: 8.6-10.5%
- Naltrexone/Bupropion: 6.1-6.4%
- Liraglutide: 6.1 – 8%

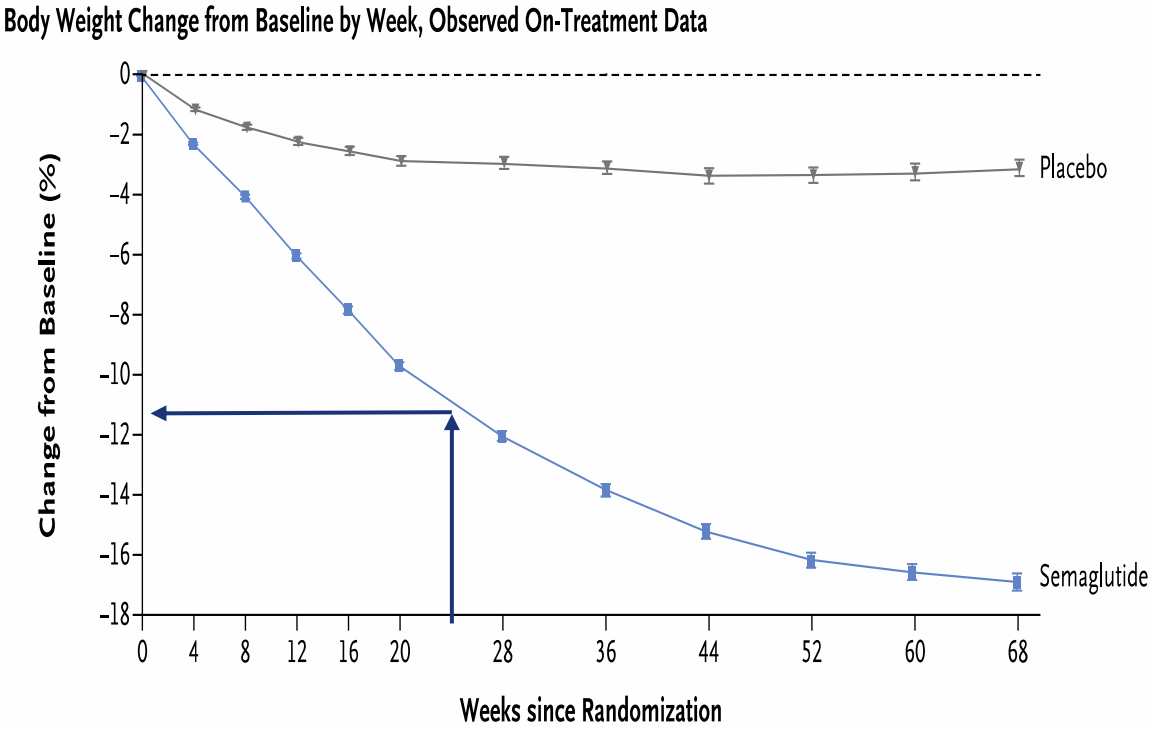
Weight loss with OMM after MBS

- Phentermine: 4.5 – 7.65%; 6.4kg
- Phentermine-Topiramate: 9.8%; additional 11kg WL
- Total numbers from post-MBS use at least 402
- Liraglutide: 6.9-9.3%

Semaglutide and Tirzepatide for the Management of Weight Recurrence After Sleeve Gastrectomy: A Retrospective Cohort Study

- N=115
- S/C semaglutide (70) or Tirzepatide (45), as tolerated
- Semaglutide 69% tolerated ≥1mg/week and Tirzepatide 64% tolerated ≥10mg/week
- Weight loss at 6/12: semaglutide 10.3% and tirzepatide 15.5%

