GLP-1 AFTER BARIATRIC SURGERY: THE PHARMACOLOGIC ENCORE

TACKLING WEIGHT REGAIN WITH SCIENCE, STRATEGY, & A LITTLE MAGIC

DR. REYNU RAJAN
CONSULTANT UPPER GI & BARIATRIC SURGEON
(MALAYSIA)

WHY THIS MATTERS

20–30% OF PATIENTS FACE WEIGHT REGAIN (WR) POST-MBS

UNDERMINES LONG-TERM SUCCESS OF SURGERY

PATIENTS & SURGEONS BOTH FRUSTRATED

King et al. Obes Surg 2024;34:123–132

UNFINISHED SYMPHONY

BARIATRIC SURGERY = POWERFUL

BUT OBESITY = CHRONIC RELAPSING DISEASE

SURGERY ALONE ≠ CURE

Rubino et al. Nat Rev Endocrinol 2023;19:263–278

DEFINING WR & IWL

WEIGHT REGAIN
≥10–15%
above nadir

INADEQUATE
WEIGHT LOSS
<50% EWL

NO UNIVERSAL CONSENSUS = INCONSISTENT REPORTING

Courcoulas et al. JAMA 2022;327:1167–1177

WHY WEIGHT RETURNS

GASTRIC POUCH ADAPTATION

BEHAVIORAL DRIFT

HORMONAL COUNTER-REGULATION:
GHRELIN ↑
GLP-1 ↓

Stefater et al. Nat Rev Endocrinol 2023;19:183–196

ENTER THE PHARMACOLOGIC ENCORE

GLP-1 RECEPTOR AGONISTS AS ADD-ON THERAPY

RESTORE HORMONAL BALANCE

EVIDENCE EMERGING IN POST-MBS WR/IWL

Wilding et al. Nat Rev Endocrinol 2023;19:301–313

MEET THE CASTS

SEMAGLUTIDE

LIRAGLUTIDE

DOES IT WORK IN INADEQUATE WEIGHT LOSS POST MBS

BARI-OPTIMISE TRIAL (LIRAGLUTIDE)

PAPAMARGARITIS JAMA SURG 2023
RCT 70 PATIENTS

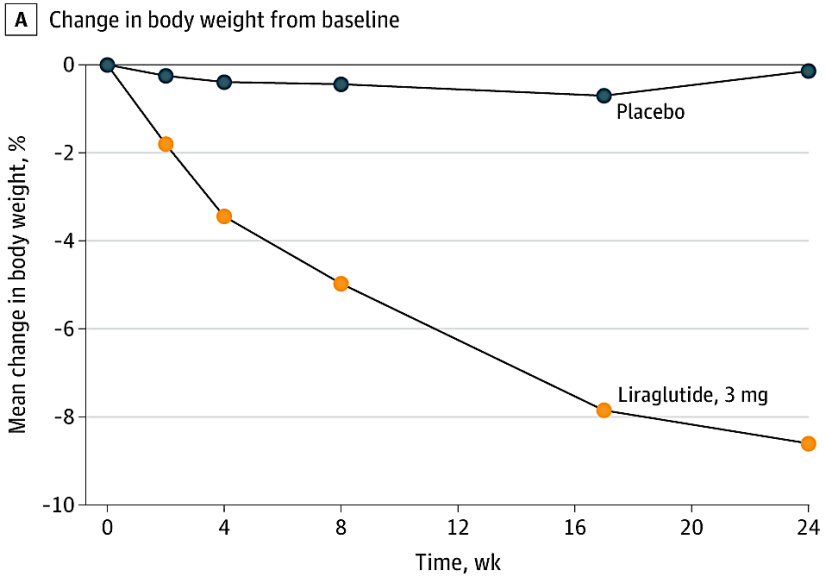
POST MBS w POOR WEIGHT LOSS : **<20% WL 1 YEAR POST MBS**

LIRAGLUTIDE 3.0 VS PLACEBO

SIGNIFICANT WEIGHT LOSS IMPROVEMENT AT 24 WEEKS

MEAN WL LIRAGLUTIDE VS PLACEBO: 8% (P<0.001)

WL w LIRAGLUTIDE DID NOT PLATEAU SUGGESTING MORE WEIGHT LOSS OVER LONGER PERIOD



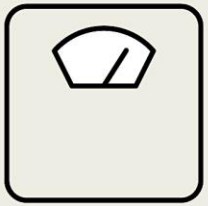
Papamargaritis et al. JAMA Surg 2023;158:671– 680

JAMA Surgery

RCT: Safety and Efficacy of Liraglutide, 3.0 mg, Once Daily vs Placebo in Patients With Poor Weight Loss Following Metabolic Surgery

POPULATION

18 Men,
52 Women



Adults ≥1 y after metabolic surgery with poor weight loss (≤20%) and a suboptimal GLP-1 response

Mean age, 47.6 y

INTERVENTION

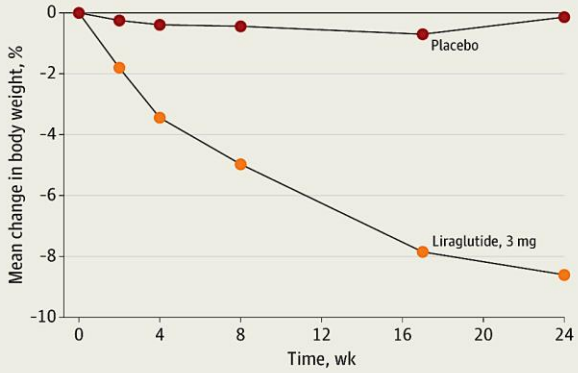
70 Patients randomized,
57 Analyzed

31 Liraglutide, 3.0 mg
Self-administration once daily of a subcutaneous injection of liraglutide, 3.0 mg, for 24 wk

26 Placebo
Self-administration once daily of placebo saline solution for the same period

FINDINGS

Liraglutide, 3.0 mg once daily, resulted in a significantly greater reduction in body weight from baseline to week 24 compared with placebo



