

Mechanisms of action of obesity surgery

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Disclosures

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GI dynamics

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Rhythm

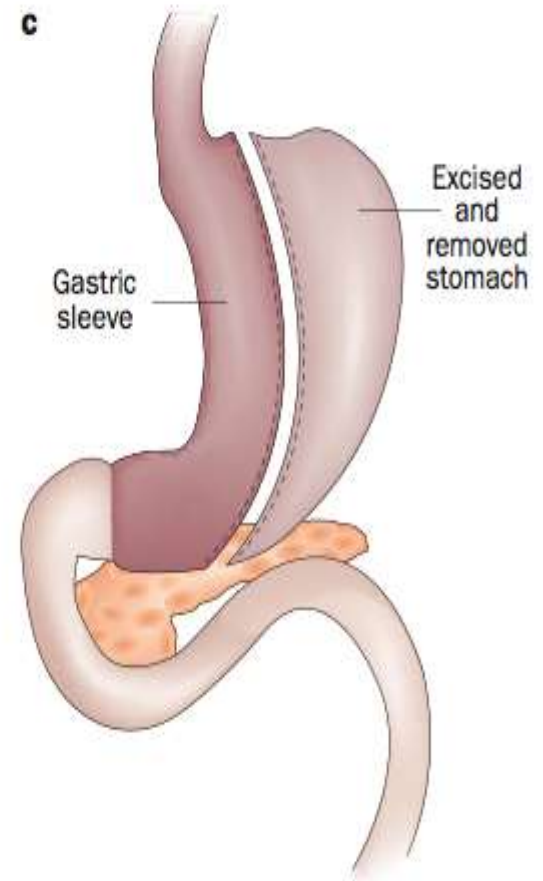
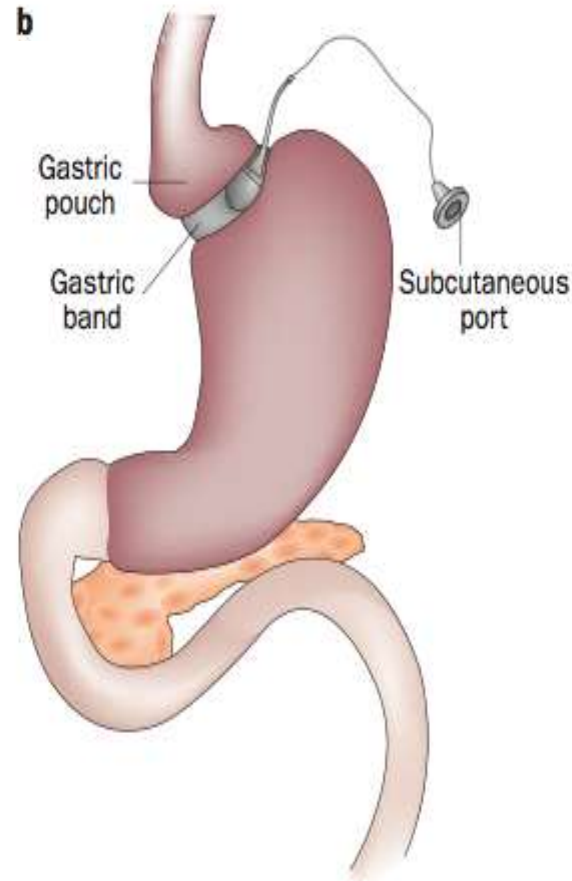
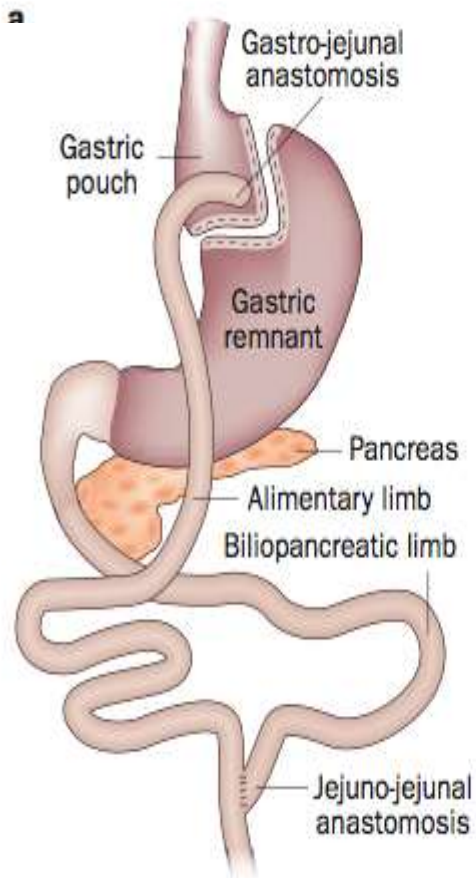
Eli Lilly