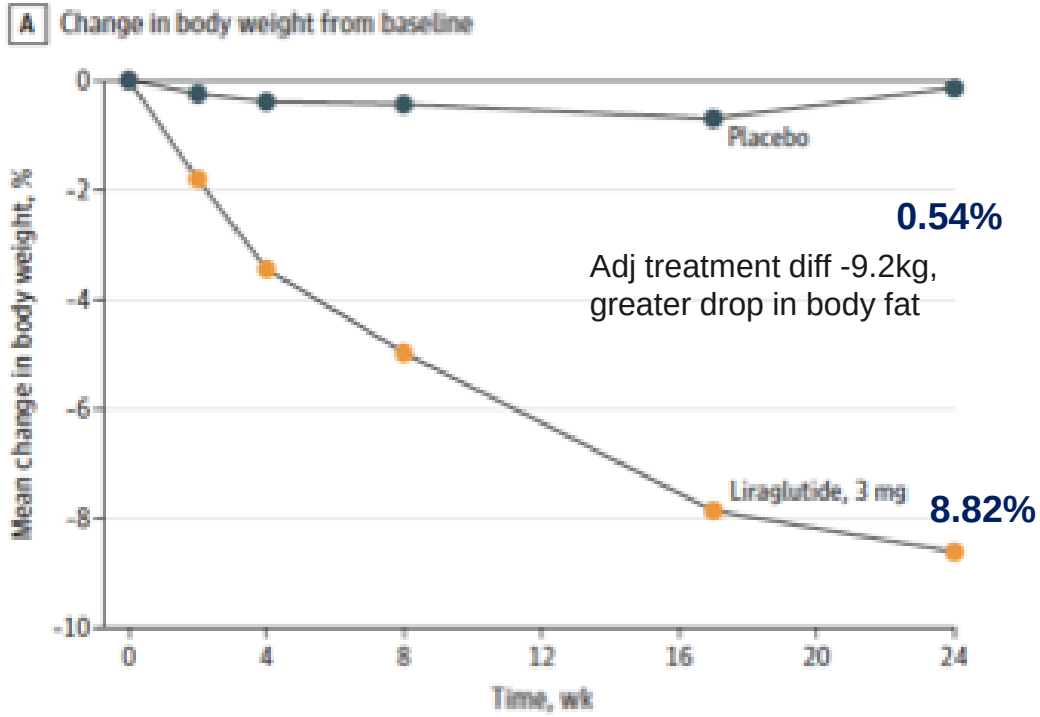


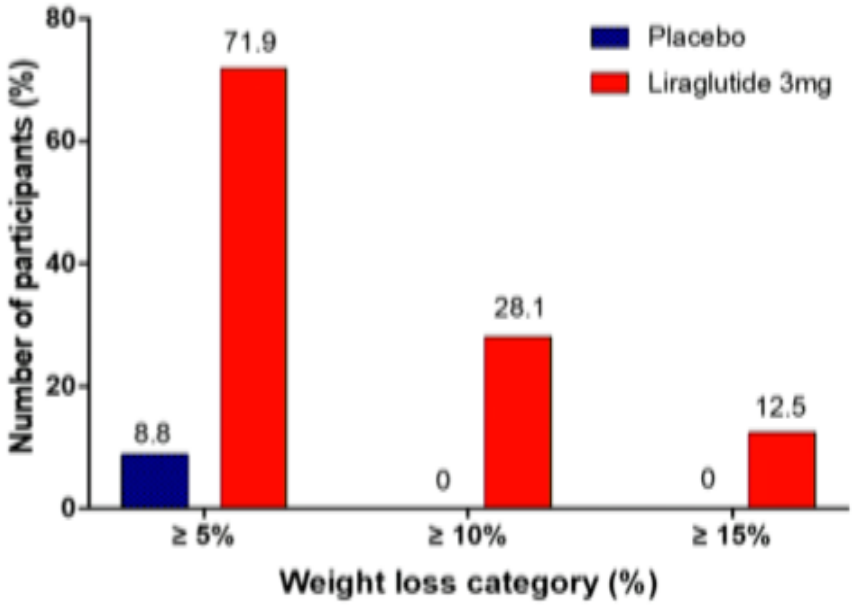


BARI-OPTIMISE: Safety and efficacy of liraglutide 3.0 mg vs placebo in patients with poor weight loss following metabolic surgery

- N=70, IWL (<20%) ≥1 yr post-MBS (SG 93%, RYGB 7%) + suboptimal GLP-1 response
- Randomized to Lira 3mg vs PBO x 24 wks, adjunct to lifestyle.

WL at 52 weeks: Overall ~7% WL from initiation [no diff between RYGB vs SG]