Mean difference: -8.0%; 95% CI, -10.4 to -5.7; *P* <.001

SETTINGS / LOCATIONS

2 Hospitals in London, United Kingdom

PRIMARY OUTCOME

Change in percentage body weight from baseline to end of 24-wk study period

Mok J, Adeleke MO, Brown A, et al. 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*. Published online July 26, 2023. doi:10.1001/jamasurg.2023.2930

DOES IT WORK IN WEIGHT REGAIN POST MBS

EFFICACY OF 12 MONTHS THERAPY w LIRAGLUTIDE & SEMAGLUTIDE ON WEIGHT REGAIN AFTER MBS: A REAL-WORLD RETROSPECTIVE OBSERVATIONAL STUDY

JENSEN BMC ENDOCRINE 2025
RETROSPECTIVE STUDY

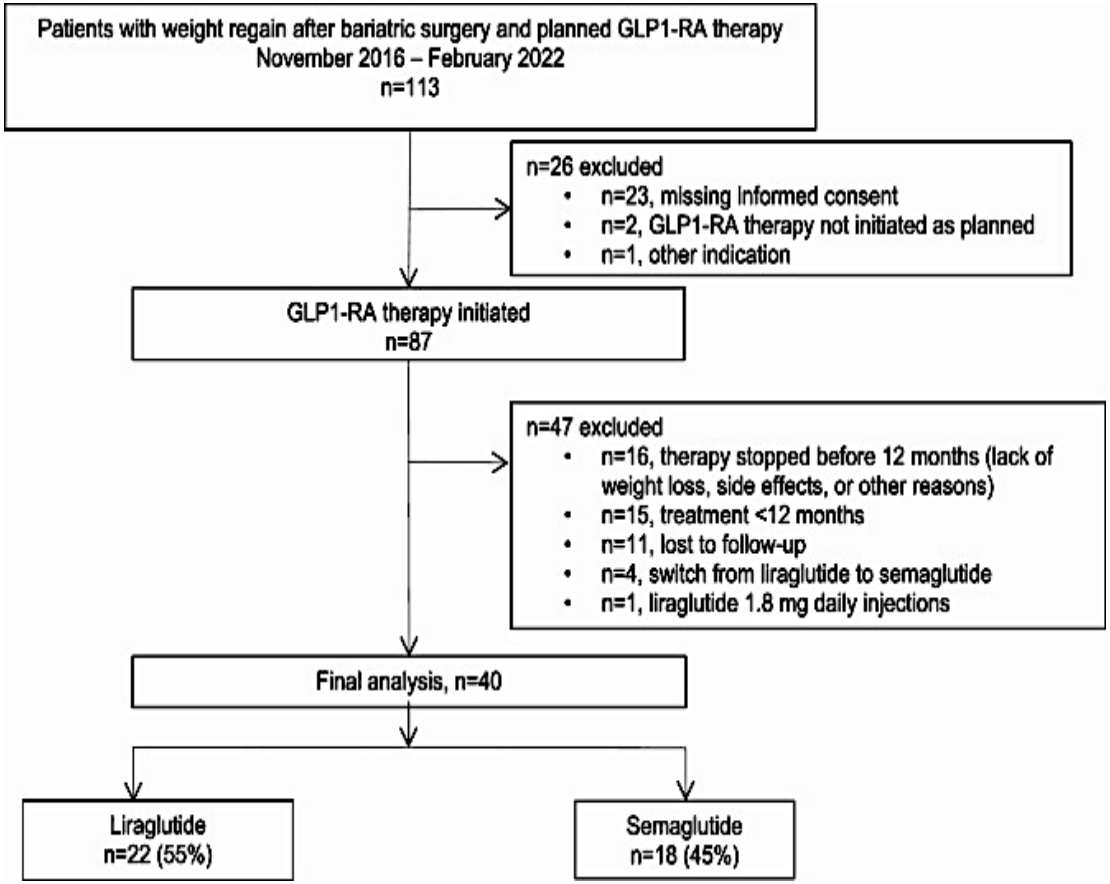
POST MBS w ANY WEIGHT REGAIN ABOVE NADIR AT 15 MONTHS POST MBS

