XXVIII IFSO World Congress

9-12 September 2025 | Santiago, Chile

Short Term vs Long Term Complications following Combined Therapy

IFSO 2025 Santiago

Combined Therapies, The Dawn of a New Era

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Disclosure Slide

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☐	Yes, please specify:

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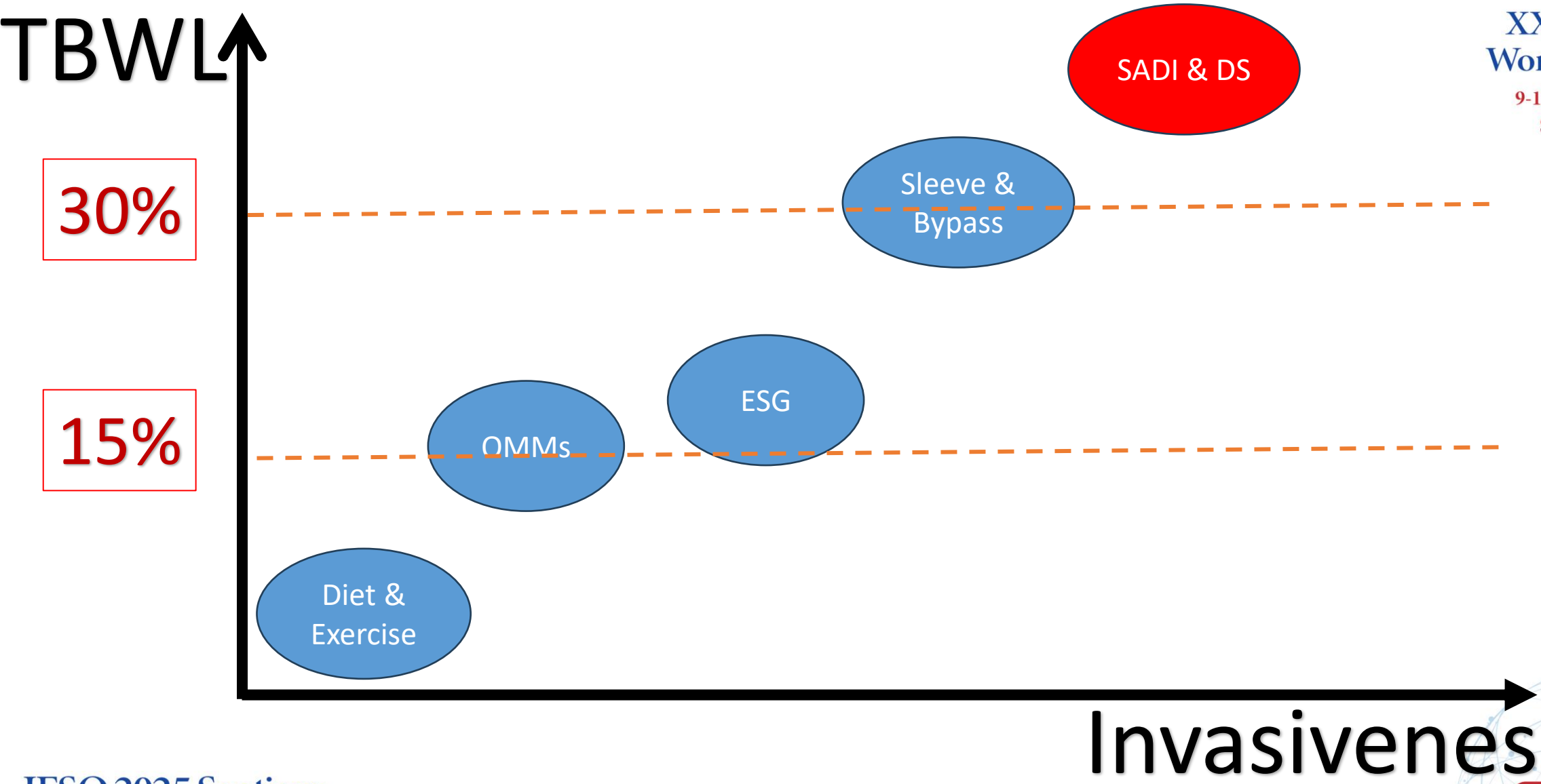
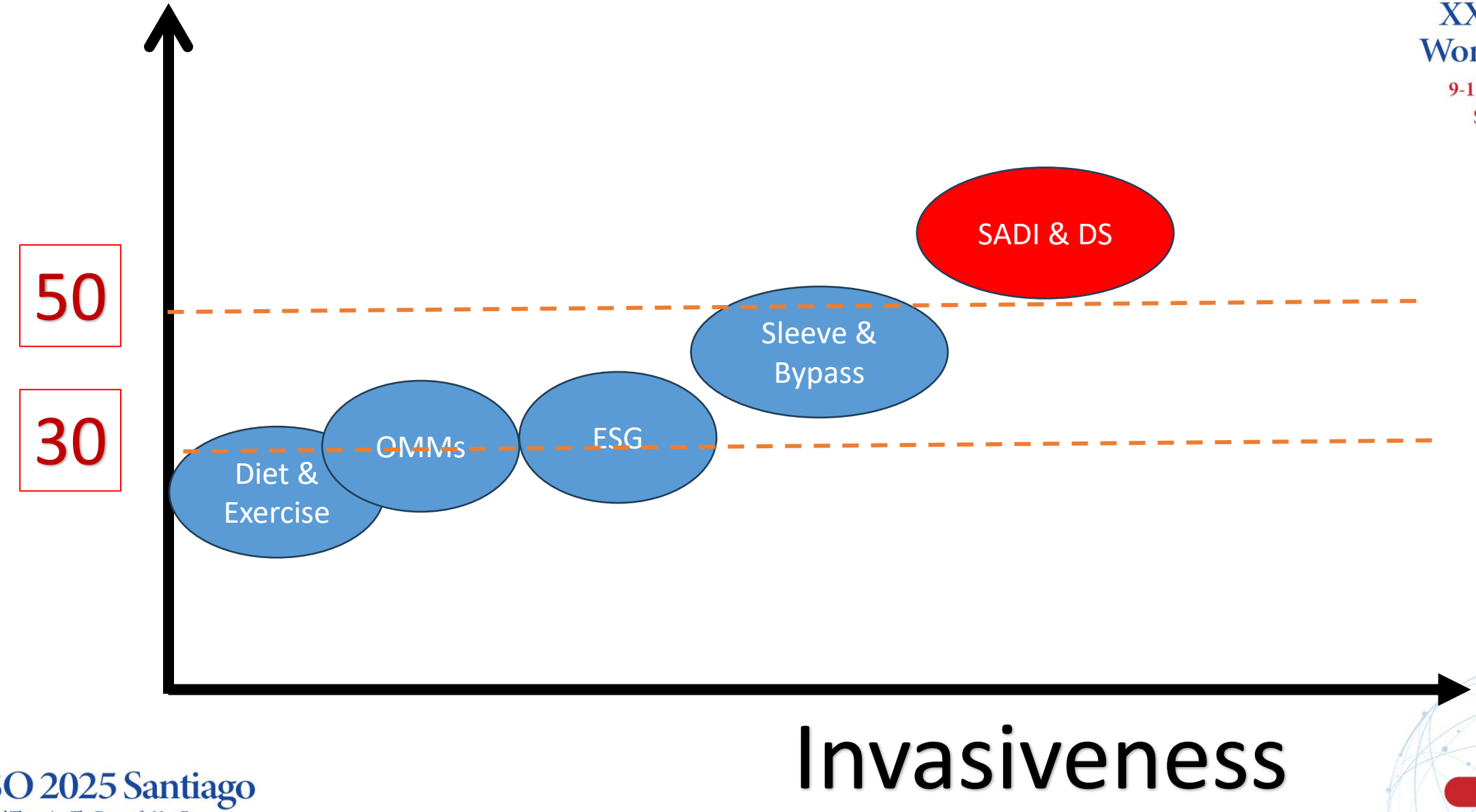
Example: company XYZ	x		x		x			