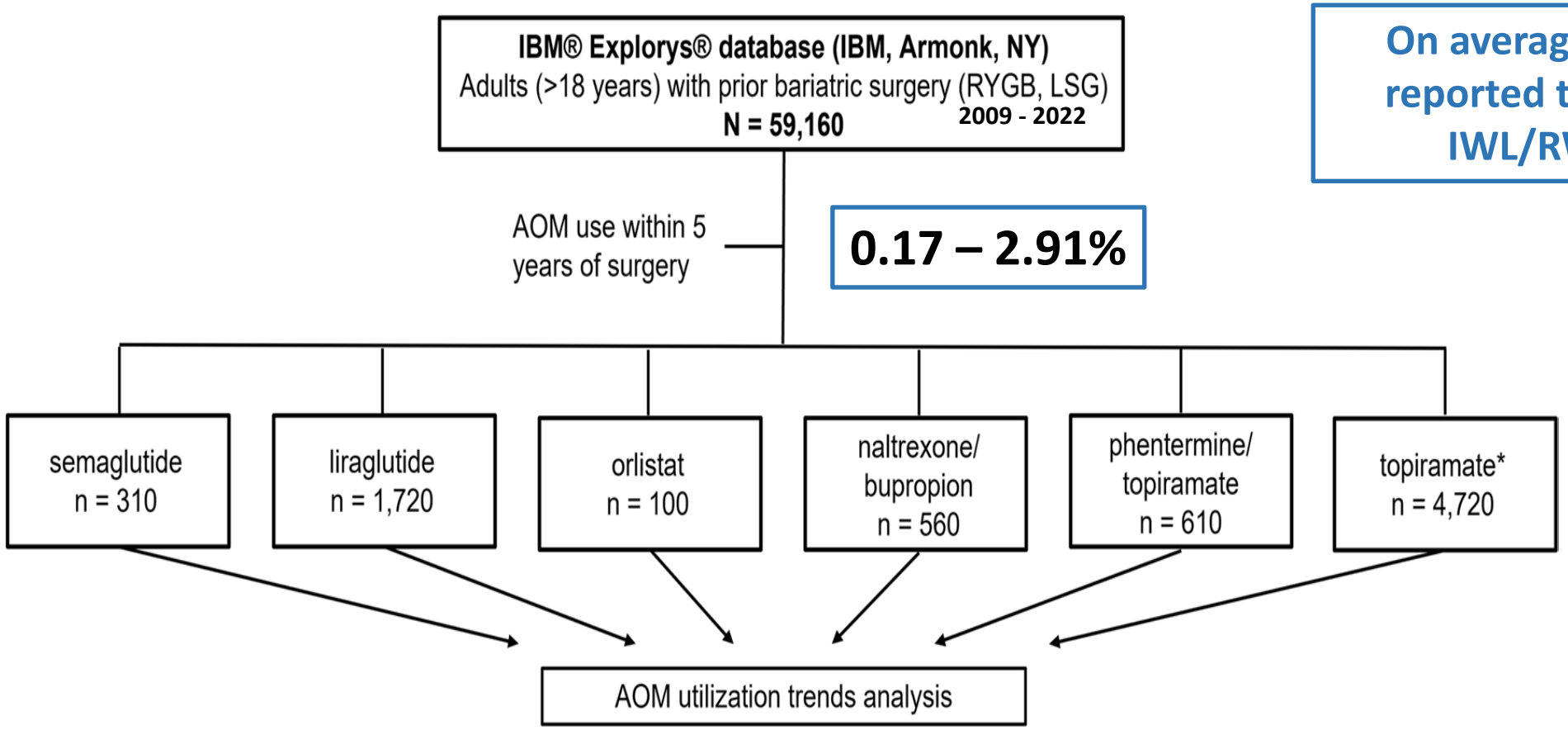




Obesity Management Medication Use after MBS

- **Indications for Use of OMM post-MBS**
- **Existing Data and Reports on Use of OMM post-MBS:**
- **Practical Considerations**

Use of Obesity Management Medication within 5 years of Metabolic Bariatric Surgery



On average, 25% reported to have IWL/RWG

TOTAL N=8020

Firkins S.A., et. al. Utilization of Anti-obesity Medications After Bariatric Surgery: Analysis of a Large National Database. Obes Surg 2024;34:1415

Timing of Initiating OMM Post-MBS can be Crucial

- **On the one hand, real-world practice, treatment inertia ++**
  - Dragged out till 5-8 years quite commonly
  - Usually for RWG rather than “plateau” or SoCR; absolute weight at OMM initiation is higher

- **On the other hand, starting OMM ”too early” before full effect of MBS is seen may result in minimal additional WL with OMM**
- **Thakur (RCT 2021)[19]:** N = 30 within 6/52 post-SG with BMI>30, Lira 3mg vs PBO for 6 mths
  - Wt change from pre-op: Lira 28.2% vs PBO 23.3% (no stat sig diff); EWL 58.7% vs 44.5% (p 0.043)

