



# OBESITY MANAGEMENT MEDICATION (OMMS) FOR RECURRENT WEIGHT GAIN - WHAT'S THE EVIDENCE?

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## Conflict of Interests

|                                                 |                                                                                                                                                              |
|-------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Grants/Research Support:                        | Fractyl<br>Novo Nordisk<br>Boehringer Ingelheim<br>Radox<br>Gila<br>Anabio<br>Eli Lilly                                                                      |
| Other Financial or Material Support/Honorarium: | Eli Lilly<br>Novo Nordisk<br>GI dynamics<br>AstraZeneca<br>Boehringer Ingelheim<br>Ethicon<br>Medtronic<br>Currax<br>BeyondBMI<br>Screen Health<br>Algorithm |



# **GLP-1 Receptor Agonist interVentlon for poor responders afTer bariAtric Surgery**

## **The GRAVITAS trial**

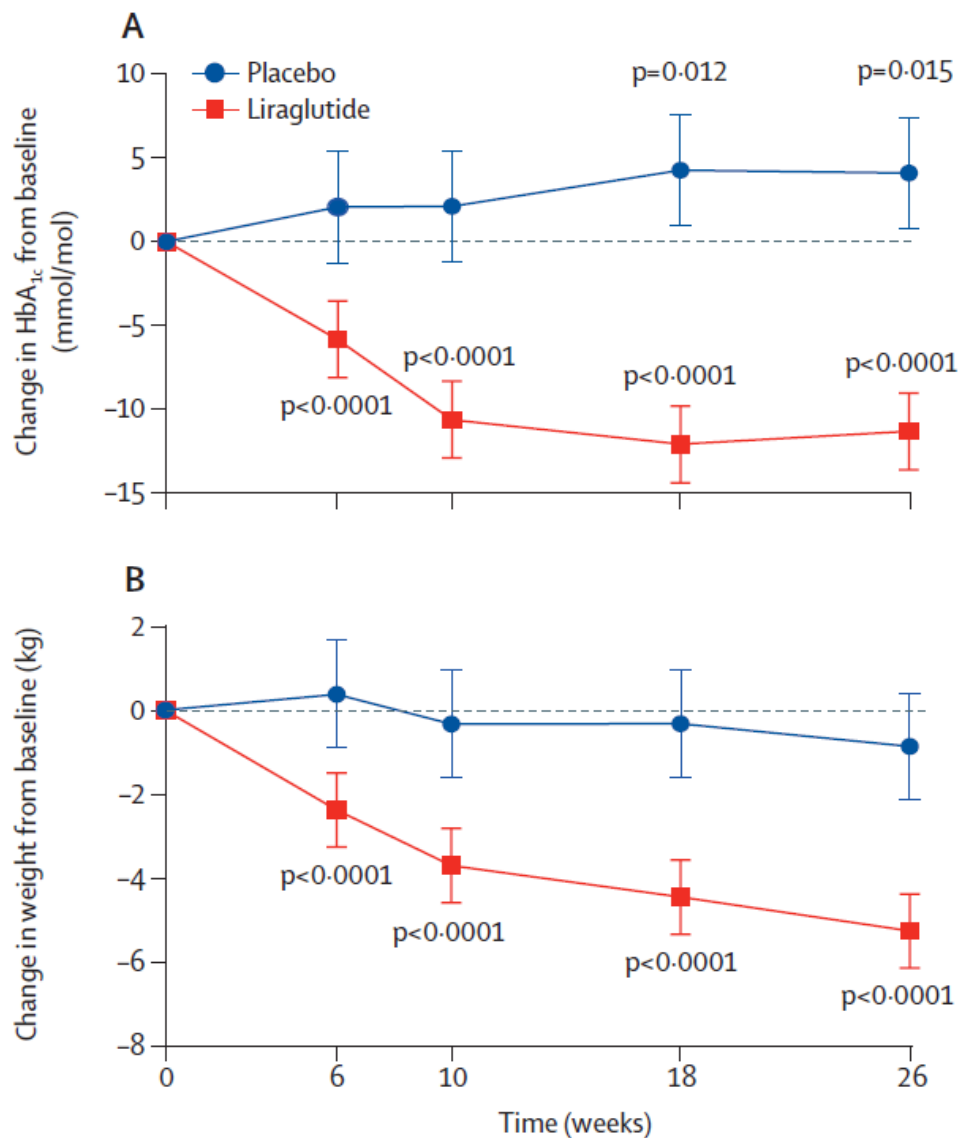