Combined Therapy

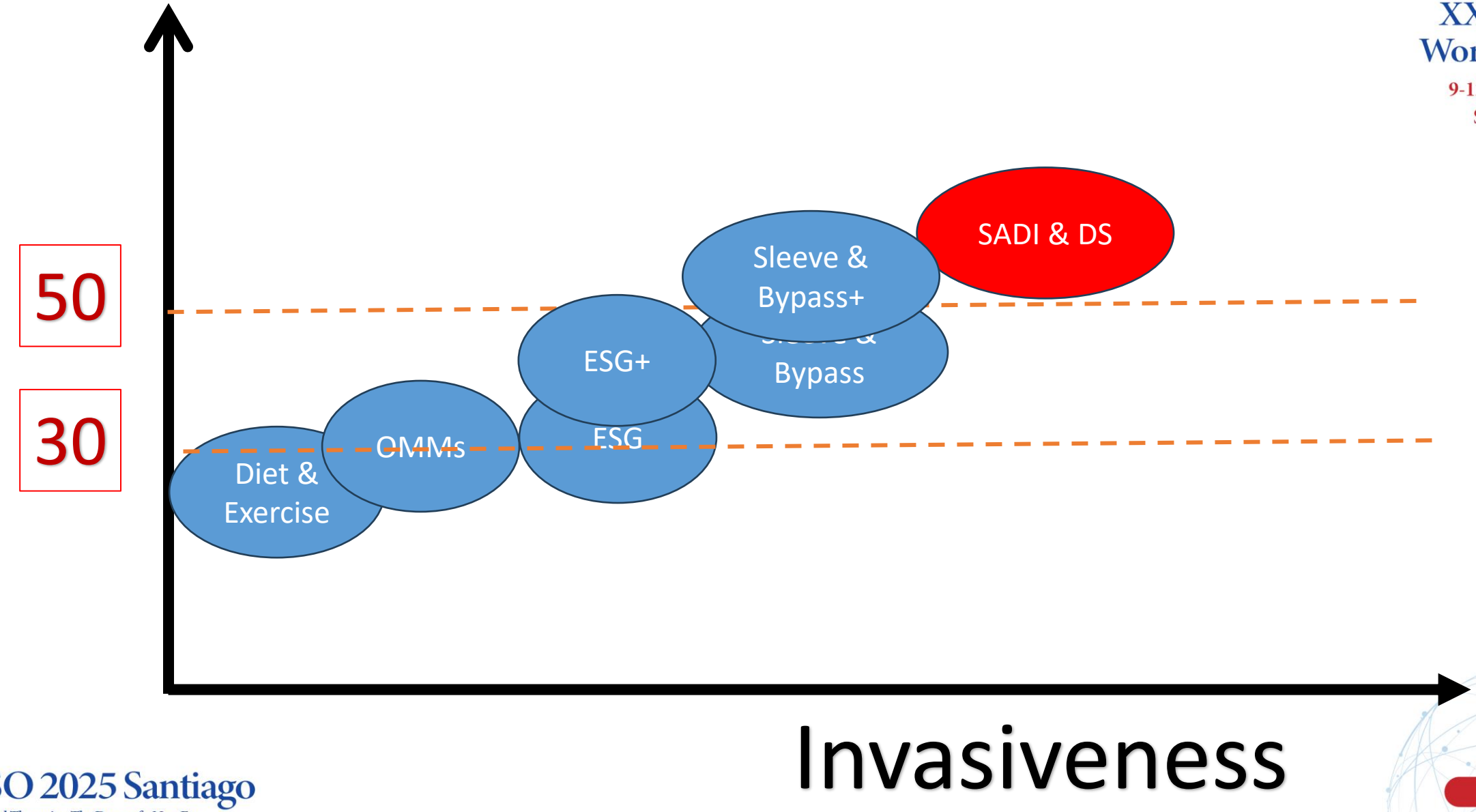
- **Bariatric surgery** = most effective long-term therapy for **severe obesity**.
- **Addition of pharmacotherapy** can:
  - Enhance **weight loss**
  - Improve **weight maintenance**
- **However**: Combination may increase risk of short and long term complications


TBWL
30%
15%
SADI & DS
Sleeve & Bypass
ESG
OMMs
Diet & Exercise
Invasiveness

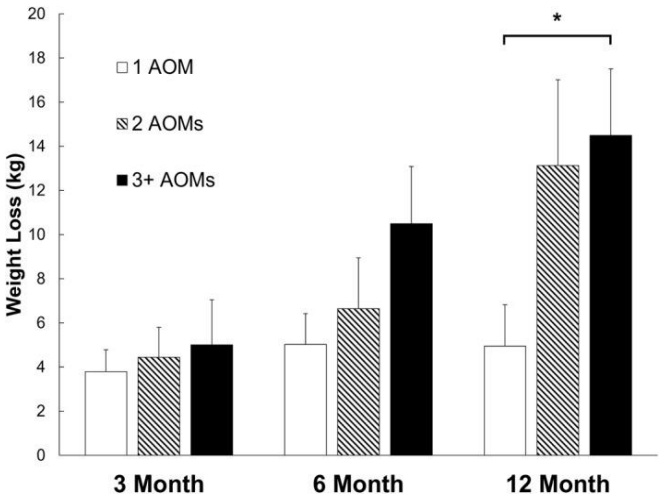
BMI Sweet Spot

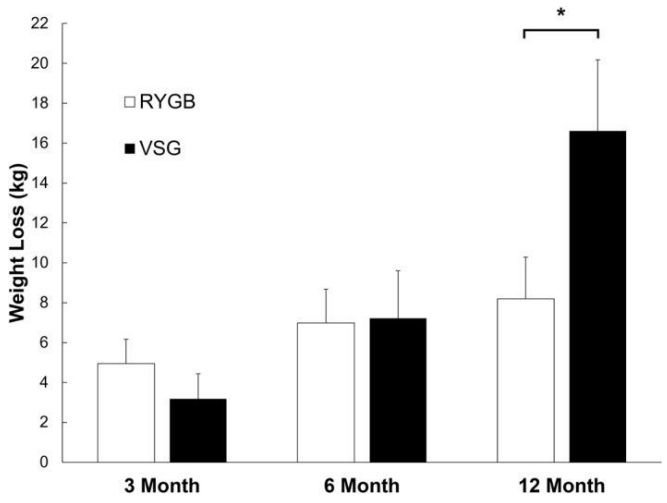


BMI Sweet Spot



Use of OMMs after Bariatric Surgery





- Wong et al (2022): patients with 10% weight regain after Bariatric Surgery prescribed GLP-1 RAs, phentermine, topiramate or metformin.
- Length of treatment and number of OMMs prescribed were found to affect weight loss
- After 12 months of treatment, patients undergoing VSG lost more weight with OMMs which needs further research

Wong G, Garner EM, Takkouche S, Spann MD, English WJ, Albaugh VL, Srivastava G. Combination Obesity Managment Medications to effectively treat bariatric surgery weight regain at an academic obesity center. Obes Sci Pract. 2022 Sep 24;9(3):203-209. doi: 10.1002/osp4.635. PMID: 37287513; PMCID: PMC10242249.