Currax

BeyondBMI

Screen Health

Obesity Surgery

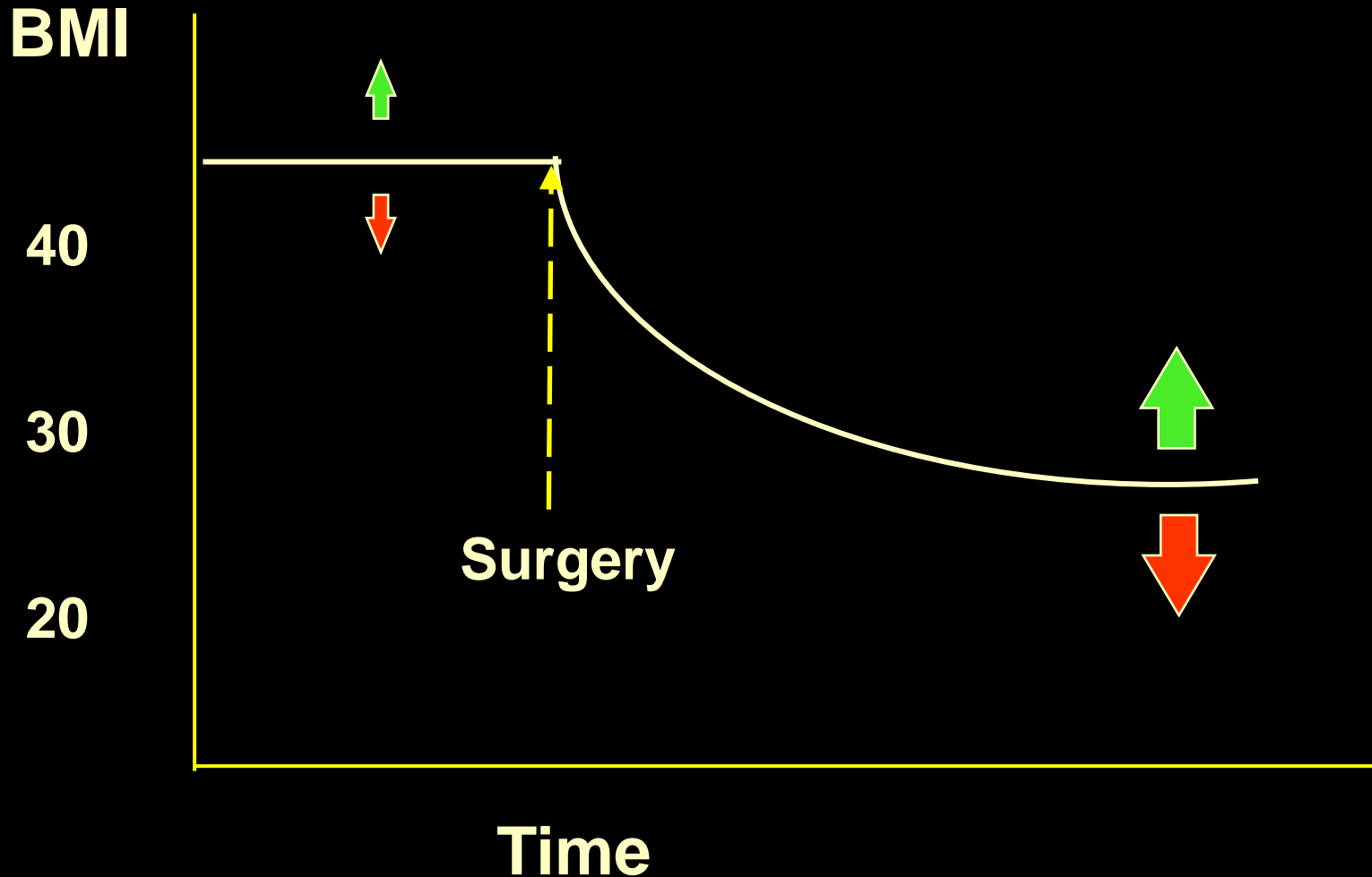


**Gastric bypass
(RYGB)**

**Gastric banding
(BAND)**

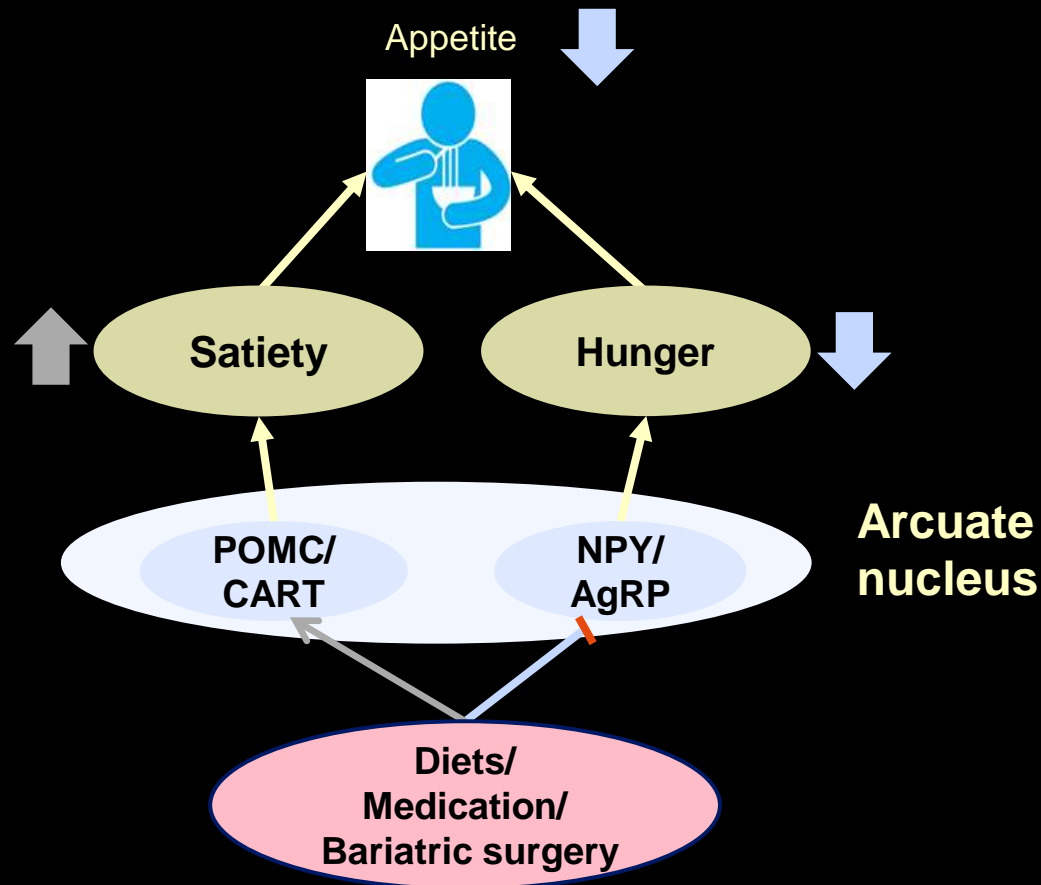
**Sleeve Gastrectomy
(VSG)**

Obesity surgery changes body weight set point



Successful obesity treatments increase satiety and reduce hunger