12 MONTHS OF LIRAGLUTIDE 3.0 VS SEMAGLUTIDE 1.0

BOTH GLP DID SO WELL

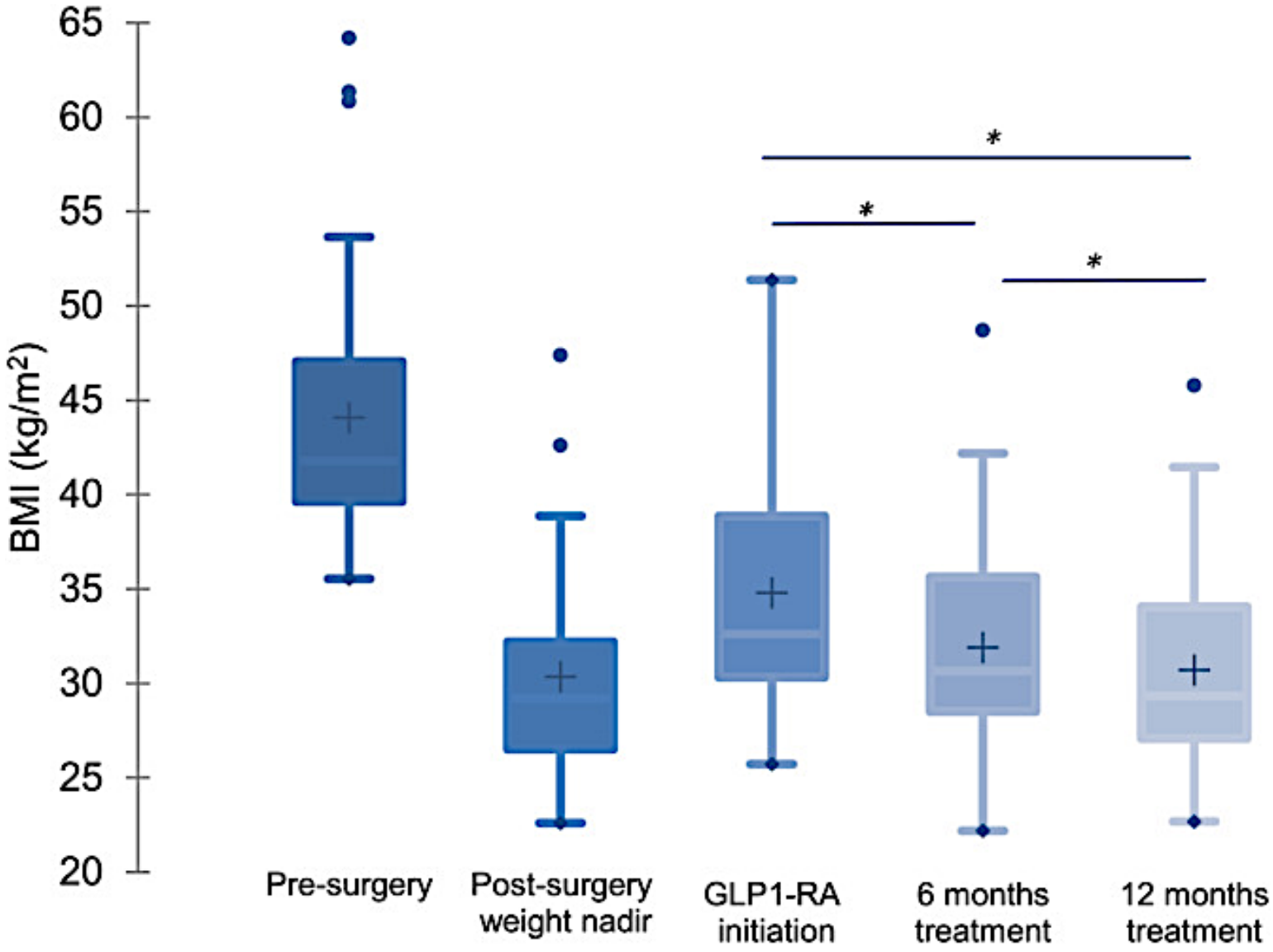
WL w SEMA > LIRA

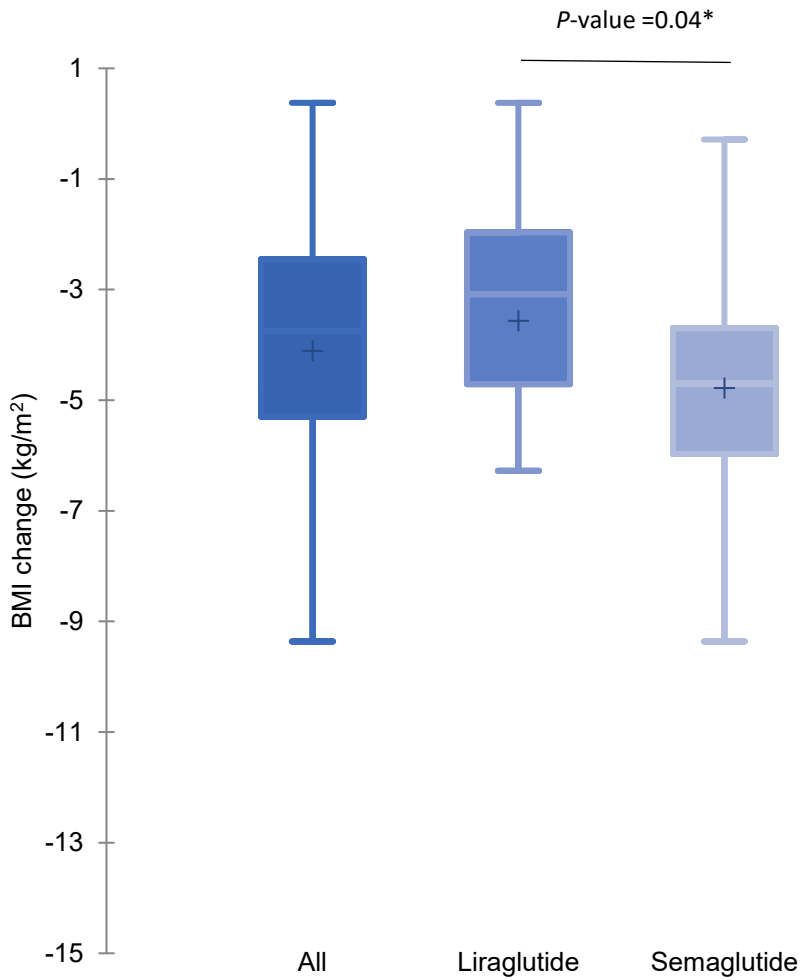
>WL WHEN GLP1 STARTED AFTER 74.5 MONTHS OF MBS