Liraglutide + Conversional RYGB

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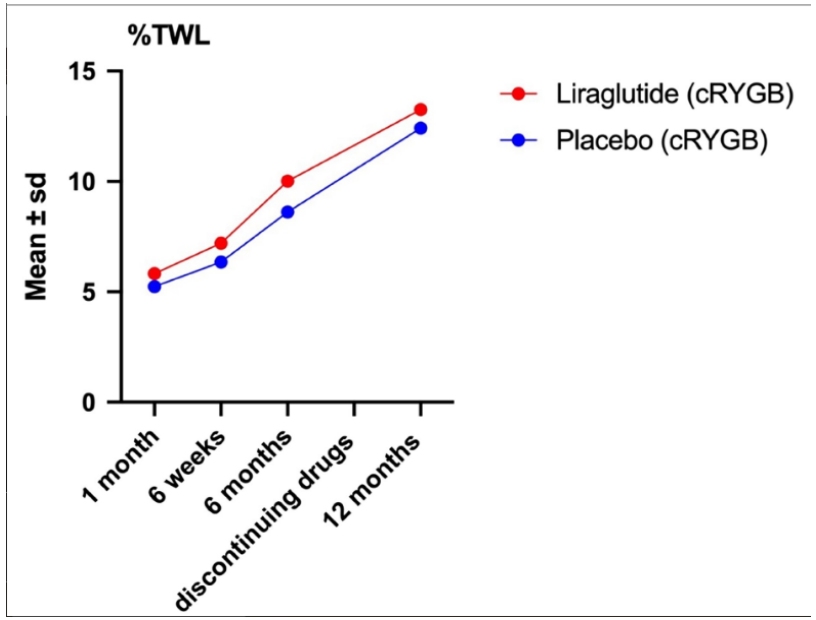
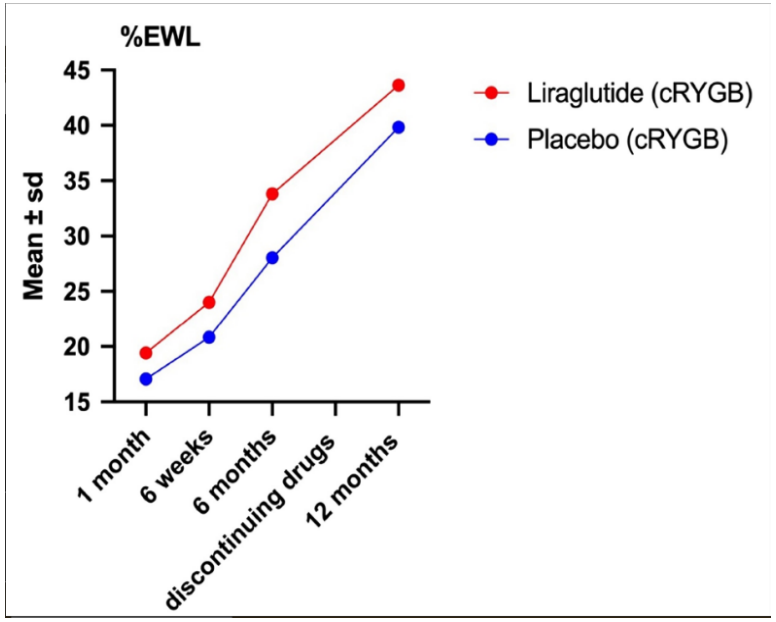