## RCT of Liraglutide

- Prospective, double-blind, placebo controlled
- 80 patients who have undergone RYGB or VSG surgery at least 12 months before randomization
- Post-op T2DM with HbA1c of  $>6.5\%$
- Recruitment stratified by surgery
- Randomised (2:1)
- Liraglutide 0.6 mg titrated up to 1.8 mg (n=54)
- Placebo (n=26)
- Treated for 6 months



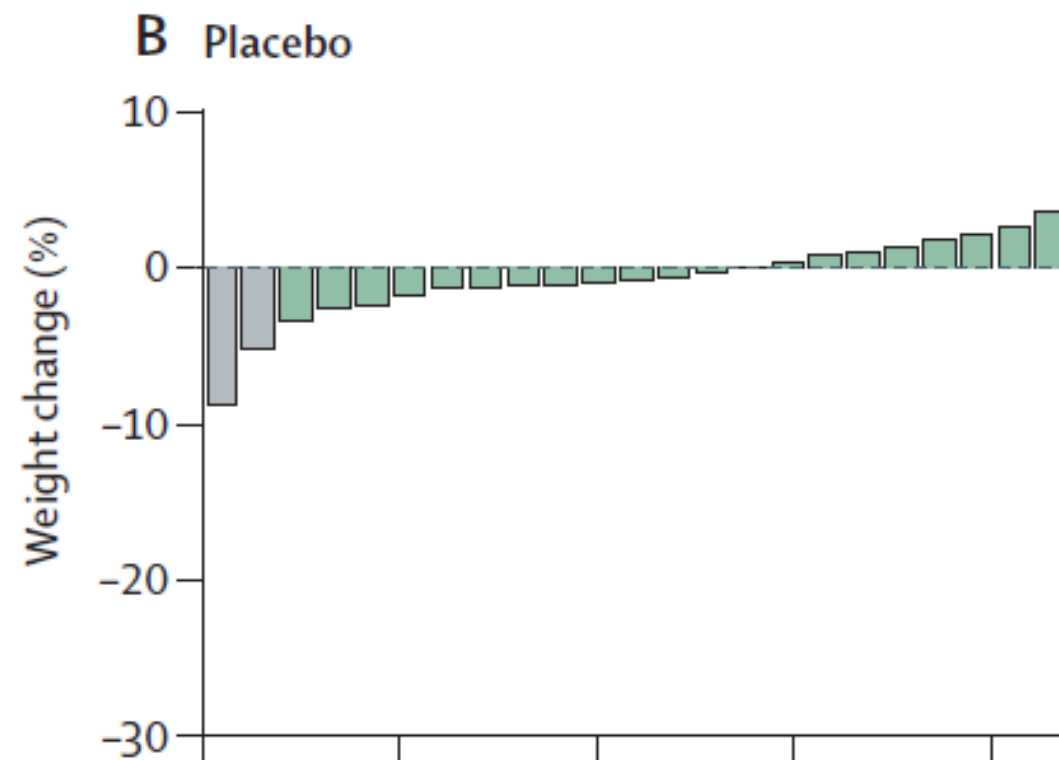
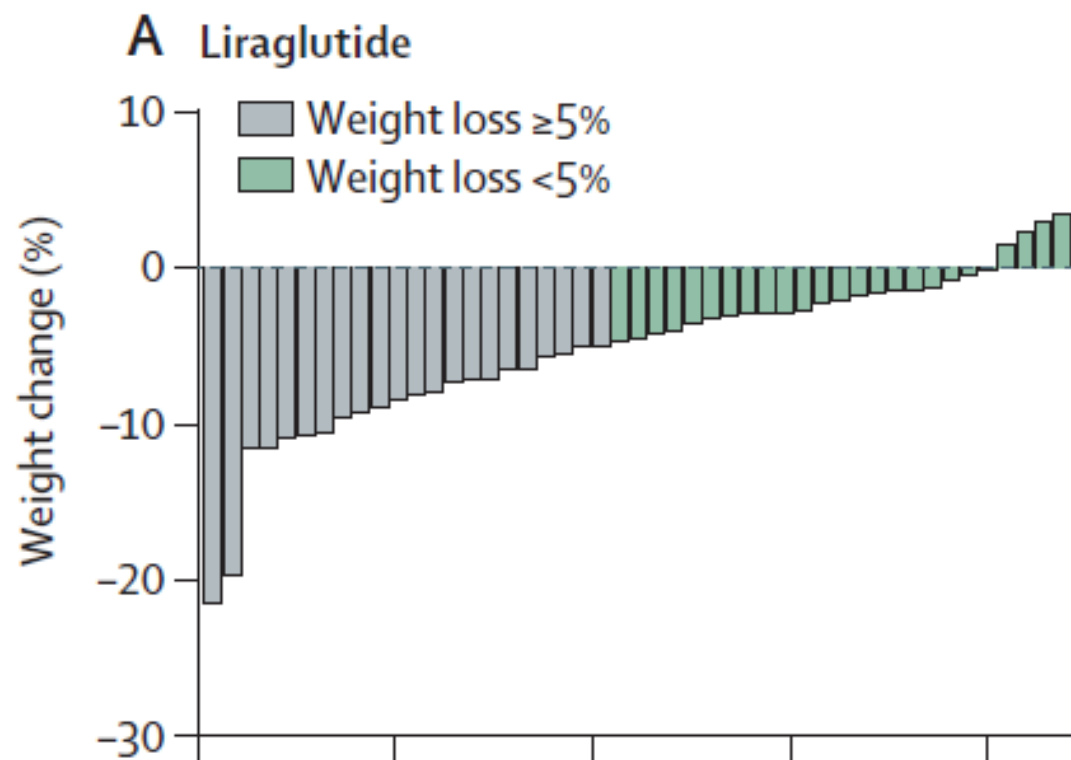
# HbA1c and weight