Via neurons in the hypothalamus



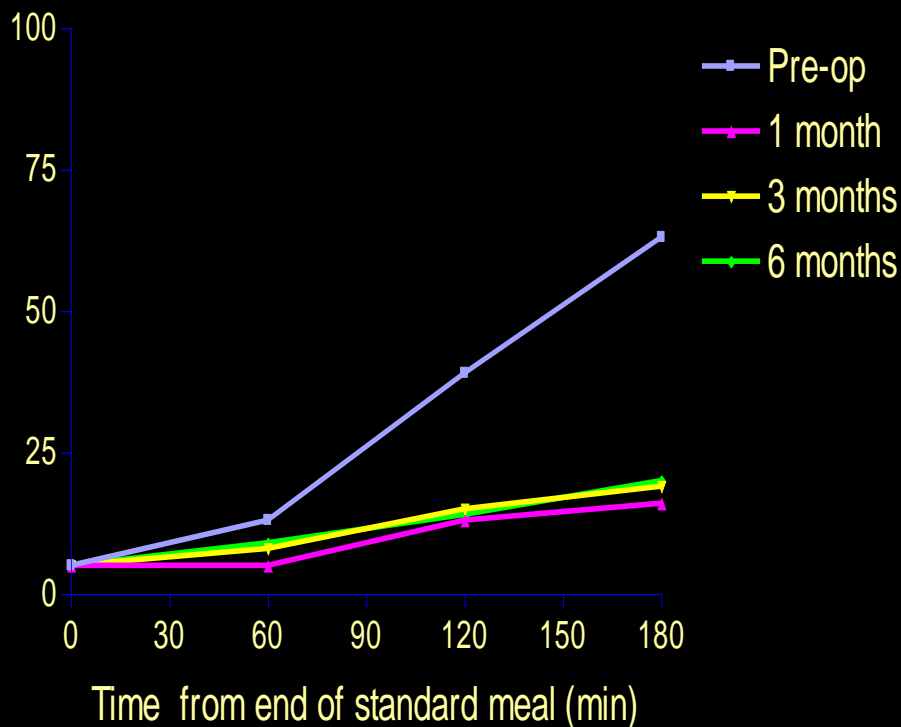
Calorie malabsorption (humans)

- Bypass: Minimal Fat malabsorption
No CHO malabsorption
- Band: ?
- Sleeve: ?

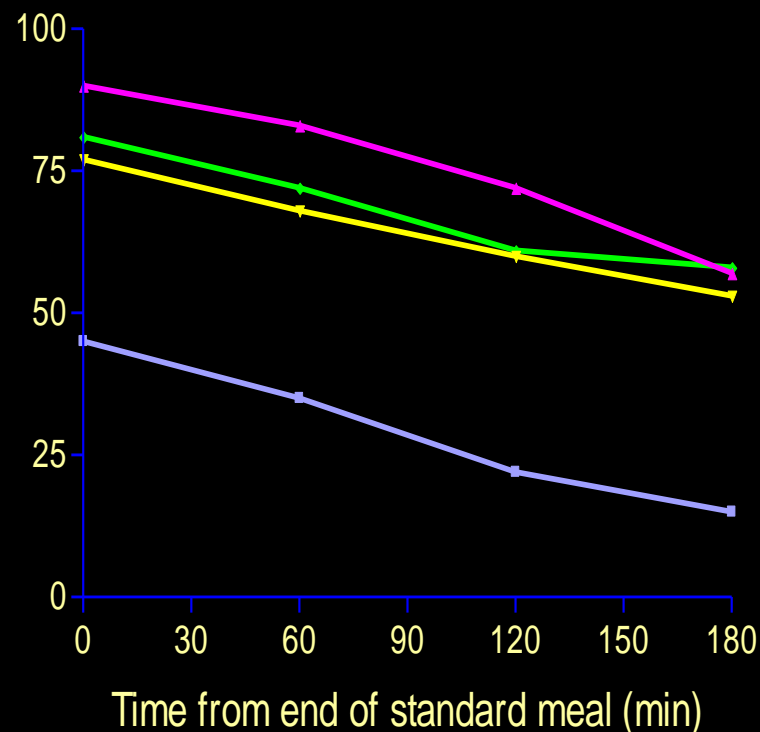
Hunger, fullness and food intake

Appetite ratings after RYGB

VAS - How hungry are you?