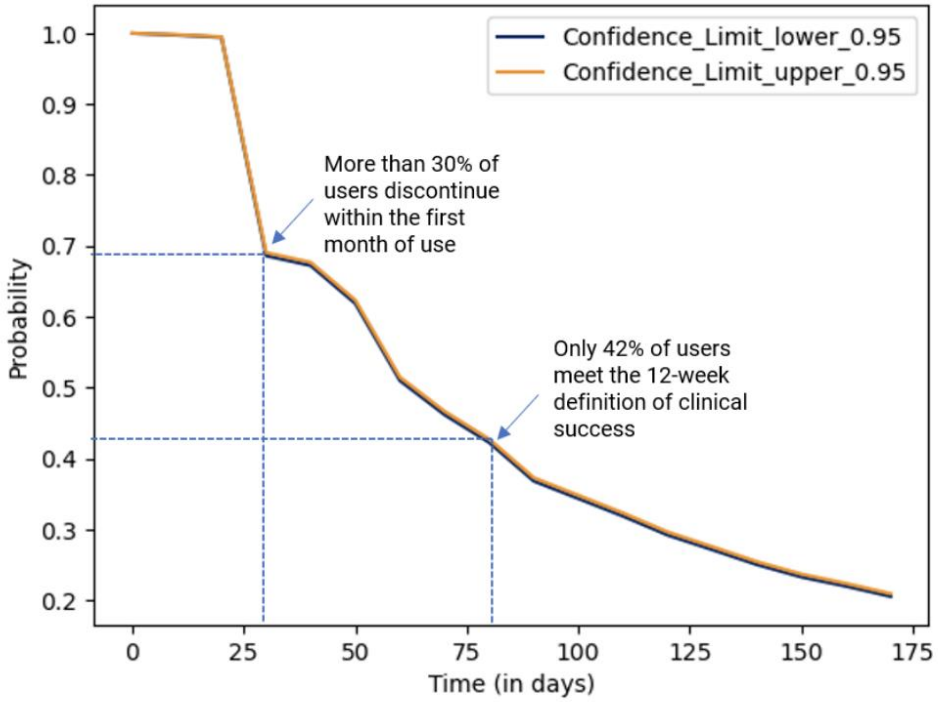


- **Adjunctive use of liraglutide with conversional RYGB** resulted in **significantly higher weight loss** compared to those undergoing conversional surgery alone
- Adverse events were **only** recorded in liraglutide group
  - GI related
- Combined therapy is promising to enhance weight loss outcomes, with careful consideration of risks

Hany, Mohamed MDa,c; Torensma, Bart MSc, PhDe; Ibrahim, Mohamed MDa; Zidan, Ahmed MDa; Agayby, Ann S.S. MDa; Abdelkhalek, Mohamed H. BScd; El Sayed, Iman MSc, PhDb. Boosting weight loss after conversional Roux-en-Y Gastric Bypass with liraglutide and placebo use. A double-blind-randomized controlled trial. International Journal of Surgery 110(3):p 1546-1555, March 2024 | DOI: 10.1097/JS9.0000000000000990

Limitations of OMM: High discontinue rate

Figure 5: Overall time to treatment discontinuation in GLP-1 users for weight management.



The probability of staying on a GLP-1 drug drops drastically between zero and six weeks. These individuals are not on a GLP-1 long enough to see a clinically meaningful benefit.

- **High Discontinuation rates** observed within the first month of treatment
- Potential barriers: cost, expectations, GI side effects
- Highlights potential for combined therapy

Perioperative Complications

- **Anesthesia / Aspiration Risk**
  GLP-1 RAs significantly delay gastric emptying, which has raised concerns **about pulmonary aspiration during** surgery even following standard fasting periods.
- **Unknown Perioperative Interactions**
  While using GLP-1s before surgery (preoperative use) in patients with extreme obesity (e.g., BMI > 70) has shown promise in **reducing post-op complications** by improving weight status, these data are preliminary

Recommendations for Discontinuing OMMs prior to Surgery

- **Most Patients**
  - Continue GLP-1 RAs through peri-op period (per 2024 multi-society guidance)
  - Standard fasting protocols adequate
- **Elevated Risk Patients**
  - High aspiration risk or delayed gastric emptying
  - Strategies: 24-hour clear liquid diet, rapid sequence induction, anesthesia precautions
- **Very High Risk / Symptomatic Patients**
  - Consider holding weekly GLP-1s for 1–2+ weeks pre-op
  - Daily formulations: may omit on day of surgery
  - Optional: point-of-care gastric ultrasound pre-op

Short term Post-op Complications: GI Symptoms / Ileus

- **GLP-1s** → nausea, vomiting, delayed gastric emptying, ileus.
- **Naltrexone/bupropion** → worsens nausea in sensitive patients.

Incidence:

- transient nausea/vomiting common in first 48-72 h. [8,12]
- ileus uncommon (<1-2%)

- **Exacerbated by OMMs**. Symptoms may be more frequent in SG due to higher intragastric pressure.
  - May also increase the risk of leak due to severe vomiting ↑ intraluminal pressure → stress on staple line

- **Management:** IV hydration, antiemetics, withhold or reduce AOM temporarily, monitor electrolytes and hydration, gradual diet advancements

GI Related Complications

- Side effects of GLP-1RAs following bariatric surgery include mild gastrointestinal adverse events
- **Most notable AEs:** (Placebo vs. Liraglutide) at 24 weeks:
- Nausea: 20% vs 51%
  - Constipation: 6% vs 26%
  - Fatigue: 6% vs 14%
- Most GI related complications are significantly associated with the use of GLP-1RAs[2]

