



Can OMMs rescue outcomes after MBS?

Alex Miras

Professor of Endocrinology, Ulster University

Visiting Professor, Imperial College London



Conflict of Interests

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



Baseline characteristics

	Total cohort	
	Placebo (n=27)	Liraglutide (n=53)
Sex		
Men	13 (48%)	20 (38%)
Women	14 (52%)	33 (62%)
Median age in years (IQR)	57.0 (52.0–64.0)	55.0 (50.0–61.0)
Diabetes duration (years)	19.6 (8.0)	16.4 (7.0)
Time since surgery (years)	3.8 (2.4)	3.8 (2.0)
HbA _{1c} (mmol/mol)	57.7 (8.2)	63.3 (15.2)
HbA _{1c} (%)	7.4 (0.75)	7.9 (1.39)
Fasting glucose (mmol/L)	7.5 (2.9)	8.2 (3.2)
Fasting insulin (mIU/L)	7.3 (1.7)	9.2 (9.0)
HOMA2 (% insulin sensitivity)	96.1 (50.2)	124.1 (81.7)
Bodyweight (kg)	103.5 (27.0)	100.7 (20.7)
BMI (kg/m ²)	37.0 (7.7)	36.1 (7.8)
Preoperative bodyweight (kg)	130.8 (29.7)	127.8 (25.7)
Nadir bodyweight after surgery (kg)	92.8 (19.6)	89.0 (18.7)
Percentage weight change after surgery (at screening)	–20.3% (12.9)	–20.9% (10.0)
Weight regain from nadir to screening (kg)	10.8 (12.6)	11.5 (8.8)
King's Obesity Staging Criteria score	10.4 (3.9)	11.2 (3.9)