Approach to Post-MBS RWG: Use of Rate of WR for Early Detection and Intervention

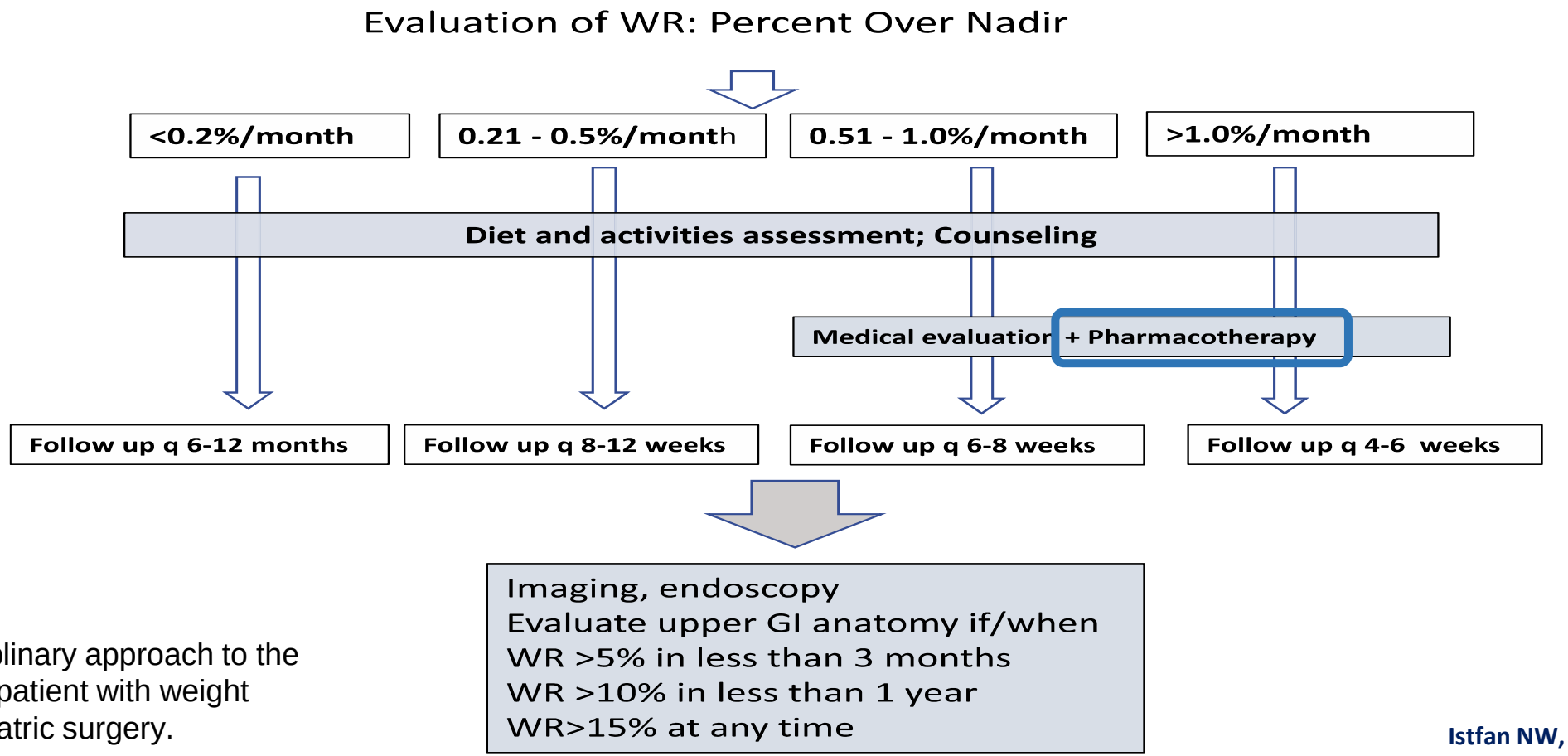
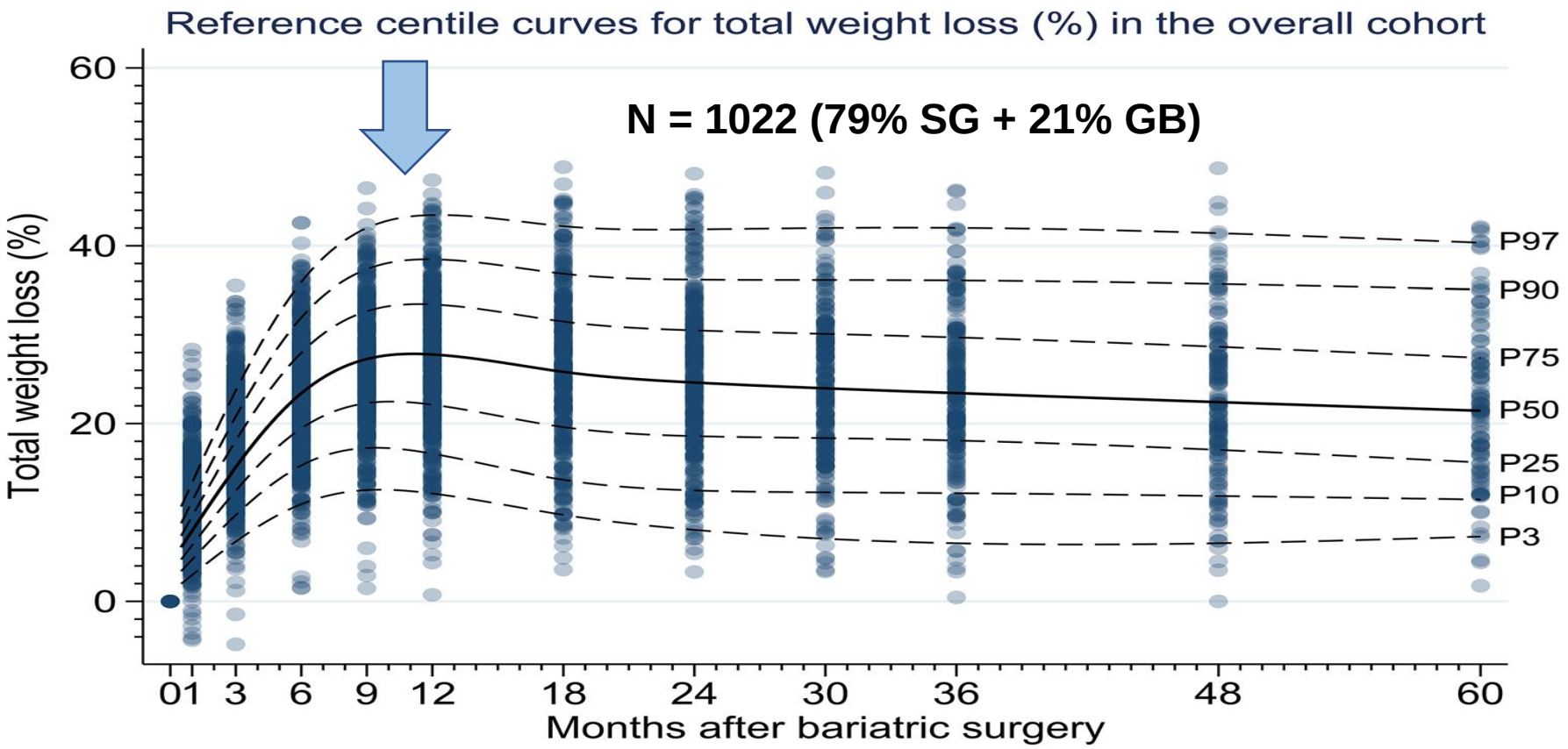


Figure 2. Multidisciplinary approach to the management of the patient with weight regain following bariatric surgery.