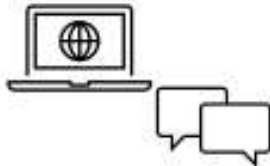
VAS - How full are you?



Study Protocol @ Ulster

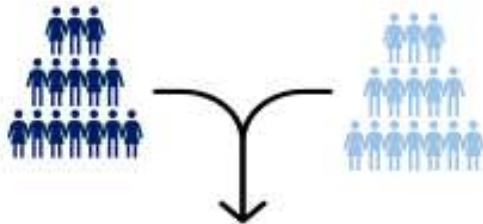
Patients: >18 yrs,
eligible for gastric
bypass surgery

Controls: >18 yrs,
Weight stable

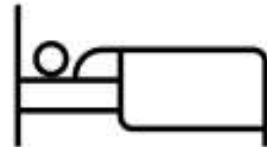


Patients
n = 31

Controls
n = 32

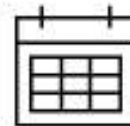


Human Intervention Studies Unit,
Ulster University
(Coleraine Campus)

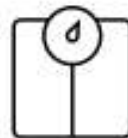


Fully residential
~ 36 hours

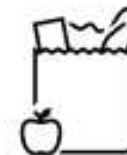
Four timepoints:
Pre-surgery (-1-month),
3-, 12-, 24- and 60
months post-surgery



Primary outcome: Energy
intake and food selection

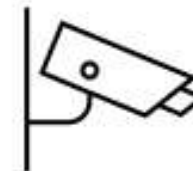


Secondary measures:
Eating behaviour, body
composition, metabolic rate,
food preferences, gut
hormone response, energy
expenditure and bone density