Miras et al Lancet D&E 2019



# Variation in response





# Liraglutide 3.0mg for suboptimal response after surgery

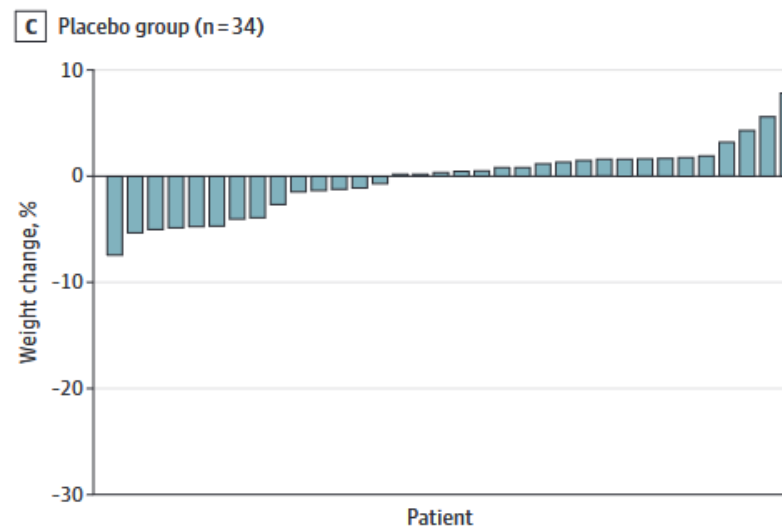
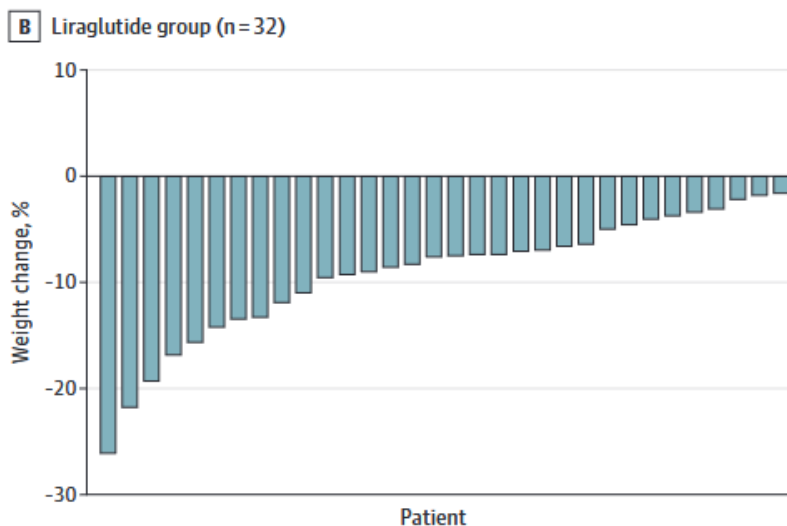
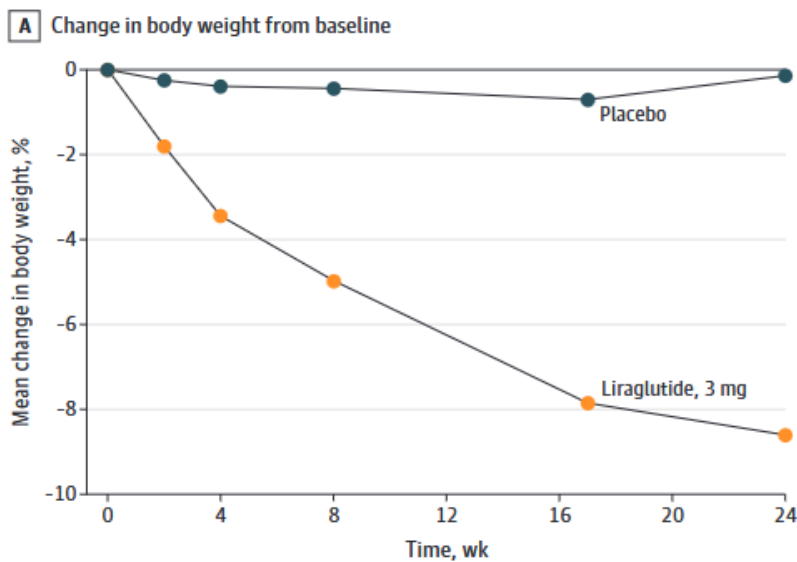
Suboptimal weight loss: 20% or less total body weight loss

and

Suboptimal GLP-1 response: 2-fold or less increase in circulating active GLP-1 between 0 and 30 minutes following the meal



# Liraglutide 3.0mg for suboptimal response after surgery





# Liraglutide 3.0mg for suboptimal response after surgery

total body weight loss of 5%- 12% for adjustable gastric band (n=21)