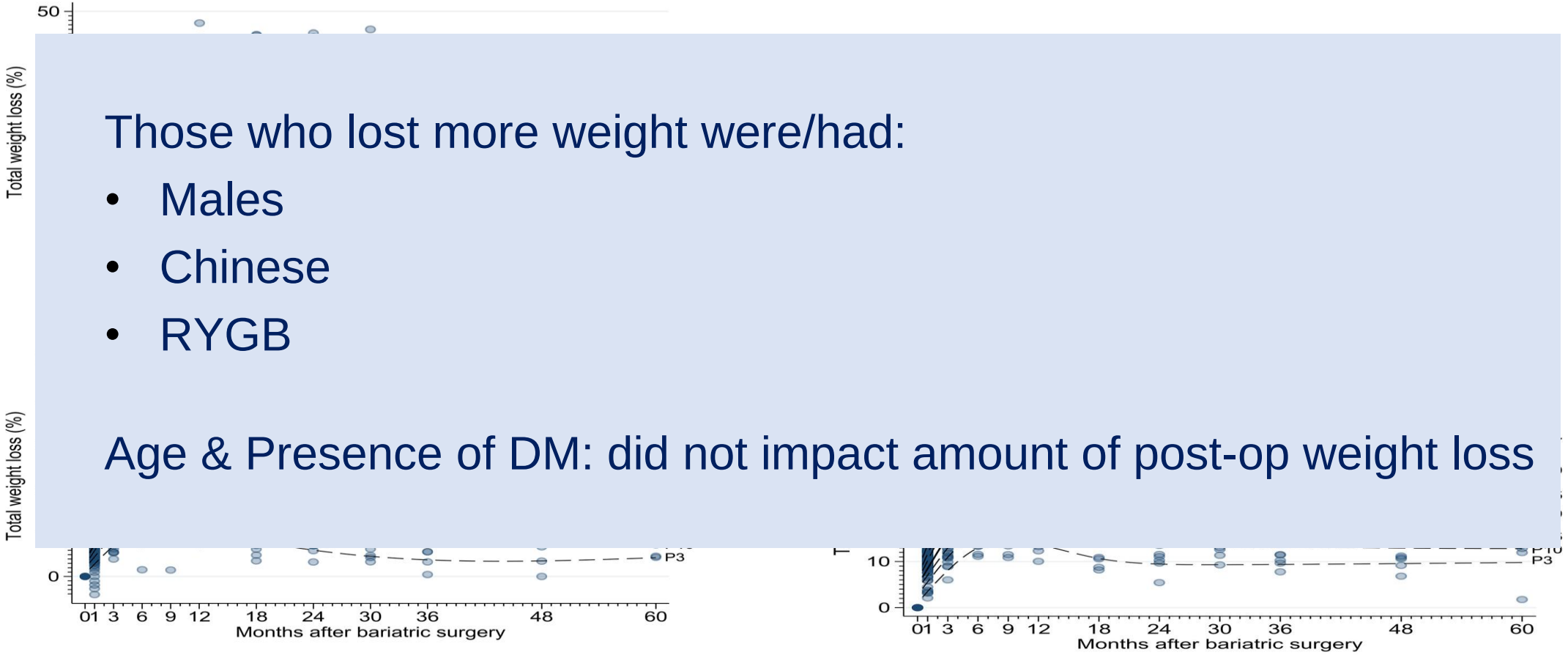
Istfan NW, et al. JCEM 2020

Studying Our Own Patient Cohorts: Detect and Intervene Early for RWG and SoCR



Tan SYT, et. al. Centile Charts for Monitoring of Weight Loss Trajectories After Bariatric Surgery in Asian Patients . Obesity Surgery (2021) 31:4781–4789

Sub-analyses by Surgery Type, Gender, Age and Ethnicity



Those who lost more weight were/had:

- Males
- Chinese
- RYGB

Age & Presence of DM: did not impact amount of post-op weight loss

Tan SYT, et. al. Centile Charts for Monitoring of Weight Loss Trajectories After Bariatric Surgery in Asian Patients . Obesity Surgery (2021) 31:4781–4789

ASK OURSELVES

- What is/are the target(s) of treatment?
  Obesity: A chronic, multifactorial, relapsing, progressive disease due to excess or abnormally distributed adipose tissue, and a disorder of energy homeostasis, resulting in adverse metabolic, biomechanical, and psychosocial health consequences

- Weight or Obesity or the Patient? e.g. heterogeneity in adiposity distribution → 2kg of ”fat loss” may be 5cm in waist circumference loss & improvement of ORC or, just better function / “breathe better” & QOL/ “no need to use CPAP machine”