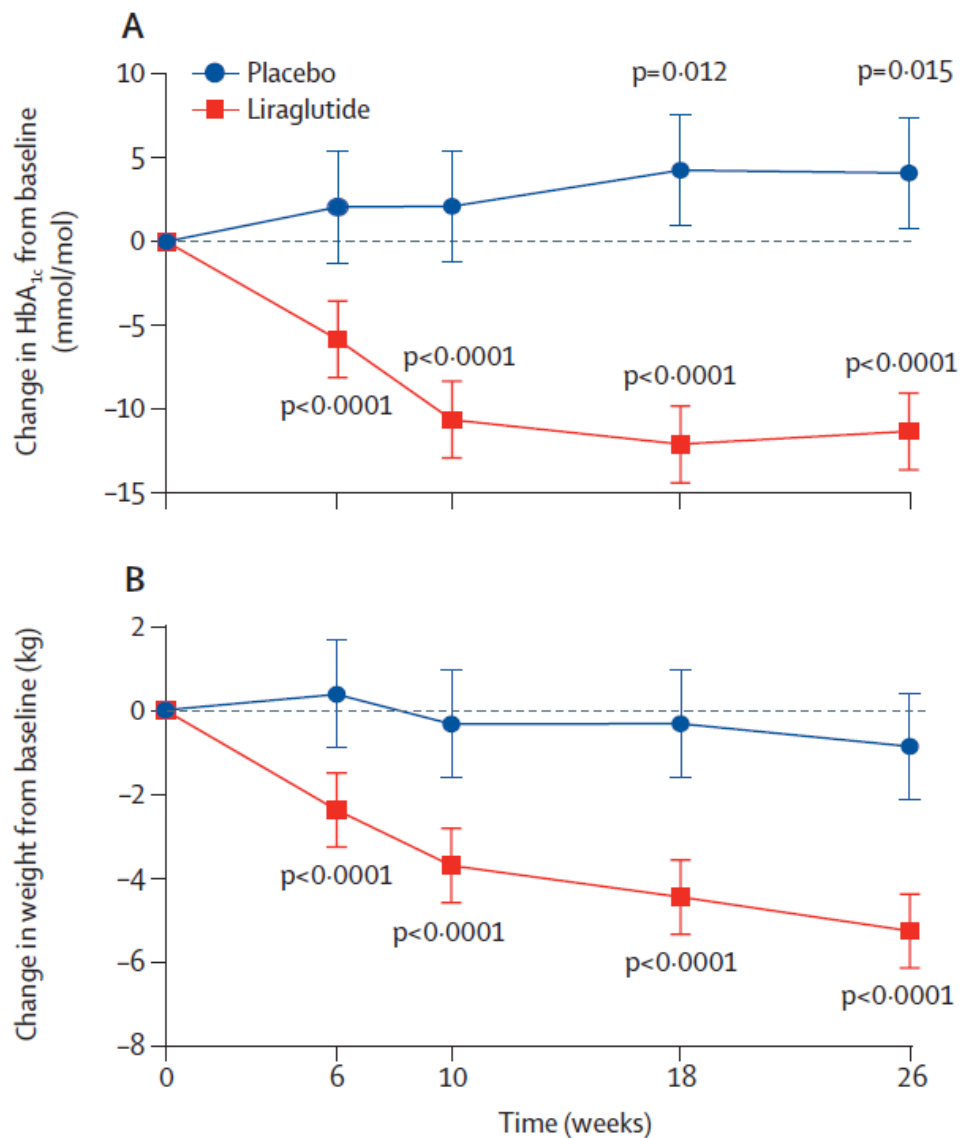
Sleeve: 19/80

RYGB: 61/80

Miras et al Lancet D&E 2019