Table 3. Adverse Events (AE)[a] in the BARI-OPTIMISE Study Population

Event	Participants who experienced an AE, No. (%)		
	Placebo (n = 35)	Liraglutide (n = 35)	Total (N = 70)
Total	20 (57)	28 (80)	48 (67)
Total AEs, No.[b]	75	37	112
Gastrointestinal events			
Nausea	7 (20)	18 (51)	25 (36)
Diarrhea	2 (6)	2 (6)	4 (6)
Constipation	2 (6)	9 (26)	11 (16)
Vomiting	1 (3)	1 (3)	2 (3)
Abdominal pain	1 (3)	2 (6)	3 (4)
Abdominal bloating	0	1 (3)	1 (1)
Dyspepsia	0	1 (3)	1 (1)
General and administration site events			
Headache	2 (6)	1 (3)	3 (4)
Injection site reaction	3 (9)	2 (6)	5 (7)
Urticaria	0	1 (3)	1 (1)
Fatigue	2 (6)	5 (14)	7 (10)
Insomnia	2 (6)	0	2 (3)
Cardiovascular events			
Dizziness	2 (6)	3 (9)	5 (7)
Palpitations	1 (3)	3 (9)	4 (6)
Infections			
Upper respiratory tract infection	2 (6)	5 (14)	7 (10)
Influenza	2 (6)	3 (9)	5 (7)
Metabolic and nutritional events			
Decreased appetite	3 (9)	11 (31)	14 (20)
Dry mouth	2 (6)	3 (9)	5 (7)
Musculoskeletal events			
Back pain	0	1 (3)	1 (1)
Arthralgia	2 (6)	2 (6)	4 (6)
Serious AEs	0	0	0

1. Mok J, Adeleke MO, Brown A, Magee CG, Firman C, Makahamadze C, Jassil FC, Marvasti P, Carnemolla A, Devalia K, Fakih N, Elkalaawy M, Pucci A, Jenkinson A,. Adamo M, Omar RZ, Batterham RL, Makaronidis J. Safety and Efficacy of Liraglutide, 3.0 mg, Once Daily vs Placebo in Patients With Poor Weight Loss Following Metabolic Surgery: The BARI-OPTIMISE Randomized Clinical Trial. JAMA Surg. 2023 Oct 1;158(10):1003-1011. doi: 10.1001/jamasurg.2023.2930. PMID: 37494014; PMCID: PMC10372755.
2. Liu L, Chen J, Wang L, Chen C, Chen L. Association between different GLP-1 receptor agonists and gastrointestinal adverse reactions: A real-world disproportionality study based on FDA adverse event reporting system database. Front Endocrinol (Lausanne). 2022 Dec 7;13:1043789. doi: 10.3389/fendo.2022.1043789. PMID: 36568085; PMCID: PMC9770009

Long Term Complications: Nutritional Deficiencies

- Mechanism:
  - Malabsorption (RYGB > SG) and reduced intake (GLP-1s, orlistat)
  - Due to reduced intake, intolerance; bypass of duodenum/jejunum (RYGB) → malabsorption; ↓ acid & intrinsic factor → impaired iron/B12 absorption.
  - Anorectic effect of GLP-1 RAs, malabsorption with orlistat

- Common deficits: iron, vitamin B12, folate, vitamin D, calcium.

- Incidence:
  - - Iron deficiency ± anemia: up to ~38% at 36 months post-RYGB; variable after SG. [A]
  - - Vitamin deficiencies (A, B12, D, folate) remain prevalent years after surgery. [B]

Long Term Complications: Gallstones & Biliary Disease

- Mechanism: biliary cholesterol supersaturation during rapid weight loss; gallbladder hypomotility. → supersaturated bile, impaired emptying

- Incidence: 10–40% in year 1 (w/o UDCA), symptomatic lower
  - RYGB & SG: both at risk, some data SG ≤ RYGB

- Management: UDCA prophylaxis (6 mo), cholecystectomy if symptomatic
  - UDCA prophylaxis reduces gallstones vs placebo in RCT meta-analyses. [L,M,N]

(Pharmacy review. MDPI 2025, Li et al. *Lipids Health Dis* 2023)

Long Term Complications: Hepatic Complications

Malnutrition-related liver injury (rare)

- Due to protein–calorie deficiency, micronutrient deficits

Drug-related DILI

- Orlistat: rare severe hepatotoxicity
- Naltrexone/bupropion: mild transaminase rises possible
- GLP-1 RAs: ↑ gallbladder risk, not intrinsic DILI

Long Term Complications: Pancreatic Complications

Acute Pancreatitis

- Mechanisms: early (edema, obstruction, hematoma), later (gallstones)
- Incidence: uncommon, ↑ risk in first 90 days
- SG approximately 2x higher early AP risk than RYGB
- GLP-1 RAs: mixed signal, low absolute risk; avoid if prior AP
- Management: standard AP care, gallstone workup/intervention

Exocrine Pancreatic Insufficiency (EPI)