**Ad lib access to 54
foods**

**Covert
weighing of food**

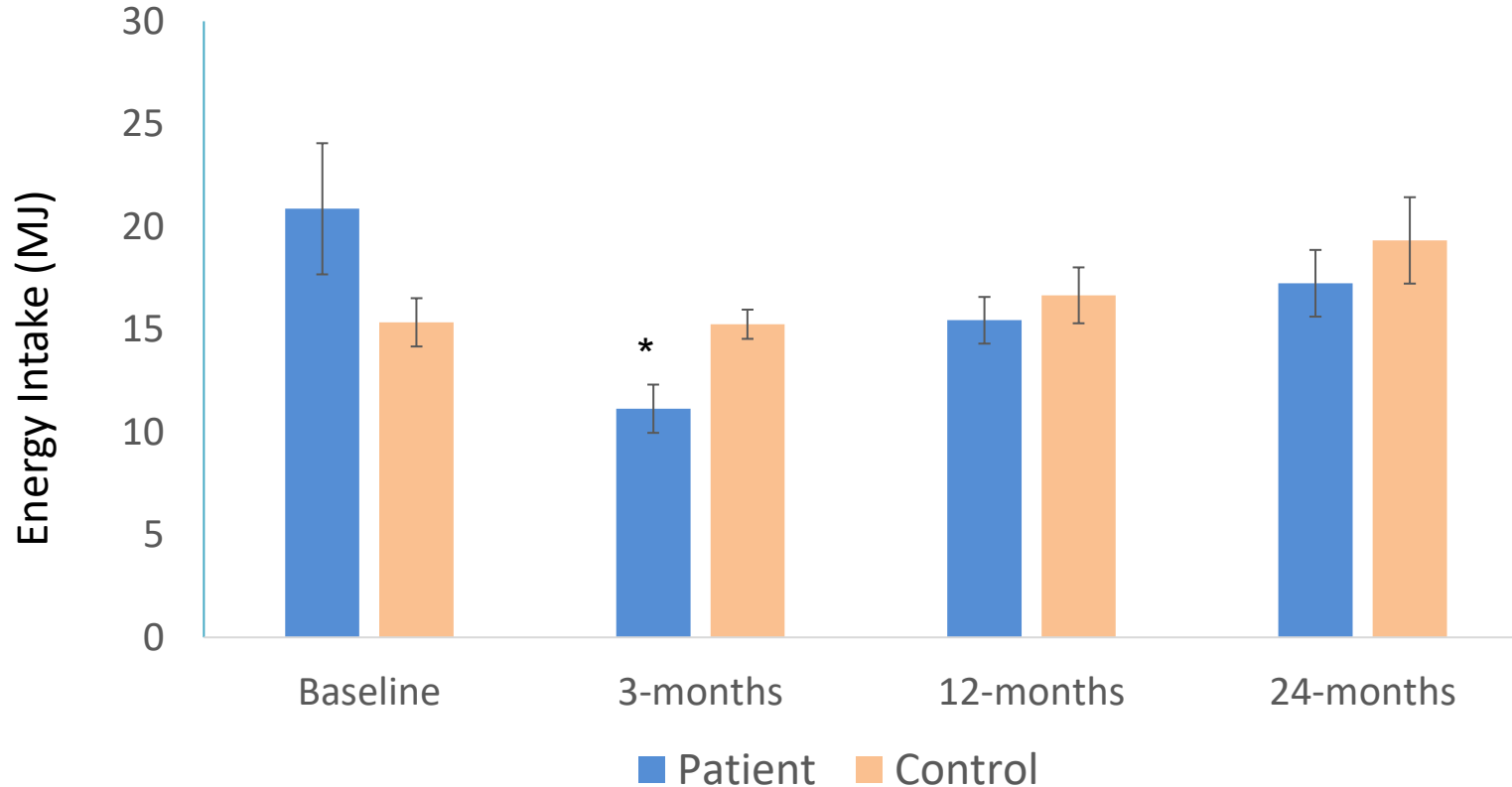


**Validation of food
intake and eating
behaviours**

**Body composition
using DXA**



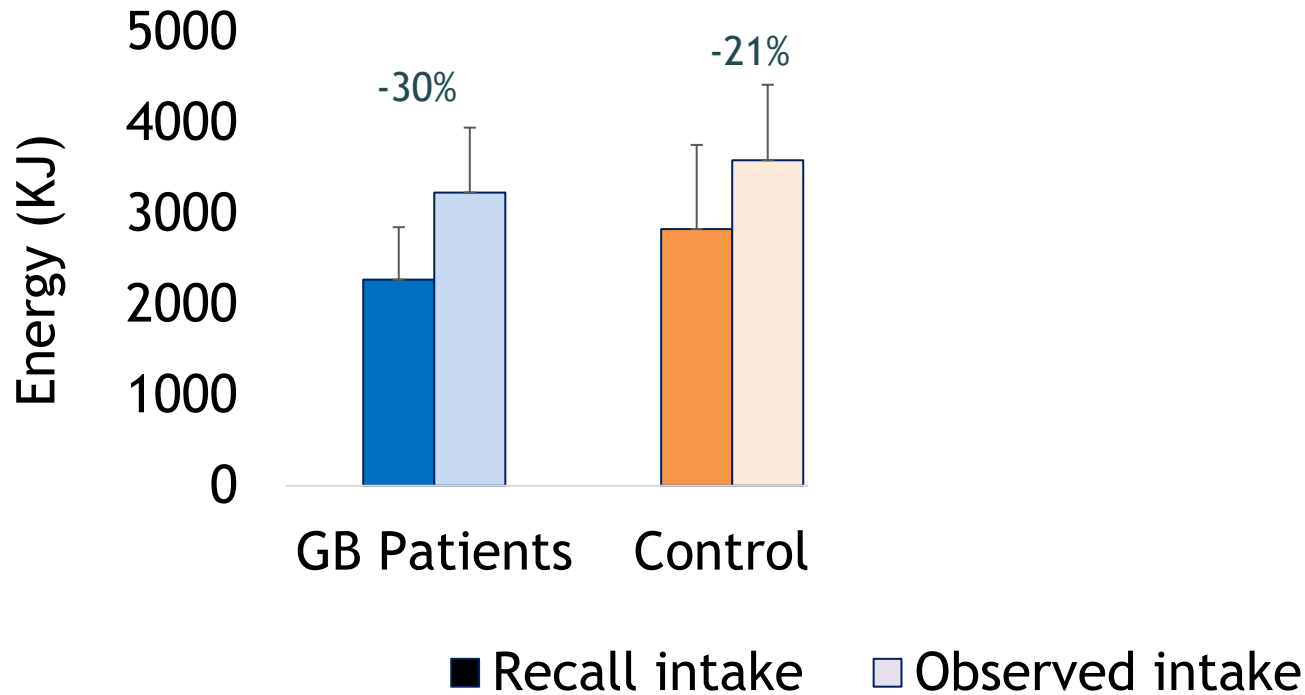
Total energy intake



* Difference from baseline
 $n = 16$ patients; $n = 16$ controls; 2-way ANOVA $p = 0.008$

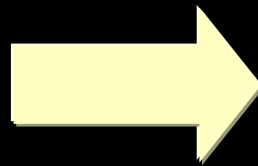
Livingstone and Price et al, J Nutrition, 2022