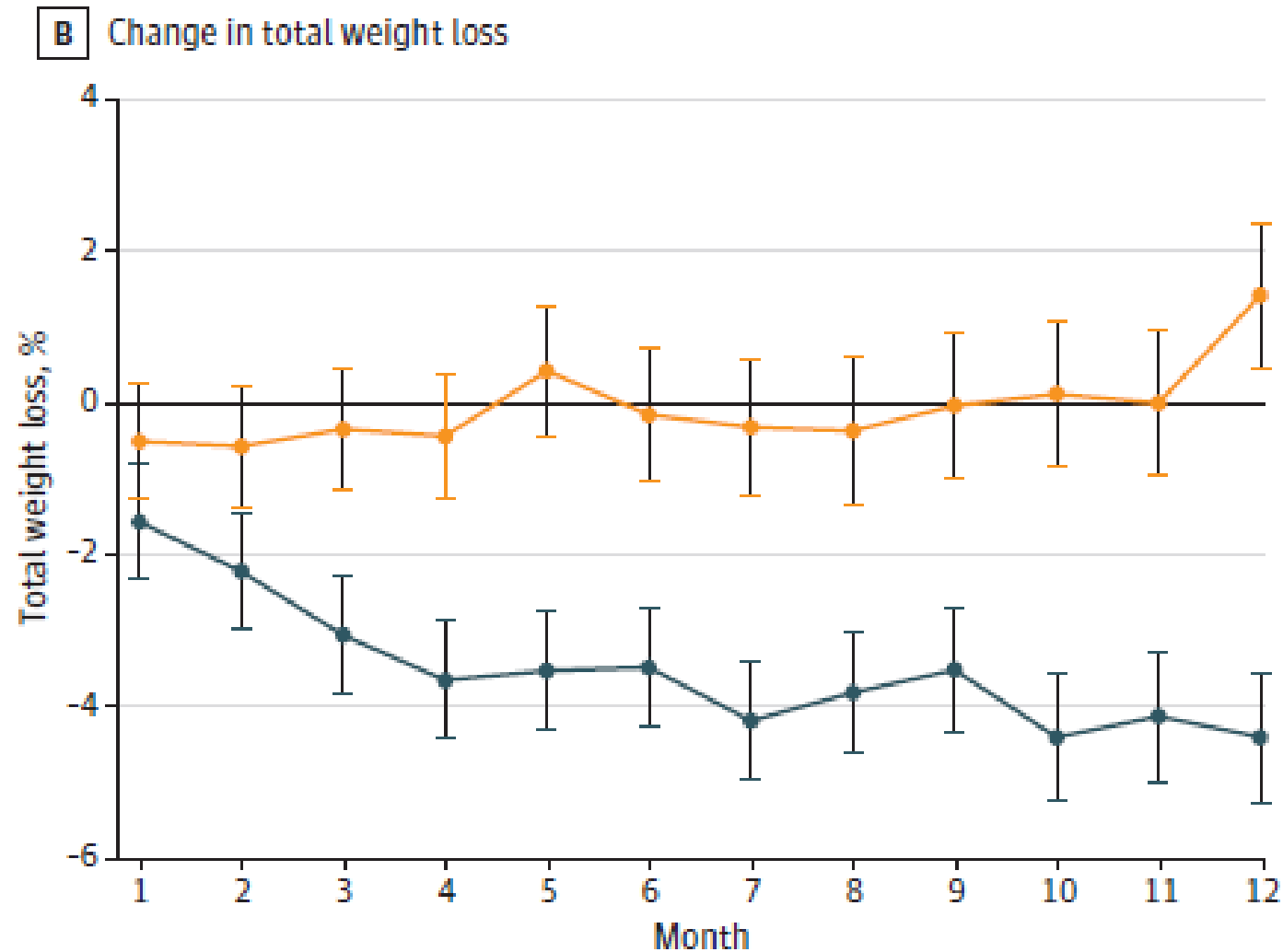
or

10% to 20% for sleeve gastrectomy (n=28)

| Characteristic                | Mean (SD)            |                  |
|-------------------------------|----------------------|------------------|
|                               | Baseline             |                  |
|                               | Liraglutide (n = 24) | Placebo (n = 24) |
| Age, y                        | 48.7 (10.5)          | 43.6 (11.4)      |
| Sex, No. (%)                  |                      |                  |
| Female                        | 22 (92)              | 20 (83)          |
| Male                          | 2 (8)                | 4 (17)           |
| Treatment for type 2 diabetes | 0                    | 0                |
| MBS procedure, No. (%)        |                      |                  |
| AGB                           | 11                   | 10               |
| SG                            | 13                   | 14               |
| Time since MBS, y             | 1.7 (0.5)            | 1.5 (0.5)        |
| BMI at date of MBS            | 48.0 (8.4)           | 45.6 (46.8)      |
| BMI at date of commencement   | 39.2 (5.2)           | 36.9 (4.3)       |
| TBWL date of commencement, %  | 16.9 (6.8)           | 17.3 (7.1)       |