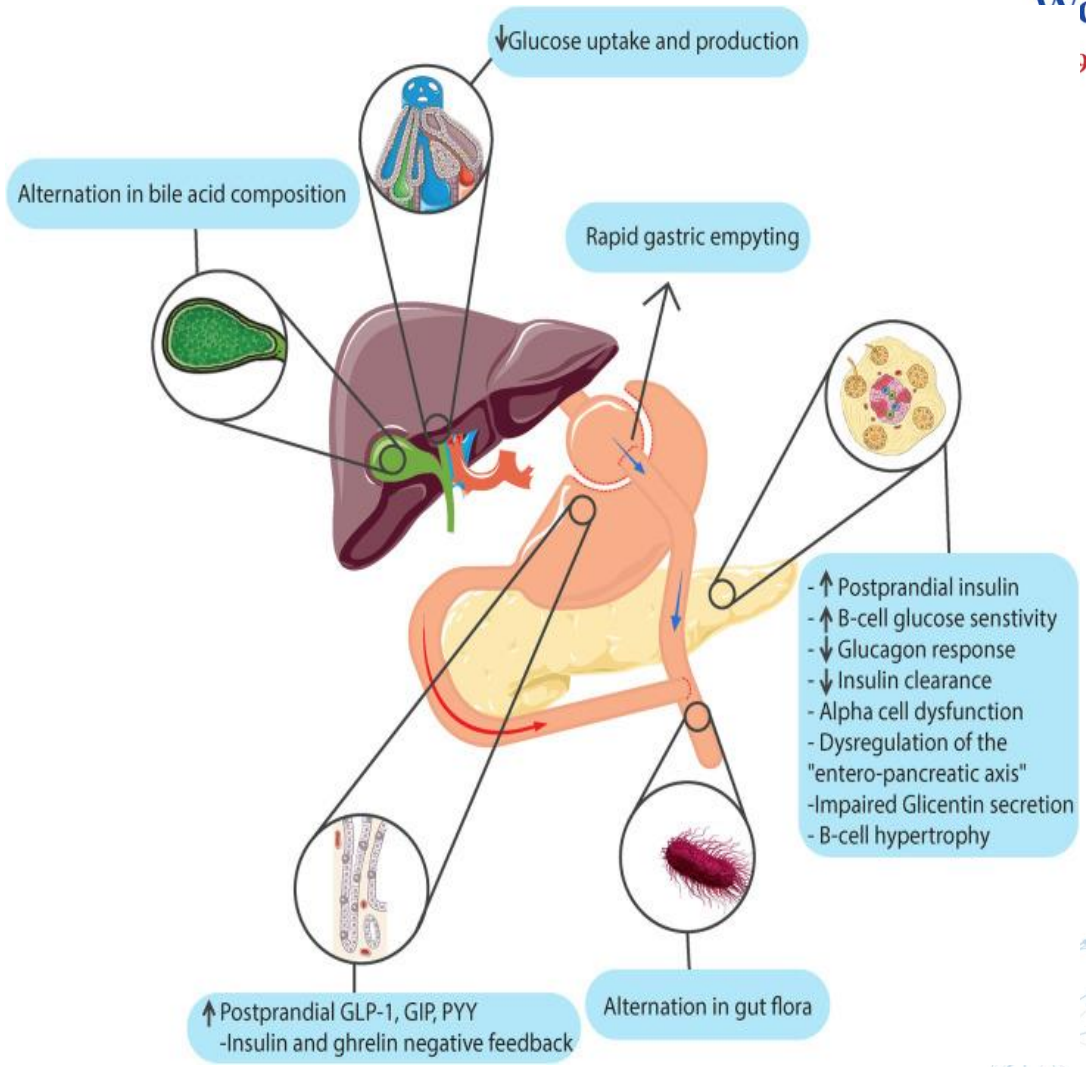
- Incidence: ~9-10% overall; higher in RYGB than SG
- Presentation: steatorrhea, fat-soluble vitamin deficiency
- Management: pancreatic enzyme replacement, nutritional support

Biliary Access after RYGB

- LA-ERCP: ~95% success, pancreatitis ~7%
- EDGE: ~98% success, shorter LOS
- Enteroscopy-assisted ERCP: less invasive, lower success

Long Term Complications: Post-Bariatric Hypoglycemia (Late Dumping)

- Rapid nutrient transit → exaggerated GLP-1/insulin response → postprandial hyperinsulinemic hypoglycemia.
- Incidence: reported range ~0.1-30% due to heterogeneity of definitions/testing; typically begins ≥1 year post-op. [U,V,W]



Ocular Complications: NAION

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Table 2. Demographic and Clinical Characteristics of Eligible, Propensity Score-Matched, and Exact-Matched Cohorts in Patients Who Were Overweight or Obese