Energy Intake misreporting



Food preferences after RYGB/VSG

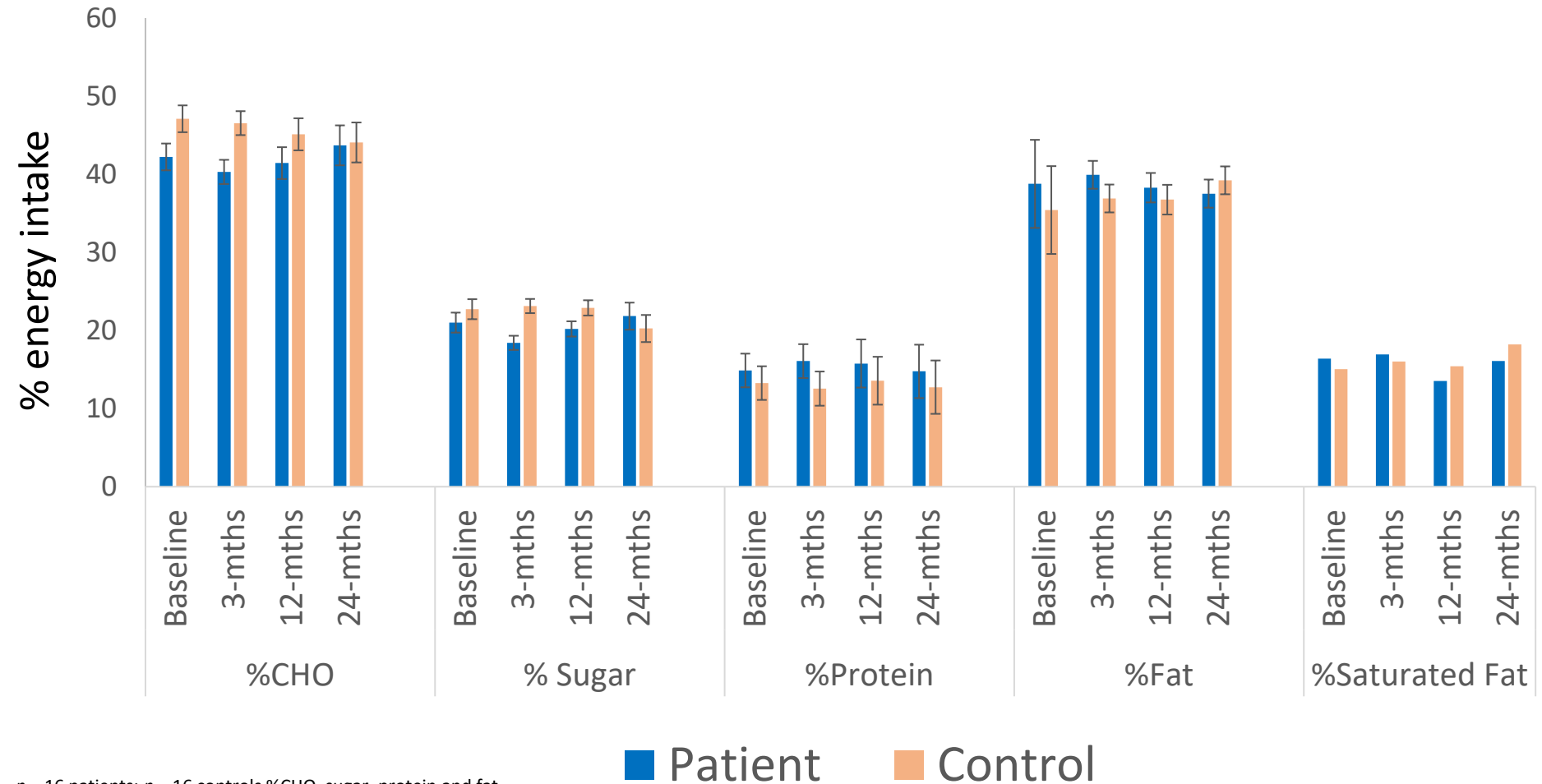
Pre-operative



Post-operative



% macronutrient contribution to total energy intake

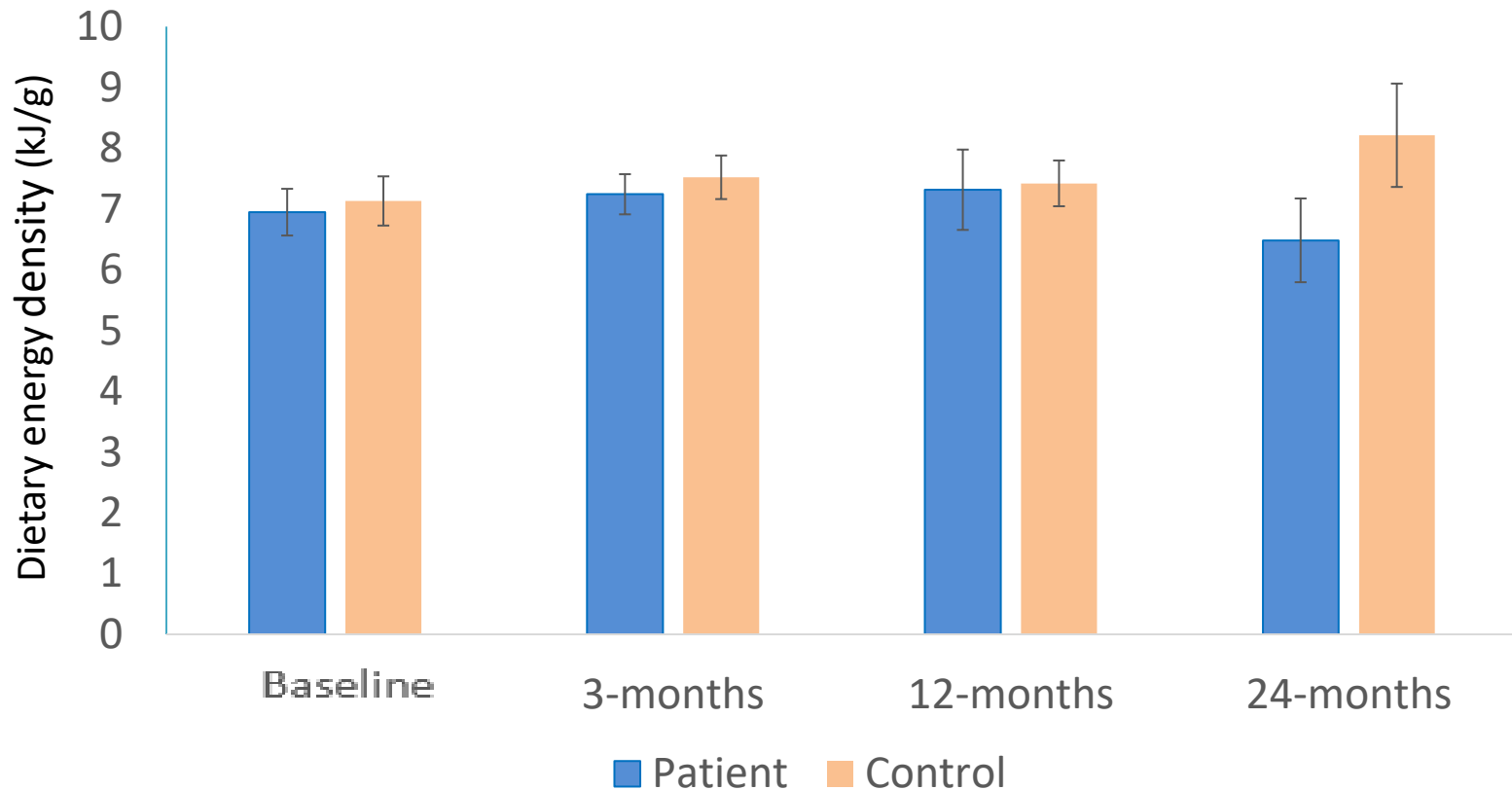


■ Patient ■ Control

Livingstone and Price et al, J Nutrition, 2022

n = 16 patients; *n* = 16 controls %CHO, sugar, protein and fat
n = 18 patients; *n* = 16 controls %saturated fat
 2-way ANOVA *p* > 0.05