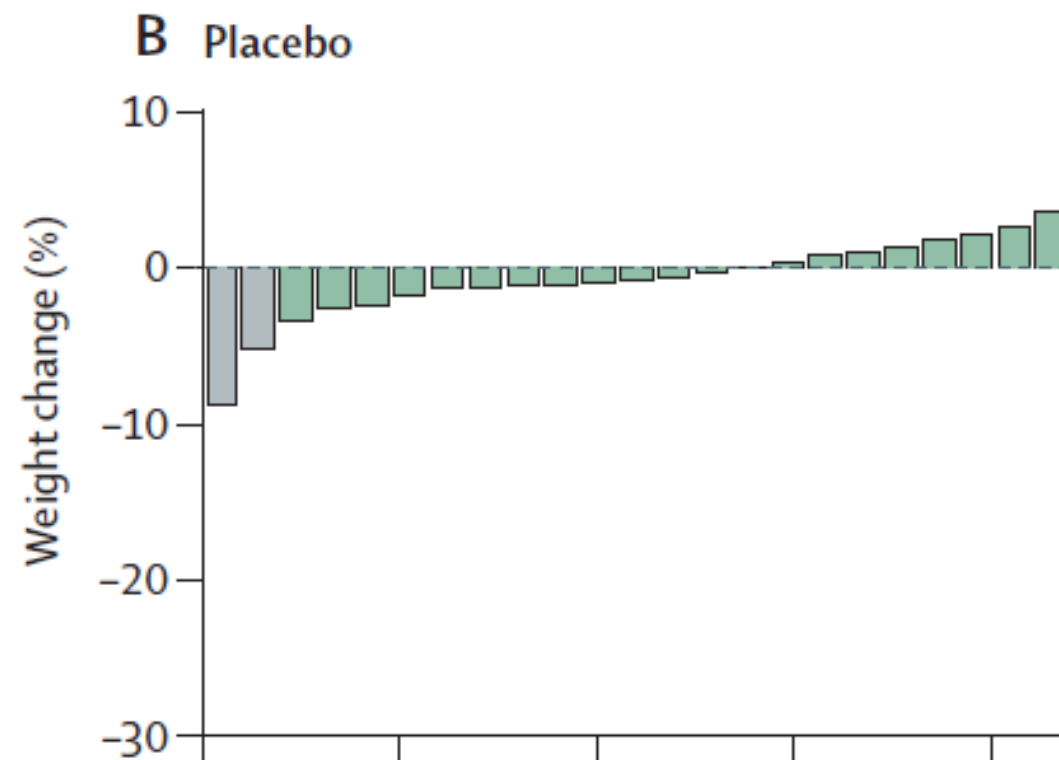
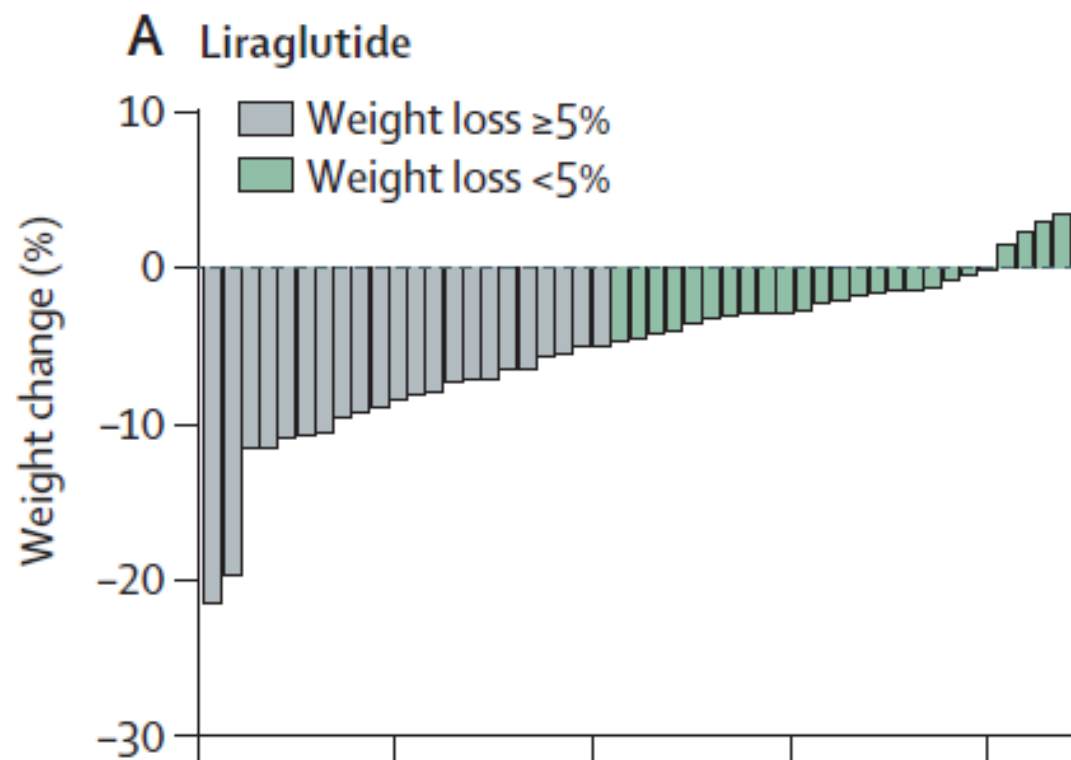
HbA1c and weight