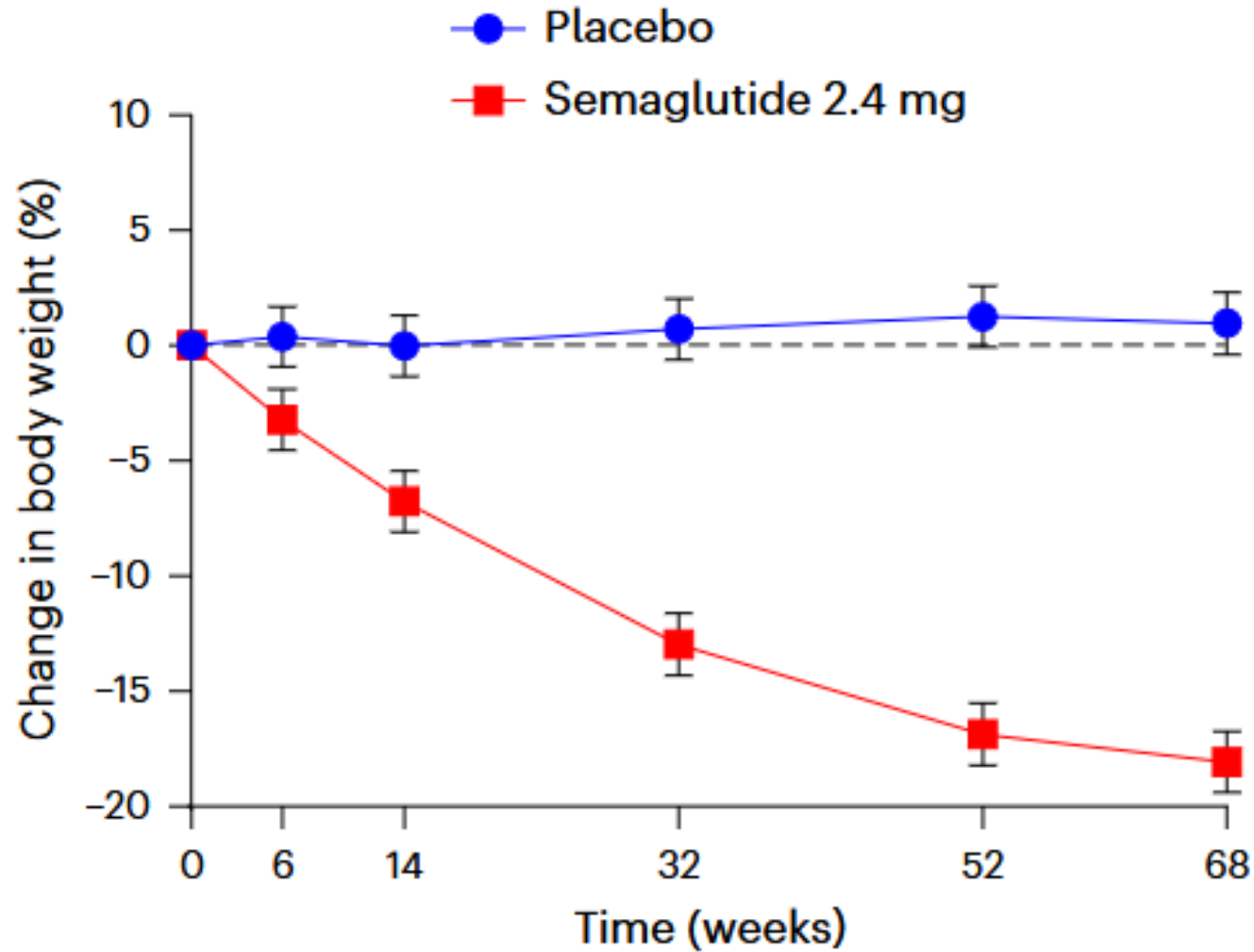


# Liraglutide 3.0mg for suboptimal response after surgery





# Semaglutide 2.4mg for suboptimal response after surgery





# Semaglutide 2.4mg for suboptimal response after surgery

| Outcome (ITT, n=63)                       | Placebo |             | Semaglutide 2.4mg |             | Adjusted mean difference <sup>a</sup> | P <sup>a</sup> |
|-------------------------------------------|---------|-------------|-------------------|-------------|---------------------------------------|----------------|
|                                           | No.     | Mean (s.e.) | No.               | Mean (s.e.) |                                       |                |
| Total body weight (kg)                    | 29      | 0.7 (2.5)   | 34                | -21.1 (2.6) | -21.7 (-26.6 to -16.8)                | <0.001         |
| BMI                                       | 28      | 0.03 (1.0)  | 33                | -7.9 (1.0)  | -7.9 (-9.8 to -6.0)                   | <0.001         |
| Fat mass (kg)                             | 28      | 0.9 (2.3)   | 33                | -15.8 (2.3) | -16.6 (-20.8 to -12.5)                | <0.001         |
| Lean soft tissue mass (%)                 | 28      | -0.8 (1.2)  | 33                | 5.5 (1.2)   | 6.3 (4.1 to 8.5)                      | <0.001         |
| Lean soft tissue mass (kg)                | 28      | -0.2 (1.2)  | 33                | -5.5 (1.2)  | -5.3 (-7.4 to -3.1)                   | <0.001         |
| HbA1c (mmol mol <sup>-1</sup> )           | 28      | 1.7 (0.8)   | 33                | -3.6 (0.8)  | -5.3 (-6.6 to -4.0)                   | <0.001         |
| HR (bpm)                                  | 28      | -6.6 (2.4)  | 34                | -4.9 (2.7)  | 1.8 (-3.0 to 6.5)                     | 0.460          |
| SBP (mmHg)                                | 28      | 2.0 (3.1)   | 34                | -3.9 (3.3)  | -5.9 (-12.0 to 0.2)                   | 0.059          |