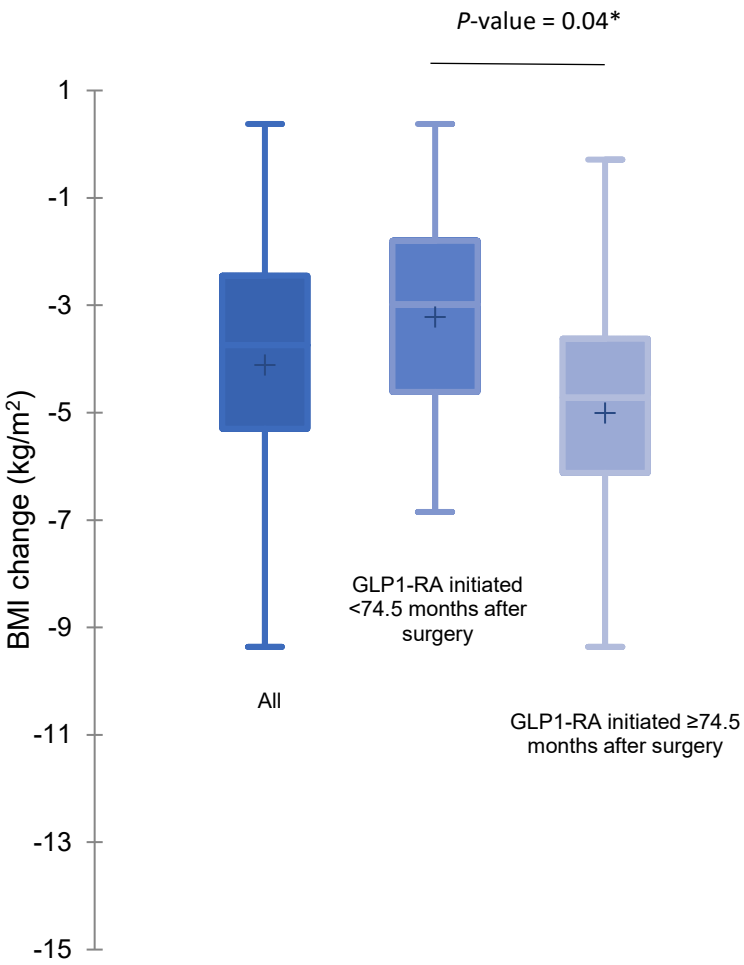


Jensen et al. BMC endocrine disorders vol. 25,1 93. 7 Apr. 2025

BOX & WHISKER PLOT : FROM REGAIN TO CONTROL




P-value =0.04*
1
-1
-3
-5
-7
-9
-11
-13
-15
BMI change (kg/m²)
All
Liraglutide
Semaglutide


P-value = 0.04*
1
-1
-3
-5
-7
-9
-11
-13
-15
BMI change (kg/m²)
All
GLP1-RA initiated <74.5 months after surgery
GLP1-RA initiated ≥74.5 months after surgery

STEP 1: CONFIRM WR/IWL

STEP 2: RULE OUT ANATOMICAL CAUSE

STEP 3: INITIATE GLP-1RA

STEP 4: COMBINE W “POUCH RESET” THRU DIET

DOES IT WORK FOR PERSISTENT T2DM AFTER MBS

ADJUNCTIVE LIRAGLUTIDE TREATMENT IN PATIENTS w PERSISTENT OR RECURRENT TYPE 2 DIABETES AFTER METABOLIC SURGERY (GRAVITAS)

DIMITRI THE LANCET 2019
RCT 80 PATIENTS

HBA1C >6.5 ONE YEAR AFTER MBS

LIRAGLUTIDE 1.8 VS PLACEBO

SIGNIFICANT HBA1C IMPROVEMENT AT 26 WEEKS

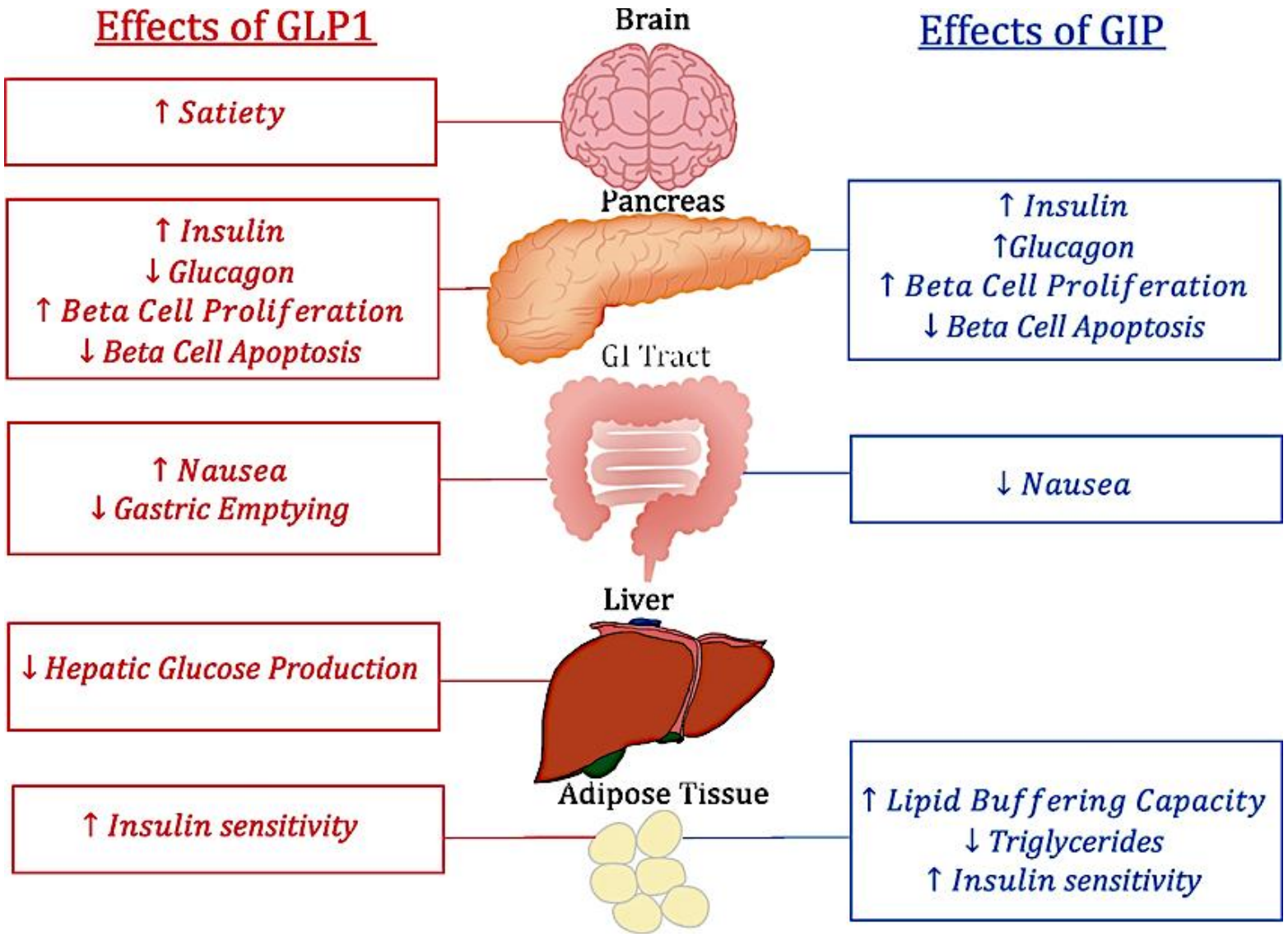
MEAN HBA1C REDUCTION -13·3 mmol/mol
p=0·0001