Miras et al Lancet D&E 2019



Variation in response





Differences VSG vs RYGB

	Baseline value	Treatment (liraglutide vs placebo)	Type of surgery (VSG vs RYGB)
HbA _{1c} (mmol/mol)	0.70 (0.48 to 0.91; p<0.0001)	-13.3 (-19.7 to -7.0; p=0.0001)	-4.67 (-11.4 to 2.0; p=0.17)
HbA _{1c} (%)	0.06 (0.04 to 0.08; p<0.0001)	-1.22 (-1.80 to -0.64; p=0.0001)	-0.43 (-1.04 to 0.18; p=0.17)
Bodyweight (kg)	0.95 (0.89 to 1.00; p<0.0001)	-4.23 (-6.81 to -1.64; p=0.0017)	-2.04 (-5.00 to 0.93; p=0.18)
Systolic blood pressure (mm Hg)	0.65 (0.47 to 0.84; p<0.0001)	2.14 (-4.52 to 8.80; p=0.52)	-3.99 (-10.80 to 2.81; p=0.25)
Diastolic blood pressure (mm Hg)	0.51 (0.33 to 0.70; p<0.0001)	2.88 (-1.67 to 7.44; p=0.21)	-1.41 (-6.36 to 3.55; p=0.57)
Total cholesterol (mmol/L)	0.58 (0.42 to 0.75; p<0.0001)	-0.03 (-0.41 to 0.35; p=0.88)	-0.36 (-0.77 to 0.05; p=0.087)
LDL cholesterol (mmol/L)	0.73 (0.55 to 0.92; p<0.0001)	0.04 (-0.29 to 0.37; p=0.82)	-0.23 (-0.58 to 0.13; p=0.21)
HDL cholesterol (mmol/L)	0.89 (0.74 to 1.03; p<0.0001)	0.03 (-0.08 to 0.15; p=0.54)	-0.03 (-0.15 to 0.09; p=0.62)
Triglycerides (mmol/L)	0.18 (0.10 to 0.25; p<0.0001)	-0.26 (-0.56 to 0.04; p=0.089)	-0.29 (-0.61 to 0.04; p=0.081)
King's Obesity Staging Criteria score	0.84 (0.70 to 0.98; p<0.0001)	0.23 (-0.87 to 1.32; p=0.68)	-0.66 (-1.86 to 0.53; p=0.27)