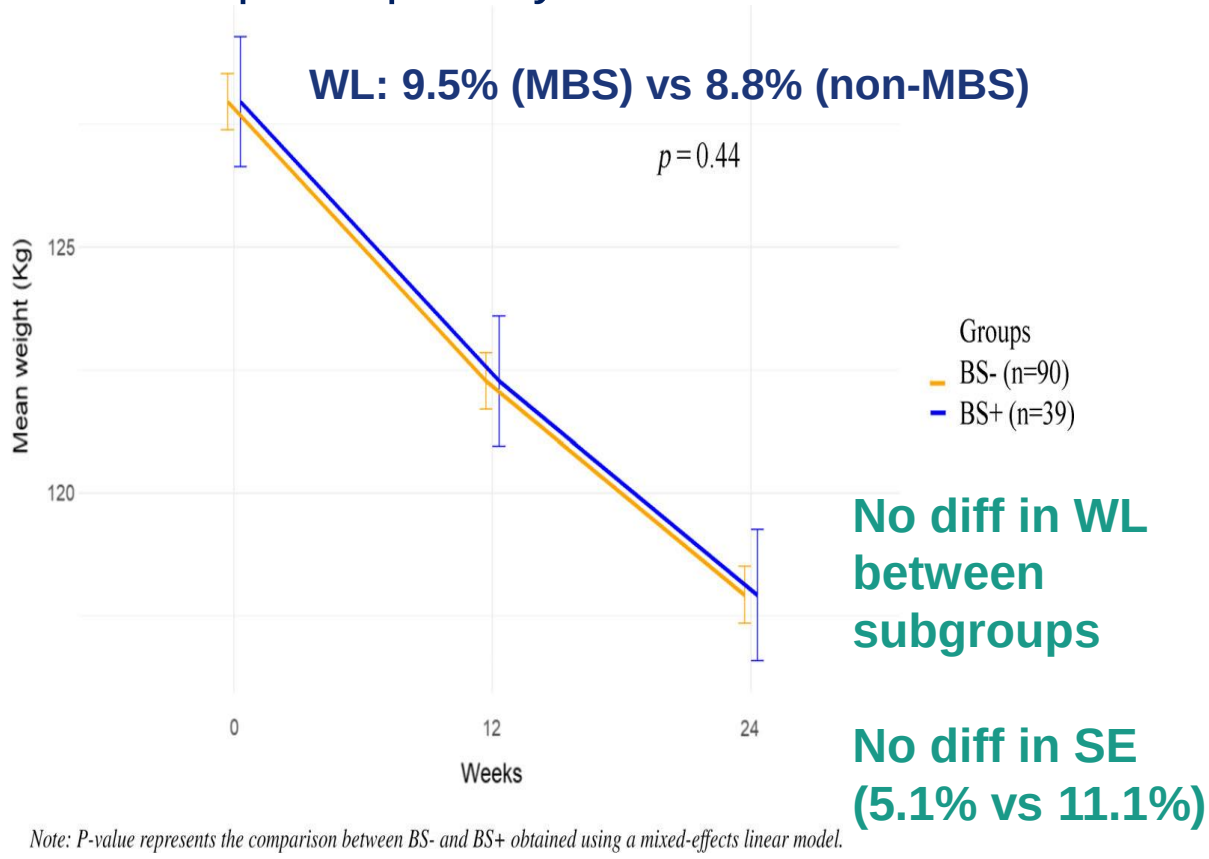
When Should OMM Be Considered After MBS? (personal conclusions)

- Lack of hard data on optimal timing to initiate OMM post-MBS → Clinical Common Sense:
  - "Weight plateau" (proactive) vs RWG (reactive)
  - Patient factors such as rate of weight regain
  - From RWG & Inadequate Weight Loss → Use Presence and severity of obesity complications as indications
- Choice of OMM guided by patient factors: no different from PwO without MBS in terms of efficacy and side effects; patient characteristics/phenotype, contraindications, preference, cost, access and those with proven benefits for ORC
- Unanswered questions remain: optimal timing,duration of use,combination treatment, newer OMM

Thank you for your kind attention!

Semaglutide 2.4mg/week in Patients with BMI>40 + ORC, with & without history of MBS: Weight Loss Efficacy over 24 weeks