	Eligible cohorts				1:2 Propensity score-matched cohorts[a]				1:1 Propensity score- and exact-matched cohorts[a]			
	No. (%)				No. (%)				No. (%)			
Characteristic	Overall (n = 979)	Non-GLP-1 RA antiobesity medication (n = 618)	Sema-glutide (n = 361)	SMD	Overall (n = 613)	Non-GLP-1 RA antiobesity medication (n = 359)	Sema-glutide (n = 254)	SMD	Overall (n = 442)	Non-GLP-1 RA antiobesity medication (n = 221)	Sema-glutide (n = 221)	SMD
NAION event	32 (3)	5 (1)	27 (7)	NA	23 (4)	3 (1)	20 (8)	NA	18 (5)	2 (1)	16 (7)	NA
Age, median (IQR), y	47 (32-59)	44 (29-58)	50 (37-60)	0.30	46 (32-58)	44 (29-59)	46 (35-58)	0.04	46 (33-59)	45 (33-59)	46 (34-58)	0.01
Sex[b]												
Female	708 (72)	454 (73)	254 (70)	0.06	463 (76)	274 (76)	189 (74)	0.04	339 (77)	167 (76)	172 (78)	<0.01
Male	271 (28)	164 (27)	107 (30)	0.06	150 (24)	85 (24)	65 (26)	0.04	103 (23)	54 (24)	49 (22)	<0.01
Race[b]												
Asian	13 (1)	8 (1)	5 (1)	<0.01	6 (1)	4 (1)	2 (1)	0.01	3 (1)	2 (1)	1 (0.5)	0.06
Black	109 (11)	55 (9)	54 (15)	0.16	70 (11)	42 (12)	28 (11)	0.01	49 (11)	23 (10)	26 (12)	<0.01
White	742 (76)	478 (77)	264 (73)	0.09	464 (76)	273 (76)	191 (75)	0.02	337 (76)	165 (75)	172 (78)	0.05
Other[c]	115 (12)	77 (12)	38 (11)	0.06	73 (12)	40 (11)	33 (13)	0.04	53 (12)	31 (14)	22 (10)	0.03
Systemic hypertension	513 (52)	273 (44)	240 (66)	0.47	340 (55)	191 (53)	149 (59)	0.03	274 (62)	137 (62)	137 (62)	<0.01
Obstructive sleep apnea	271 (28)	125 (20)	146 (40)	0.41	193 (31)	93 (26)	100 (39)	<0.01	136 (31)	68 (31)	68 (31)	<0.01
Type 2 diabetes	269 (27)	91 (15)	178 (49)	0.69	163 (27)	86 (24)	77 (30)	0.02	130 (29)	65 (29)	65 (29)	<0.01
Hyperlipidemia	370 (38)	173 (28)	197 (55)	0.53	243 (40)	130 (36)	113 (44)	0.03	184 (42)	92 (42)	92 (42)	<0.01
Coronary artery disease	297 (30)	158 (26)	139 (39)	0.26	191 (31)	106 (30)	85 (33)	0.01	143 (32)	72 (33)	71 (32)	0.04
Chronic kidney disease	100 (10)	40 (6.5)	60 (17)	0.27	66 (11)	33 (9)	33 (13)	<0.01	37 (8)	18 (8)	19 (9)	0.02
MEN type 2	0	0	0	0.00	0	0	0	0.00	0	0	0	<0.01
Thyroid tumors	9 (1)	7 (1)	2 (1)	0.07	5 (1)	4 (1)	1 (0.4)	0.05	5 (1)	3 (1)	2 (1)	0.05
Pancreatitis	54 (6)	32 (5)	22 (6)	0.03	32 (5)	21 (6)	11 (4)	<0.01	20 (5)	7 (3)	13 (6)	0.01
Amiodarone exposure	47 (5)	20 (3)	27 (7)	0.16	25 (4)	14 (4)	11 (4)	0.01	16 (4)	8 (4)	8 (4)	0.04
PDE5 inhibitor exposure	68 (7)	29 (5)	39 (11)	0.19	46 (8)	23 (6)	23 (9)	<0.01	36 (8)	20 (9)	16 (7)	0.04

Abbreviations: GLP-1 RA, glucagon-like peptide 1 receptor agonist; MEN, multiple endocrine neoplasia; NA, not applicable; NAION, nonarteritic anterior ischemic optic neuropathy; PDE5, phosphodiesterase type 5; SMD, standardized mean difference.

[a] Propensity score matching and exact matching were performed from the same eligible cohorts.

[b] Self-reported.

[c] Includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, declined, patient does not know, race not listed, or unavailable.

- Recent studies have found an increased risk of Non-Arteritis Anterior Ischemic Optic Neuropathy (NAION) in patients taking GLP-1s
- A retrospective matched cohort study by Hathaway et al. (2024) found that 20 NAION events occurred in obese patients taking semaglutide
- According to the results of this study, patients taking semaglutide for T2DM or obesity may be at an increased risk for NAION

Hathaway IY, Shah MP, Hathaway DB, et al. Risk of Nonarteritic Anterior Ischemic Optic Neuropathy in Patients Prescribed Semaglutide. JAMA Ophthalmol 2024; 142: 732–739

Integrated Management: The Path Forward

Structured monitoring protocols: Implement standardized follow-up schedules and laboratory panels specifically designed for combined therapy patients

Multidisciplinary Care Team: Coordinate care between surgery, endocrinology, nutrition, primary care, and specialized consultants as needed

Individualized Treatment Plans: Develop patient-specific protocols considering surgical procedure, medication choice, comorbidities, and risk factors

Enhanced Patient Education: Create comprehensive materials addressing the unique needs and risks of patients undergoing combined therapy