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

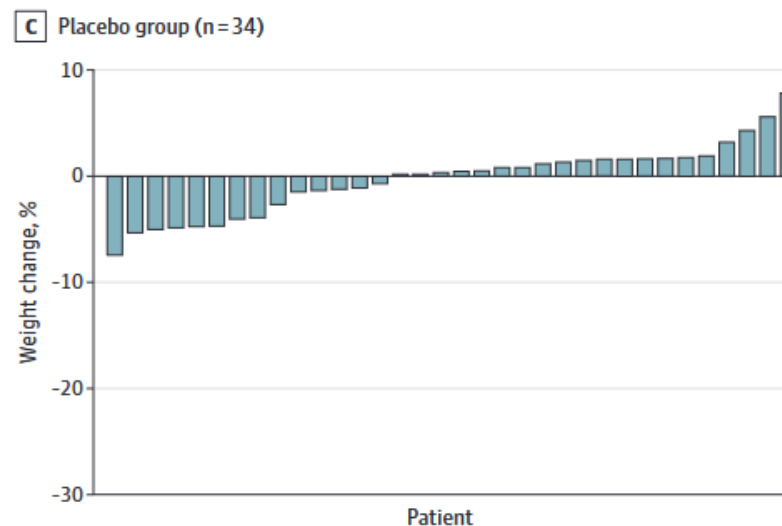
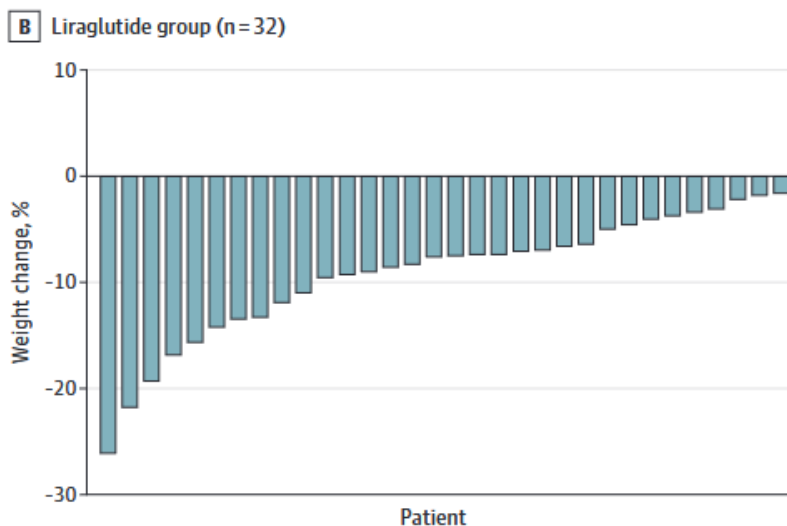
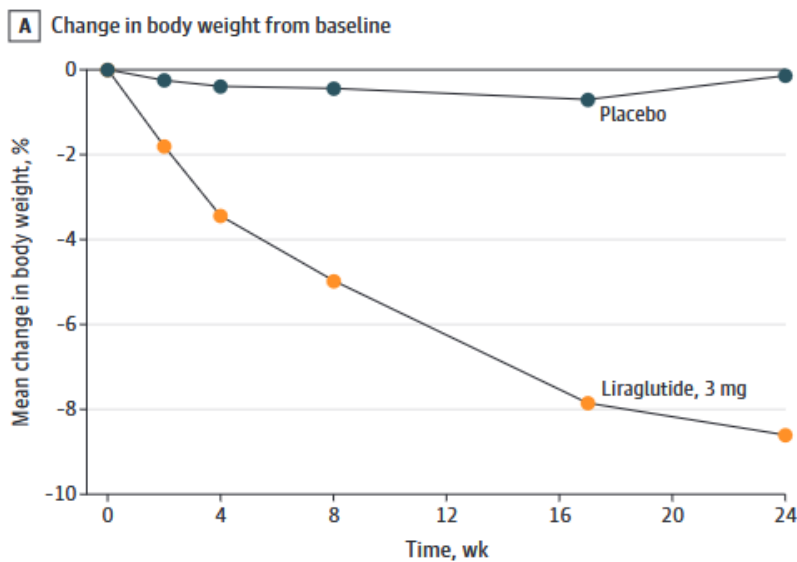