TYPE OF SURGERY DID NOT IMPACT THE OUTCOME WITH LIRAGLUTIDE

Miras, Alexander Dimitri et al. *The lancet. Diabetes & endocrinology* vol. 7,7 (2019): 549-559

THE MOST TRENDING UNION

WHEN
GLP1 RECEPTOR AGONIST
WEDS
GIP


Effects of GLP1
Brain
Effects of GIP
↑ Satiety
↑ Insulin
↓ Glucagon
↑ Beta Cell Proliferation
↓ Beta Cell Apoptosis
Pancreas
↑ Insulin
↑Glucagon
↑ Beta Cell Proliferation
↓ Beta Cell Apoptosis
GI Tract
↑ Nausea
↓ Gastric Emptying
↓ Nausea
Liver
↓ Hepatic Glucose Production
Adipose Tissue
↑ Insulin sensitivity
↑ Lipid Buffering Capacity
↓ Triglycerides
↑ Insulin sensitivity

2025
IS THE YEAR OF
TIRZEPATIDE

SEMAGLUTIDE & TIRZEPATIDE FOR THE MANAGEMENT OF WEIGHT RECURRENCE AFTER SLEEVE GASTRECTOMY: A RETROSPECTIVE COHORT STUDY

RETROSPECTIVE 115 PATIENTS

WEIGHT REGAIN >10% FROM NADIR AFTER LSG

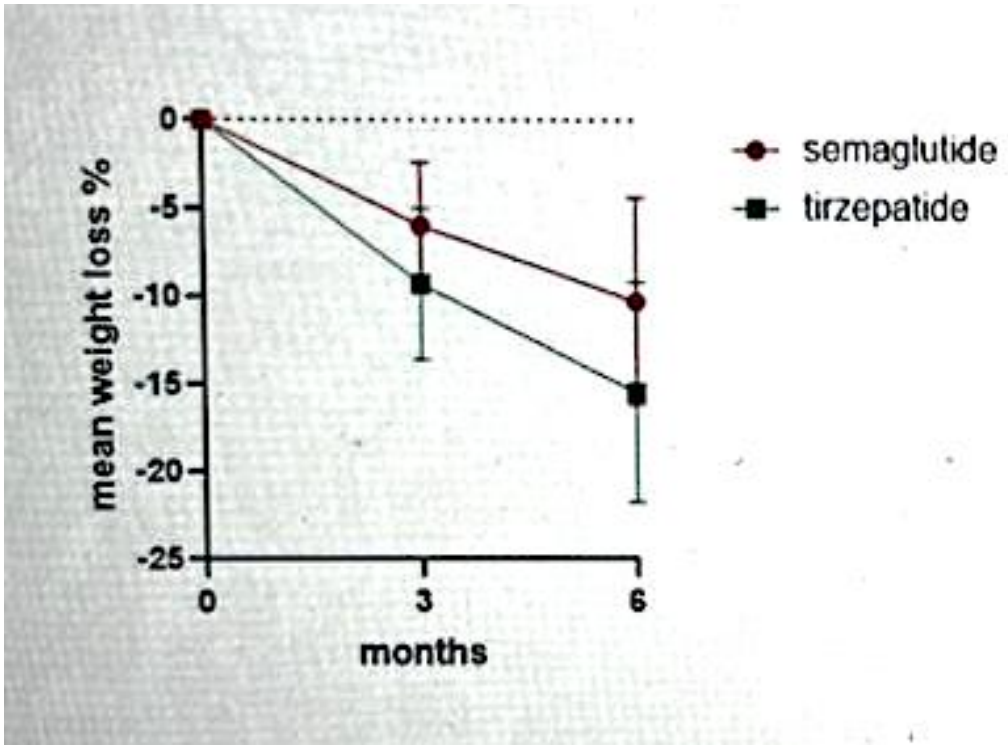
70 semaglutide
45 tirzepatide.