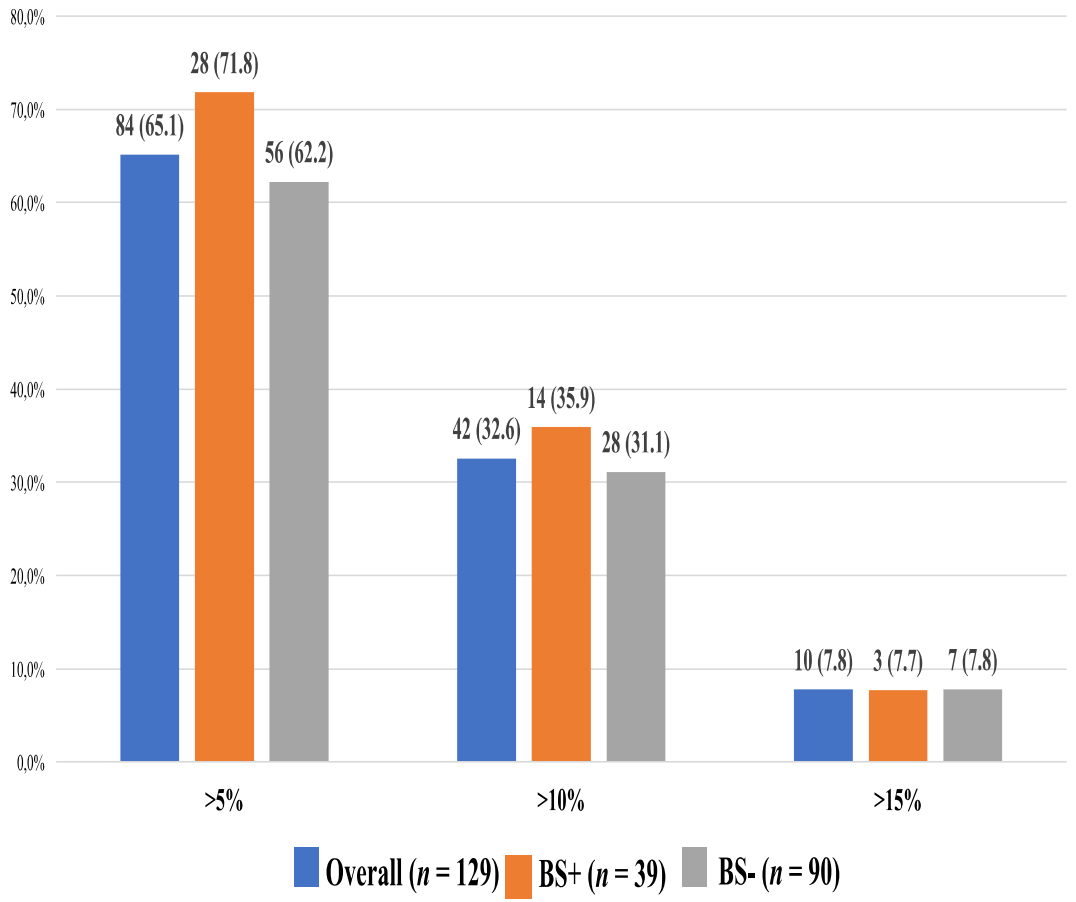
Retrospective
N = 39 MBS (72% SG, rest RYGB) vs 90 non-MBS
Mean time post-op: 8.4 yrs



Note: P-value represents the comparison between BS- and BS+ obtained using a mixed-effects linear model.