Liraglutide 3.0mg for suboptimal response after surgery

Characteristic	Mean (SD)		
	Placebo (n = 35)	Liraglutide, 3.0 mg (n = 35)	Overall trial (N = 70)
Age, y	48.4 (10.6)	46.7 (10.8)	47.6 (10.7)
Sex, No. (%)			
Female	26 (74)	26 (74)	52 (74)
Male	9 (26)	9 (26)	18 (26)
Diabetes status, No. (%)			
Type 2 diabetes	4 (11)	5 (14)	9 (13)
No diabetes	31 (89)	30 (86)	61 (87)
Metabolic surgical procedure, No. (%)			
RYGB	3 (9)	2 (6)	5 (7)
SG	32 (91)	33 (94)	65 (93)
Duration since surgery, mo	49.1 (33.7)	55.1 (33.3)	52.1 (33.4)
Percentage weight loss since surgery	7.4 (7.4)	7.0 (7.8)	7.2 (7.6)
Body mass index ^a	44.6 (8.3)	41.6 (6.9)	43 (7.5)



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)

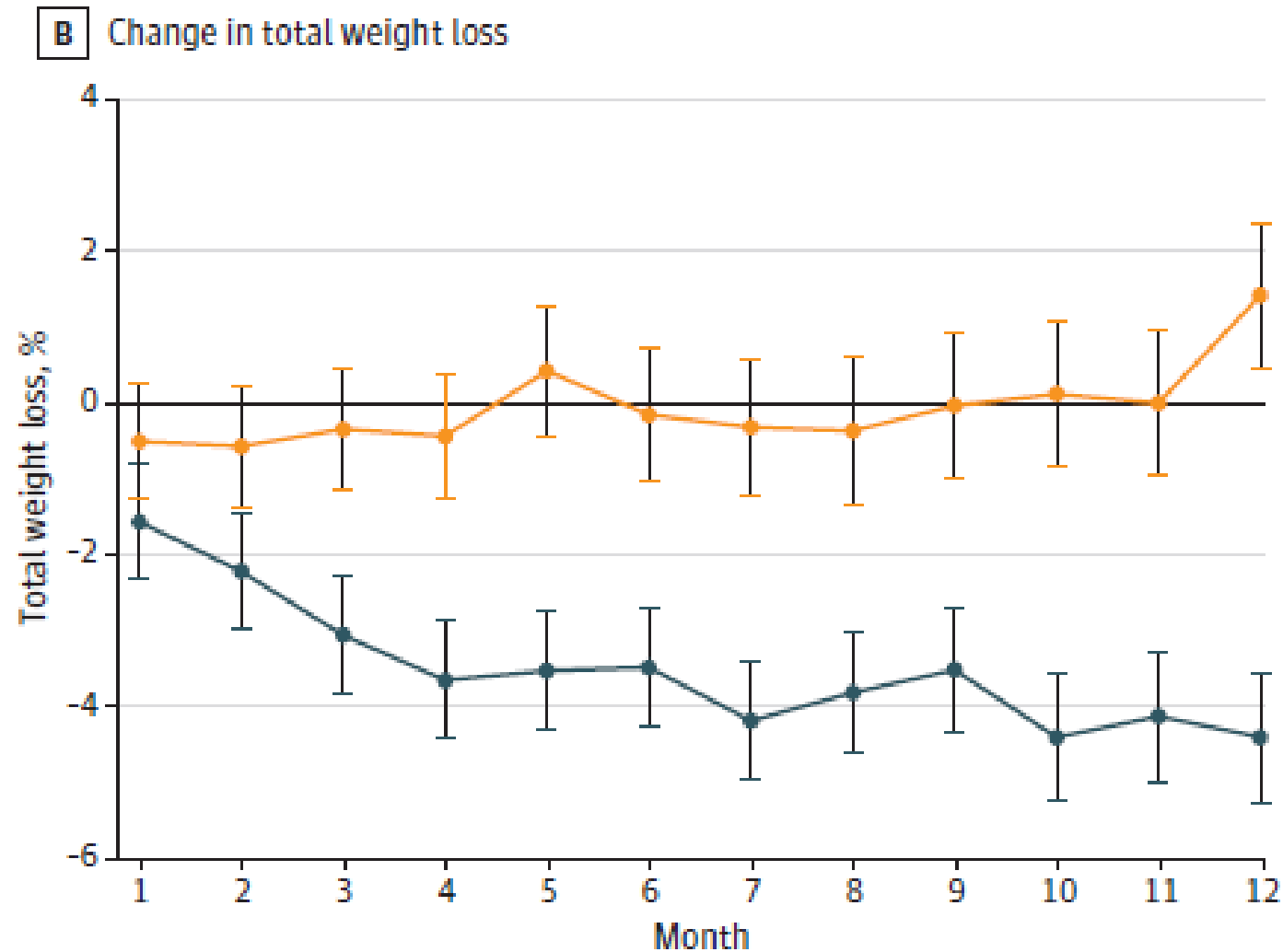
or

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)



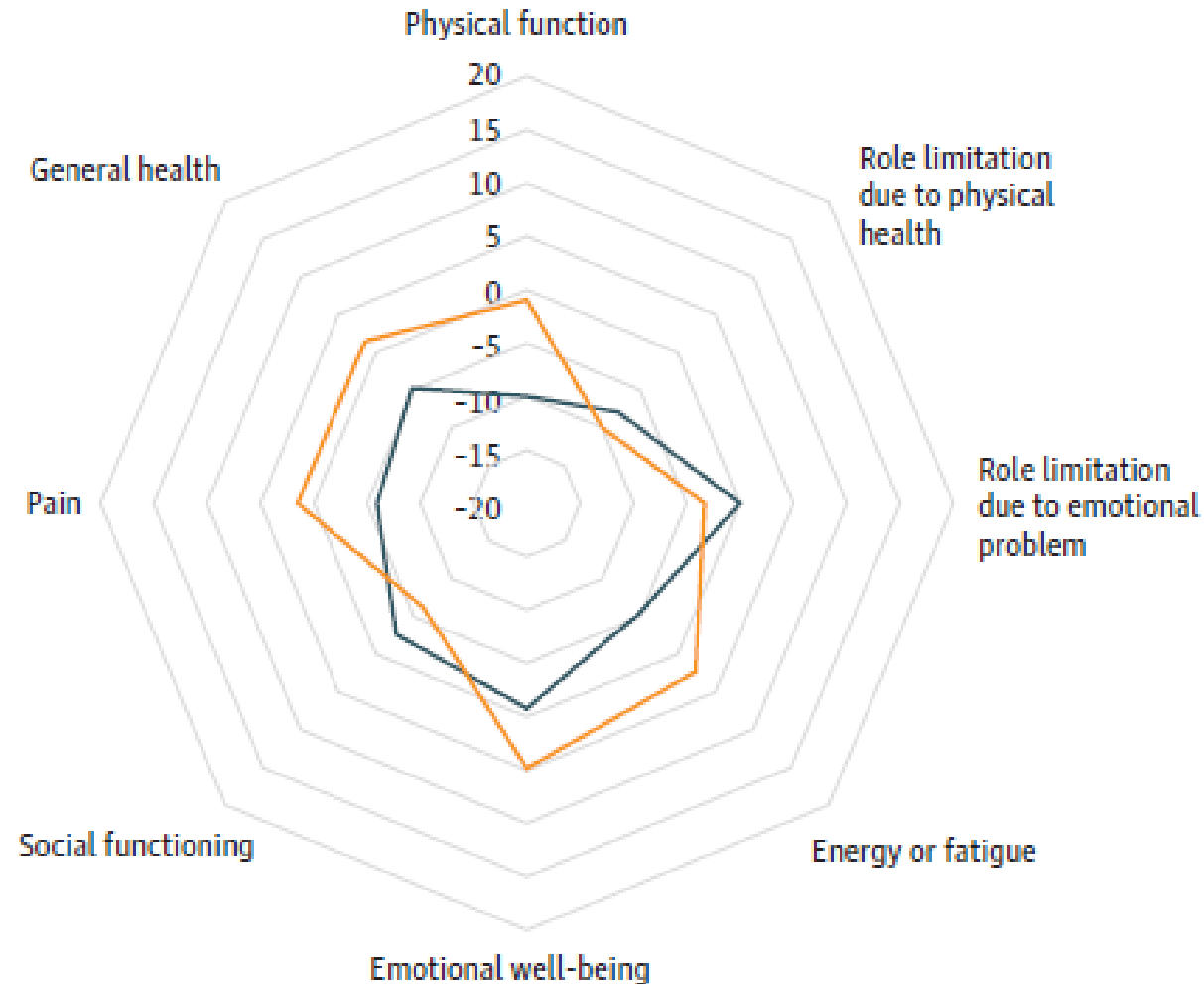
Liraglutide 3.0mg for suboptimal response after surgery