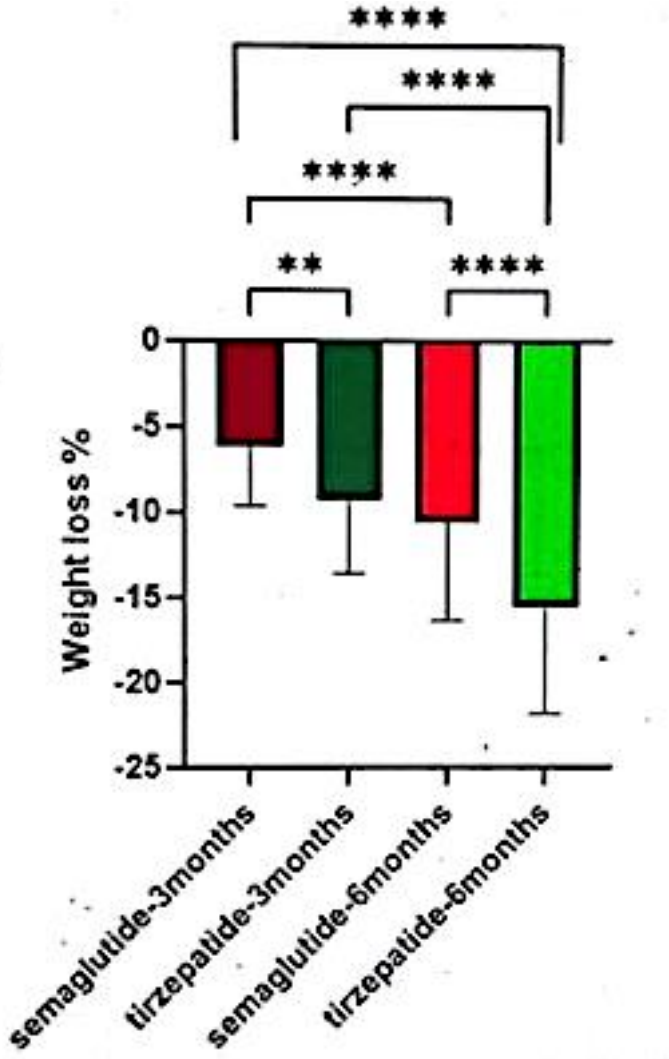
SIGNIFICANT WL AT 6 MONTHS

MEAN WEIGHT LOSS:

SEMA 5.9% (P<0.05)
TIRZEPATIDE 6.3% (P<0.05)
TIRZEPATIDE > SEMA (P<0.02)

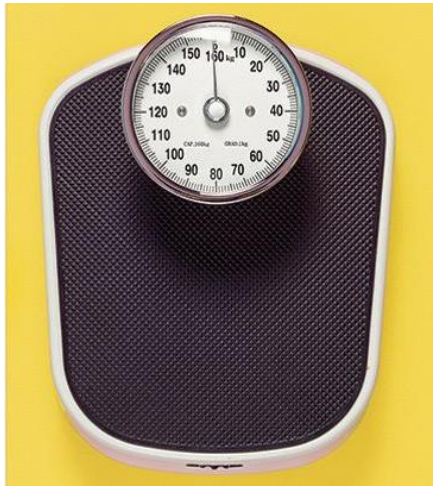
Jamal, Mohammad et al. *Obesity surgery* vol. 34,4 (2024): 1324-1332. doi:10.1007/s11695-024-07137-0

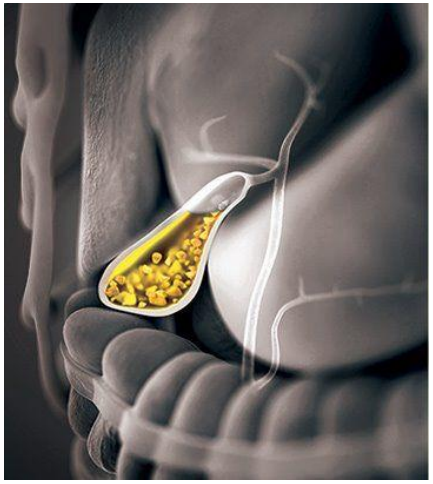

mean weight loss %
0
-5
-10
-15
-20
-25
0
3
6
months
semaglutide
tirzepatide


****
****
****
**
****
Weight loss %
0
-5
-10
-15
-20
-25
semaglutide-3months
tirzepatide-3months
semaglutide-6months
tirzepatide-6months

SAFETY FIRST : NO FREE LUNCH

GALLBLADDER & BILIARY RISK.





KRISTENSEN LANCET 2019
META ANALYSIS – 56 RCTs
103371 PATIENTS

GLP1-RA INCREASES RISK OF:
GB/BILIARY DISEASE (RR 1.27 , CI 1.1 – 1.47)

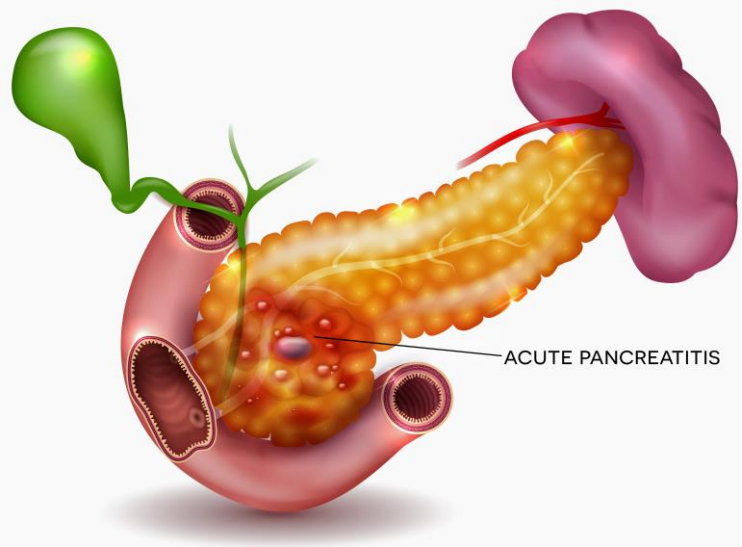
LINKED TO RAPID WEIGHT LOSS AND GALL STONE FORMATION

IMPORTANT RELEVANCE FOR BARIATRIC SURGERY PATIENTS WHO ARE ALREADY AT A HIGHER GALLSTONE RISK

Kristensen SL, Rørth R, Jhund PS, et al. Lancet Diabetes Endocrinol. 2019;7(10):776-785

SAFETY FIRST : NO FREE LUNCH

PANCREATITIS RISK



BETHEL ET AL 2021
META ANALYSIS – 7 RCTs
55921 PATIENTS

NO INCREASE OF PANCREATITIS INCIDENCE (HR 1.0 , CI 0.78-1.4)

NO INCREASE RISK OF PANCREATIC CANCER (HR 1.1 , CI 0.77-1.63)

REASSURING OUTCOME BUT REQUIRES VIGILENCE IN CASES WITH PRIOR HISTORY OF PANCREATITIS OR GALLSTONE DISEASE

Bethel MA, Patel RA, Merrill P, et al. A meta-analysis. Diabetes Care. 2021;44(3):663-671.