| DBP (mmHg)                                | 28      | 5.85 (2.3)  | 34                | 1.64 (2.5)  | -4.2 (-8.7 to 0.3)                    | 0.068          |
| Total cholesterol (mmol l <sup>-1</sup> ) | 28      | 0.2 (0.2)   | 33                | -0.3 (0.2)  | -0.5 (-0.9 to -0.1)                   | 0.014          |
| Triglycerides (mmol l <sup>-1</sup> )     | 28      | 0.2 (0.1)   | 33                | -0.3 (0.1)  | -0.5 (-0.8 to -0.23)                  | <0.001         |
| HsCRP mg l <sup>-1</sup>                  | 28      | 1.4 (1.5)   | 31                | 0.4 (1.6)   | -1.0 (-3.9 to 2.0)                    | 0.517          |
| IWQOL-Lite                                |         |             |                   |             |                                       |                |
| Total                                     | 27      | 9.3 (3.9)   | 33                | 23.7 (4.1)  | 14.3 (6.5 to 22.1)                    | <0.001         |
| Physical function                         | 27      | 7.3 (4.0)   | 34                | 23.0 (4.2)  | 15.7 (7.7 to 23.7)                    | <0.001         |
| Self-esteem                               | 27      | 17.3 (5.7)  | 34                | 34.2 (5.9)  | 16.9 (5.5 to 28.3)                    | 0.004          |
| Sex life                                  | 27      | 5.2 (6.4)   | 31                | 17.8 (6.5)  | 12.7 (-0.7 to 26.0)                   | 0.062          |
| Public distress                           | 27      | 11.1 (5.6)  | 34                | 20.4 (5.8)  | 9.3 (-1.9 to 20.4)                    | 0.103          |
| Work                                      | 27      | 8.4 (5.0)   | 32                | 18.5 (5.1)  | 10.1 (0.1 to 20.1)                    | 0.048          |



# Thoughts

Pharmacotherapy works after bariatric surgery

GLP-1 treatments work despite elevations in endogenous GLP-1 levels

Some hints the effect may be synergistic

Heterogeneity of response

No safety signals

Lack of data on hard outcomes

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