Liraglutide 3.0mg for suboptimal response after surgery

C Difference between pretreatment and posttreatment





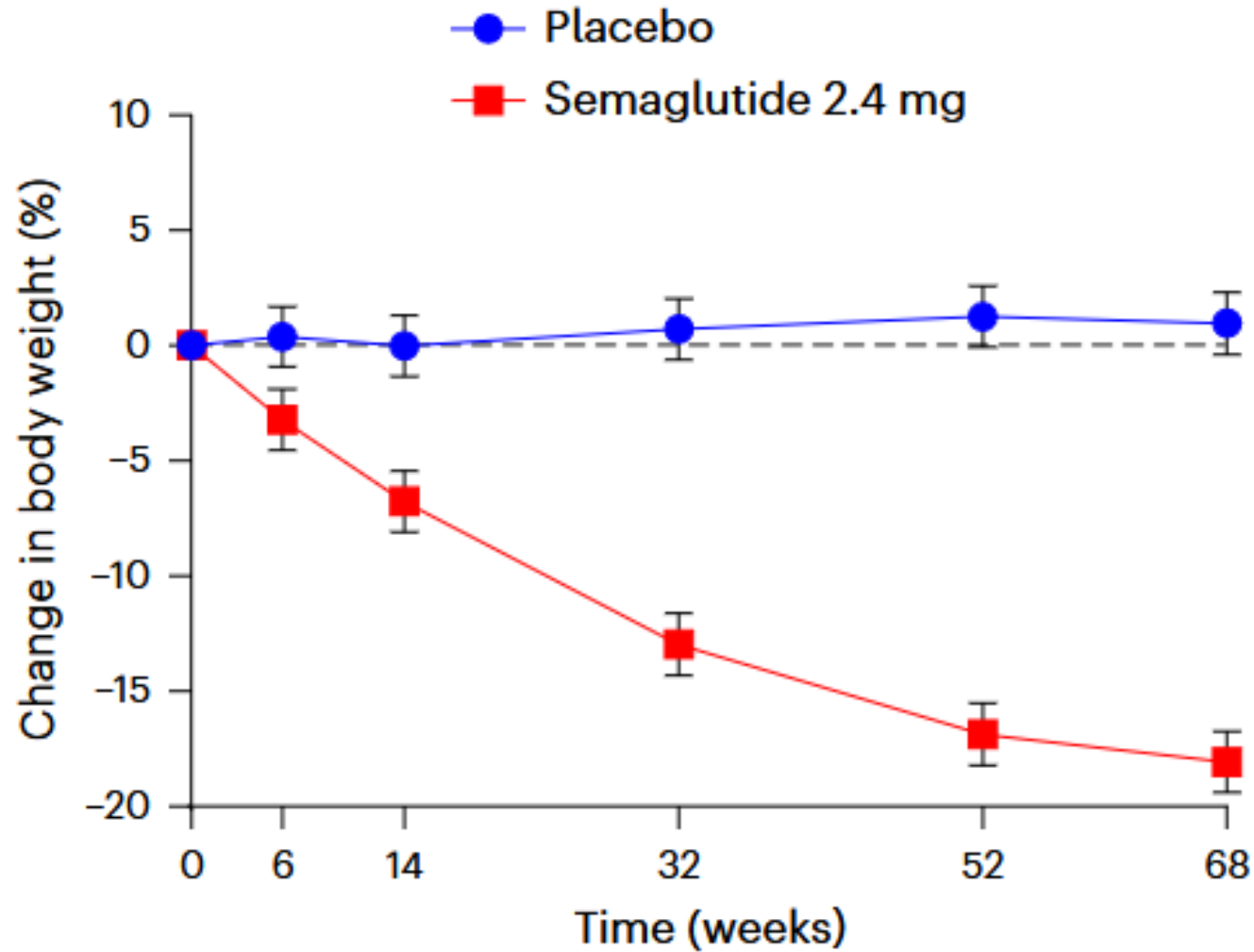
Semaglutide 2.4mg for suboptimal response after surgery