ELIXA (LIXISENATIDE)
LEADER (LIRAGLUTIDE)
SUSTAIN 6 (SEMAGLUTIDE)
EXSCEL (EXENATIDE)
HARMONY (ALBIGLUTIDE)
REWIND (DULAGLUTIDE)
PIONEER 6 (ORAL SEMAGLUTIDE)

SAFETY FIRST : NO FREE LUNCH

PANCREATITIS RISK

MONAMI ET AL 2017
META ANALYSIS
113 RCTs
48267 PATIENTS

NO INCREASE OF PANCREATITIS INCIDENCE (OR 0.93, CI 0.65-1.34)

NO INCREASE OF PANCREATIC CANCER (OR 0.94, CI 0.52-1.70)

INCREASE GALLSTONE RISK (OR 1.3, CI 1.01-1.68)

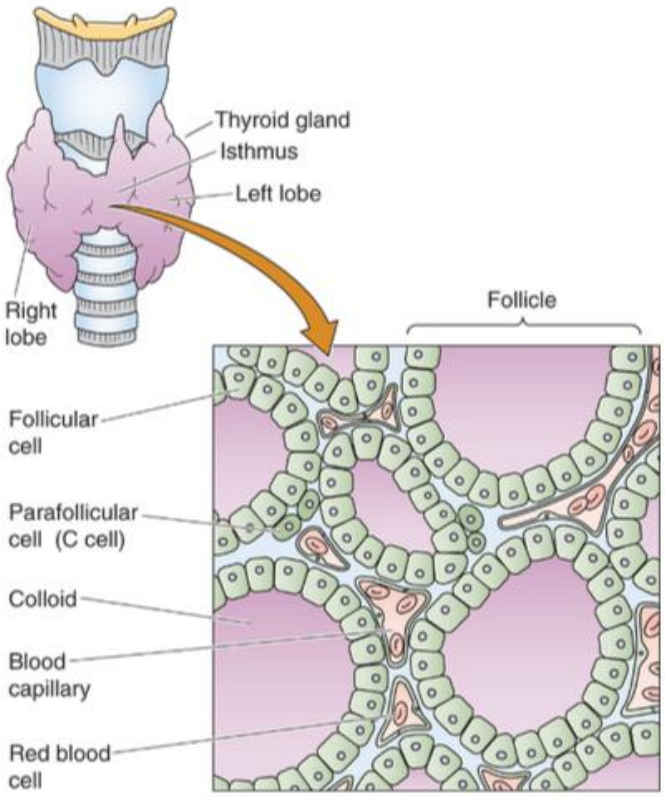
MASSON ET AL 2024
SEMAGLUTIDE SPECIFIC RCTs
21 RCTs
34721 PATIENTS

NO INCREASE OF PANCREATITIS INCIDENCE (OR 0.70, CI 0.5-1.20)

REASSURING OUTCOME BUT REQUIRES VIGILENCE IN CASES WITH PRIOR HISTORY OF PANCREATITIS OR GALLSTONE DISEASE

SAFETY FIRST : NO FREE LUNCH

THYROID CANCER RISK



NARRATIVE REVIEW
DISCUSSED:
RCT, META ANALYSIS, REGULATORY SAFETY REPORTS (FDA)

NO REPORTED HUMAN CASES OF MTC
NO INCREASE IN SERUM CALCITONIN DURING FOLLOW UP

NO INCREASE RISK OF PANCREATIC CANCER (HR 1.1 , CI 0.77-1.63)

BLACK BOX WARNING CONTINUE TO EXIST AS A PRECAUTION BY REGULATORY BODIES

Nauck MA, Meier JJ. Are GLP-1 receptor agonists safe? Eur J Endocrinol. 2019;181(6):R211-R234.

IN RATS LIRAGLUTIDE CAUSED

46-56% (F>M) BENIGN C CELL ADENOMAS
6-14% (M>F) C CELL CARCINOMAS

RODENT THYROID C CELLS EXPRESS GLP1 RECEPTORS ABUNDANTLY

↓

WHEN EXPOSED CHRONICALLY TO GLP1-RA, THEIR C CELLS GET ACTIVATED AND GET HYPERPLASIA, INCREASING RISK OF CANCER

↓

HUMAN C CELLS HAVE NEGLIGABLE TO ABSENT GLP1 RECEPTOR EXPRESSION THUS SHOWS NO FUNCTIONAL RESPONSE TO GLP1-RA

SAFETY FIRST : NO FREE LUNCH

GASTROPARESIS

LEE MM ET AL 2025
META ANALYSIS
55 RCTs
106395 PATIENTS

NO INCREASE OF GASTROPARESIS/ILEUS/OBSTRUCTION (RR 1.85, CI 0.89-3.85)

END POINTS FOR GALLSTONE DISEASE AND GERD WAS SIGNIFICANT

NAUCK MA ET AL 2024
META ANALYSIS
36 RCTs
1800 PATIENTS

FOR SOLID:
MEAN DIFFERENCE IN GASTRIC EMPYTING TIME DELAYED BY 36 MIN (CI 24-48)