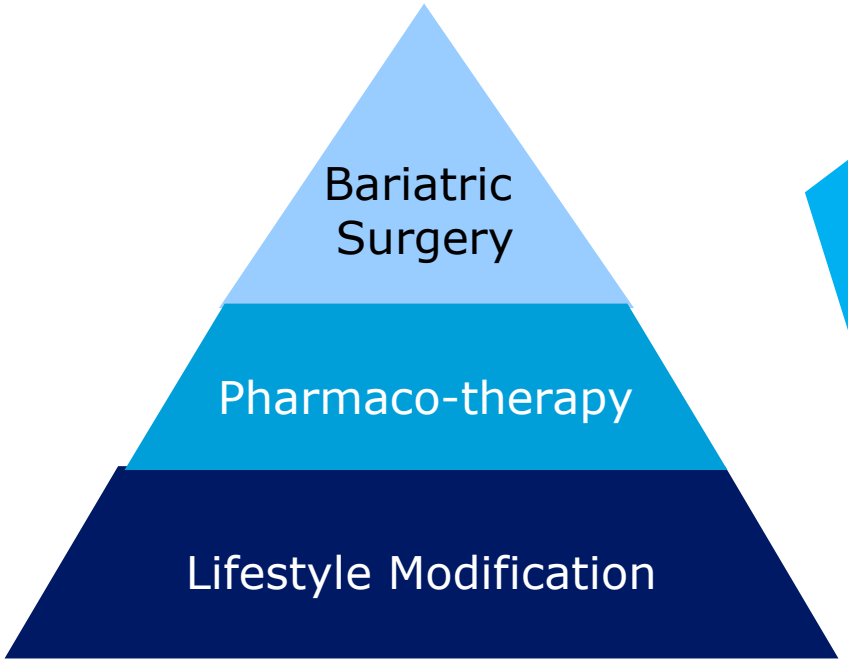
No diff in WL between subgroups

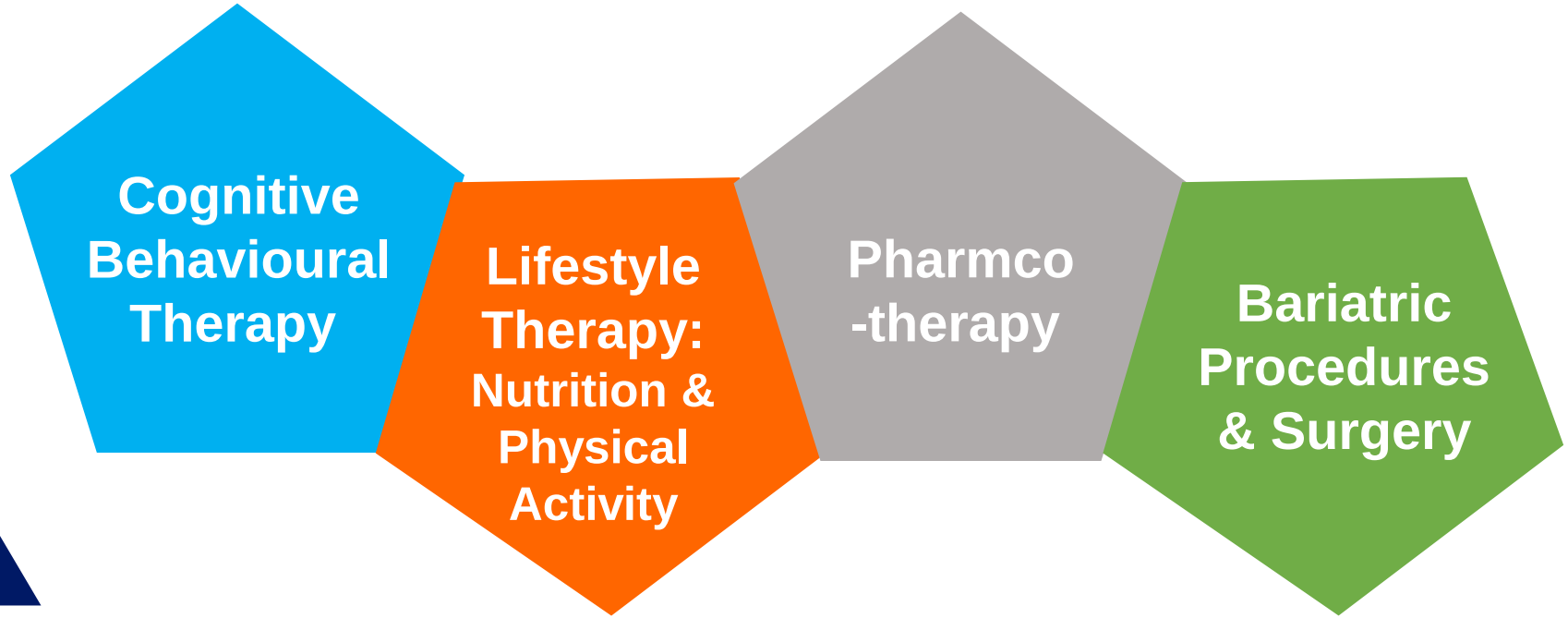
No diff in SE (5.1% vs 11.1%)



[24]Bonnet J, et al. Obesity (Silver Spring). 2024;32:50–58

Obesity Management:
Pyramid vs Adjunctive (Multi-modal) Approach





Dutch Study of 868 patients at 5 years post-RYGB (91%) & SG (9%): RWG variable depending on definition used

Definition	Patients with weight regain, *n* (%)
I. An increase of > 10 kg from nadir	325 (37%)
II. An increase of > 25%EWL from nadir	180 (21%)
III. An increase in BMI of 5 kg/m^2 from nadir	169 (20%)
IV. Weight regain to a BMI > 35 kg/m^2 after successful loss	141 (16%)
V. Any weight regain	759 (87%)
VI. An increase of > 15% of total body weight at nadir	211 (24%)

%EWL percent excess weight loss, *BMI* body mass index, *m* meters, *nadir* lowest weight measured after surgery

16 – 87% of patients with RWG

In general, ~ 50% of patients regain 5% from 2 yrs post-MBS; 25%–35% regain ≥ 15% of in 2–5 years

Voorwinde V., et.al. Definitions of Long-Term Weight Regain and Their Associations with Clinical Outcomes. **OBES SURG (2020) 30:527–536**

RCTs involving Liraglutide use after MBS

- **Hany 2021 (BOOST-LIRA)[20]:** N=80; Lira use vs PBO in conversional RYGB, treated from 6 wks till 6 mths post-op and followed up to 12 months.
  - Total WL after MBS at 12 months: Lira 24.15±2.35% vs PBO 22.70±2.13% (p<.001)
  - %TWL of >20% at 6 months: Lira 15.8% vs PBO 0% (p=.029)
  - Comparable changes in metabolic biomarkers in both groups; AE 27.5% (lira) vs 0% (PBO)

- **Mok 2023 (BARI-OPTIMISE)[21]:** N=70, IWL (<20%) ≥1 yr post-MBS (SG 93%, RYGB 7%) + suboptimal GLP-1 response; Lira 3mg vs PBO x 24 wks, adjunct to lifestyle.
  - WL at 24 wks: Lira 8.82% vs PBO 0.54% (Adj treatment diff -9.2kg, greater drop in body fat, adj treatment diff -4.9kg)
  - WL at 52 weeks: Overall ~7% WL from surgery at [no diff between RYGB vs SG]

For T2D Management post-MBS:

- Miras 2019 (GRAVITAS)[22]: **for T2D relapse**; Lira 1.8mg x 24 wks.
- Coelho 2023 (GLIDE)[23]: N=27 with T2D, Lira 1.8mg in those with A1c > 6.5%, within 6 wks after LAGB, treated for 6 mths, followed up for 12 months; HbA1c & weight significantly higher in Lira group (compared to PBO) at 12 months. (underpowered to show above changes)

Weight loss with Semaglutide 1mg post-MBS

Comparing categorical weight loss with Semaglutide 1mg/week with that of Semaglutide 2.4mg/week in STEP 1