Mean (s.d.)/n (%)	Overall trial (n=70)
Age (years)	47.3 (10.3)
Sex, n (%)	
Female	58 (82.9)
Male	12 (17.1)
Weight (kg)	115 (12.6)
BMI	41.5 (6.5)
BMI, kg m ⁻² , n (%)	
<35	7 (10)
≥35 to <40	29 (41.4)
≥40	34 (48.6)
Weight on DOS (kg)	124.5 (21.5)
BMI on DOS (kg m ⁻²)	44.9 (6.4)
Post-surgery maximum %WL	23.1 (9.1)
Nadir BMI (kg m ⁻²)	34.5 (5.8)
%WL since DOS	7.5 (7.6)
Post-surgery outcome	
Weight regain, n (%)	39 (55.7)
Suboptimal initial weight loss, n (%)	31 (44.3)
Ethnicity, n (%)	
Asian	2 (2.9)
Black	16 (22.9)
White	47 (67.1)
Mixed/other	5 (7.1)
Surgical procedure n (%)	
SG	55 (78.6)
GB	15 (21.4)
Time since surgery (months)	83.9 (43.1)
Diabetes status, n (%)	
T2D	7 (10.0)
Normoglycemia/pre-diabetes	63 (90.0)
HbA1c (mmol mol ⁻¹)	38.0 (5.0)
Change in meal-stimulated GLP-1 (pg ml ⁻¹)	7.6 (3.0, 29.5)

Stanley et al, Nature Medicine, 2026



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 ^a	P ^a
	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 ⁻¹)	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 ⁻¹)	28	0.2 (0.2)	33	-0.3 (0.2)	-0.5 (-0.9 to -0.1)	0.014
Triglycerides (mmol l ⁻¹)	28	0.2 (0.1)	33	-0.3 (0.1)	-0.5 (-0.8 to -0.23)	<0.001
HsCRP mg l ⁻¹	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

Acknowledgements



a.miras@ulster.ac.uk

Ulster University

Louise Dubras
Victor Gault
Peter Flatt
Mark Tully
Ruth Price
Patrick Swan
Grace Curry
Muzamil Hussain

Western Trust

Neil Black
Lesley Hamilton
Tracy Donaghy
Frank McCarroll
Aaron Peace

Imperial College London

Steve Bloom
Tony Goldstone
Anna Kamocka
Vasha Kaur
Shahd Alabdulkader
Brett Johnson
Suhaniya Samarasinghe
Alhanouf Al-Alsheikh
Migena Luli
Julian Teare
Tricia Tan
Harvinder Chahal
Samantha Scholtz
Ahmed Ahmed
Sanjay Purkayastha
Krishna Moorthy
Sherif Hakky
Christos Tsironis

University College Dublin

Carel W le Roux
Neil Docherty
Werd Al-Najim

University Hospitals Coventry / University of Warwick

Harpal Randeva
Vinod Menon
Bianca Leca

King's College London

George Dimitriadis
Spyros Panagiotopoulos
Ameet Patel
Francesco Rubino
Royce Vincent

King Saud University, Saudi Arabia

Ghalia Abdeen
Madhawi Aldhwayan

North Bristol NHS Trust

Dimitris Pournaras

University College London/ Whittington

Chetan Parmar

University of Wurzburg

Florian Seyfried