FOR LIQUID:
NO CLINICALLY MEANINGFUL DELAY (+4 MINS)

PHYSIOLOGIC SLOWING IS NOT GASTROPARESIS – IMPROVES WITH USE OVER TIME

CLINICAL CRITERIA FOR GASTROPARESIS

AMERICAN COLLEGE OF GASTROENTEROLOGY

SYMPTOMS	> 3 MONTHS, EARLY SATIETY, POST PRANDIAL FULLNESS, VOMITING, BLOATING
OBJECTIVE EVIDENCE (SCINTIGRAPHY)	>60% RETENTION @ 2 HOURS >10% RETENTION @ 4 HOURS
EXCLUSION OF MECHANICAL OBSTRUCTION	ENDOSCOPY / IMAGING

EXPLORING PATIENT PERSPECTIVES ON SHARED DECISION MAKING ABOUT BARIATRIC SURGERY

OBJECTIVE: TO ASSESS PATIENT PERSPECTIVES ON THE LEVEL OF SHARED DECISION MAKING (SDM)

167 PARTICIPANTS.

MEAN AGE:
43.8 YEARS (SD 13.5)

BMI WAS 48 KG/M^2 (SD 8.63)

81% WERE FEMALE & 73% WERE WHITE.

>60% BELIEVED SURGERY = CURE
WHY DO I NEED MEDICATION?

PATIENTS WITH HIGHER BMI AND YOUNGER AGE MORE LIKELY TO EXPECT SURGERY = CURE

>50% REPORTED THEIR DOCTORS DID NOT EXPLAIN CHRONICITY OF OBESITY OR RISK OF WEIGHT REGAIN

40% FELT THEY WERE ENGAGED IN SHARED DECISION MAKING ABOUT LONG TERM TREATMENT PLAN

OBES SCI PRACT. 2024 NOV 26;10(6):E779. DOI: 10.1002/OSP4.779

SCIENCE VS REALITY: THE COST BARRIER

- **HIGH LIST PRICES AND RESTRICTIVE FORMULARIES LIMIT ACCESS TO GLP-1 THERAPIES**

- **INSURANCE PATHWAYS ARE OFTEN NARROW AND ADMINISTRATIVELY BURDENSOME**

- **INEQUITIES PERSIST ACROSS SYSTEMS, DELAYING INITIATION EVEN WHEN MEDS ARE INDICATED**

Citation: ICER. Affordable Access to GLP-1 Obesity Medications: Strategies to Guide Market Action and Policy Solutions. Institute for Clinical and Economic Review. 2025.

BARRIERS TO GLUCAGON-LIKE PEPTIDE-1 AGONIST (GLP-1RA) USE FOR WEIGHT MANAGEMENT: INSIGHTS FROM REAL-WORLD PATIENT PERSPECTIVES.

High awareness of GLP-1RA drugs, but real concerns around:

COST
ACCESS (insurance)
SAFETY AND SIDE EFFECTS
STIGMA

remains significant barriers to adoption—even among users.

WHAT'S COMING NEXT ?
THE PHARMACOLOGIC FUTURE

AMYLIN RECEPTOR AGONIST

AMYLIN IS CO-SECRETED WITH INSULIN BY BETA CELLS

SLOWS GASTRIC EMPYTING, REDUCES APETITE

PHASE 2 TRIALS – CAGRISEMA

RCT 338 ADULTS BMI>30 NO DM
68 WEEKS

CAGRILINTIDE 2.4MG+SEMA 2.4MG WEEKLY
15.6% MEAN WEIGHT LOSS

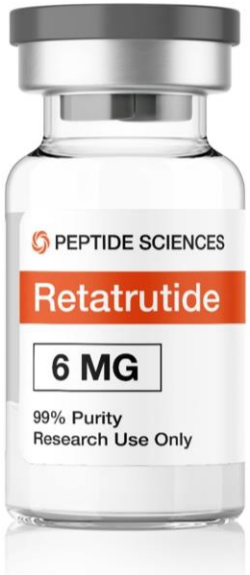
SEMA 2.4MG WEEKLY
8% MEAN WEIGHT LOSS

CAGRILINTIDE 2.4MG WEEKLY
6.4% MEAN WEIGHT LOSS

PLACEBO
0.8% MEAN WEIGHT LOSS

COMBO CAGRI + SEMA STATISTICALLY SIGNIFICANT WEIGHT LOSS

WHAT'S COMING NEXT ?
THE PHARMACOLOGIC FUTURE



NOVEL TRI RECEPTOR AGONIST
(GLP1, GIP, GLUCAGON RA)

DEVELOPED BY ELI LILLY
NICKNAME TRIPLE G
(GODZILLA OF WEIGHT LOSS JABS)

PHASE 2 TRIALS – 24% WEIGHT LOSS 11 MONTHS
PHASE 3 TRIAL PENDING

GREAT DEBATES:
UNDERGOING THE KNIFE VERSUS PILL-POPPING

FIVE PUNCHLINES

- GLP-1RAS EFFECTIVE POST-MBS WR/IWL
- SEMAGLUTIDE > LIRAGLUTIDE
- TIRZEPATIDE: RISING STAR
- MAINTENANCE IS KEY
- METABOLIC BENEFITS IS A PLUS

Brosnihan P et al. (2025)

GLP-1 AFTER BARIATRIC SURGERY: THE PHARMACOLOGIC ENCORE

TACKLING WEIGHT REGAIN WITH SCIENCE, STRATEGY, & A LITTLE MAGIC

DR. REYNU RAJAN
CONSULTANT UPPER GI & BARIATRIC SURGEON
(MALAYSIA)

"THE TRUE ENCORE ISN'T SURGERY OR DRUG ALONE — IT'S THE DUET."

DR. REYNU RAJAN