Dietary energy density



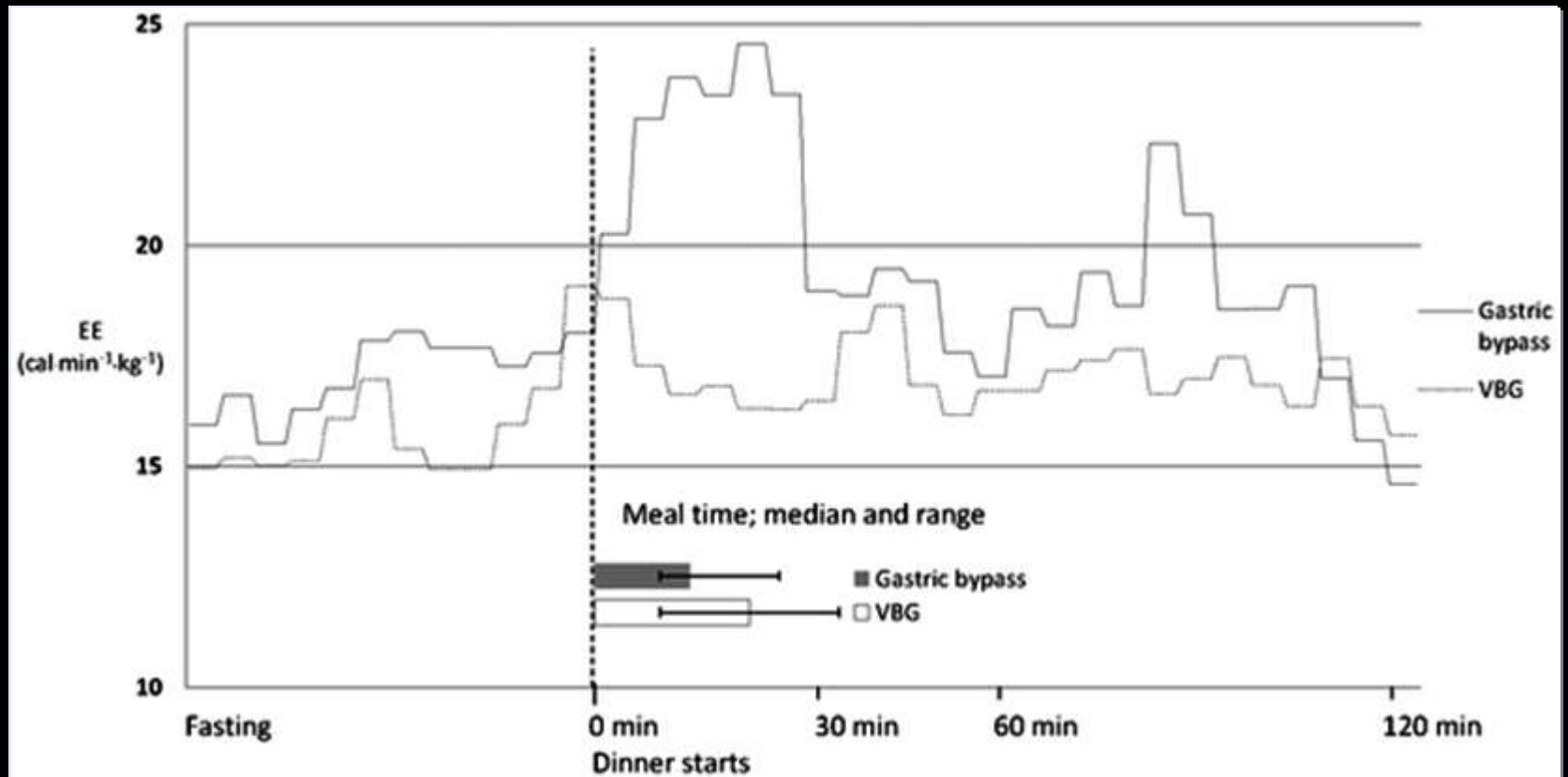
* Difference from baseline

$n = 15$ patients; $n = 16$ controls; 2-way ANOVA $p = 0.72$

Livingstone and Price et al, J Nutrition, 2022

Energy expenditure

Energy Expenditure



Energy expenditure

Table 2. Energy expenditure

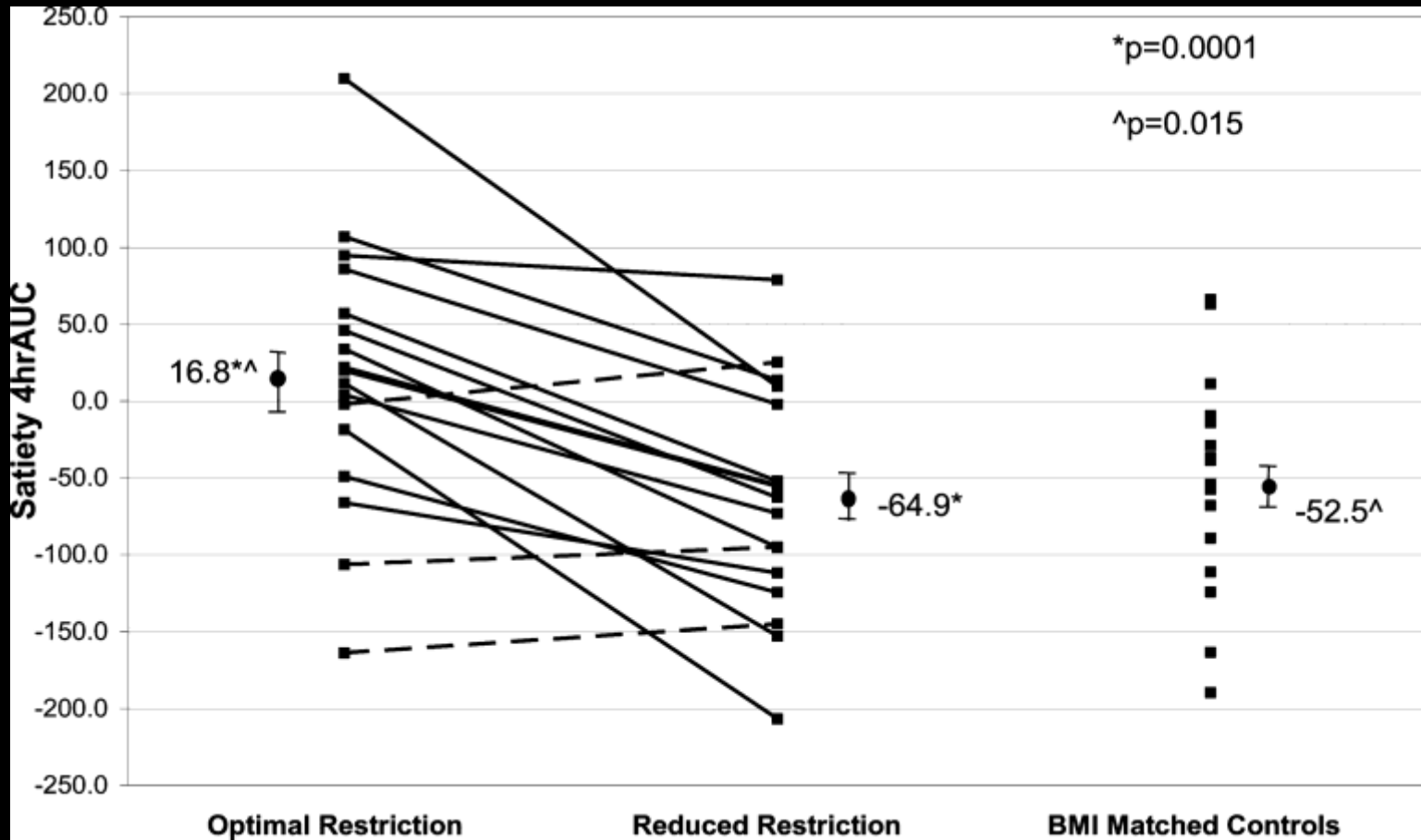
Outcome (kcal per day)	RYGB week 7	CON week 7	RYGB week 11	CON week 11	Difference between RYGB and CON at week 11	P-values for the difference between RYGB and CON at week 11 adjusted for week 7
24-h EE	2393 (2313–2473)	2404 (2324–2484)	2248 (2197–2298) ^a	2310 (2259–2361) ^a	–62 (–121 to –4)	0.05 ^b
BMR	2241 (2118–2364)	2117 (1994–2240)	2046 (1975–2117) ^a	2181 (2109–2252)	–135 (–242 to –28)	0.02
PPEE	2788 (2661–2914)	2863 (2737–2990)	2603 (2505–2702) ^a	2684 (2586–2783) ^a	–81 (–193 to 32)	0.17
SEE	1845 (1781–1910)	1786 (1722–1851)	1738 (1704–1773) ^a	1770 (1735–1804) ^a	–31 (–71 to 9)	0.14

Abbreviations: BMR, basal metabolic rate; CON, control; 24-h EE, 24-h energy expenditure; PPEE, postprandial EE; RYGB, Roux-en-Y gastric bypass; SEE, sleep energy expenditure. Model-derived parameter estimates with 95% CI at weeks 7 and 11. Estimates are adjusted for body composition and spontaneous physical activity and week 11 estimates and P-values are furthermore adjusted for baseline (week 7). ^aHighlights a within-group difference from weeks 7 to 11 ($P < 0.01$). ^bExact P-value = 0.048.

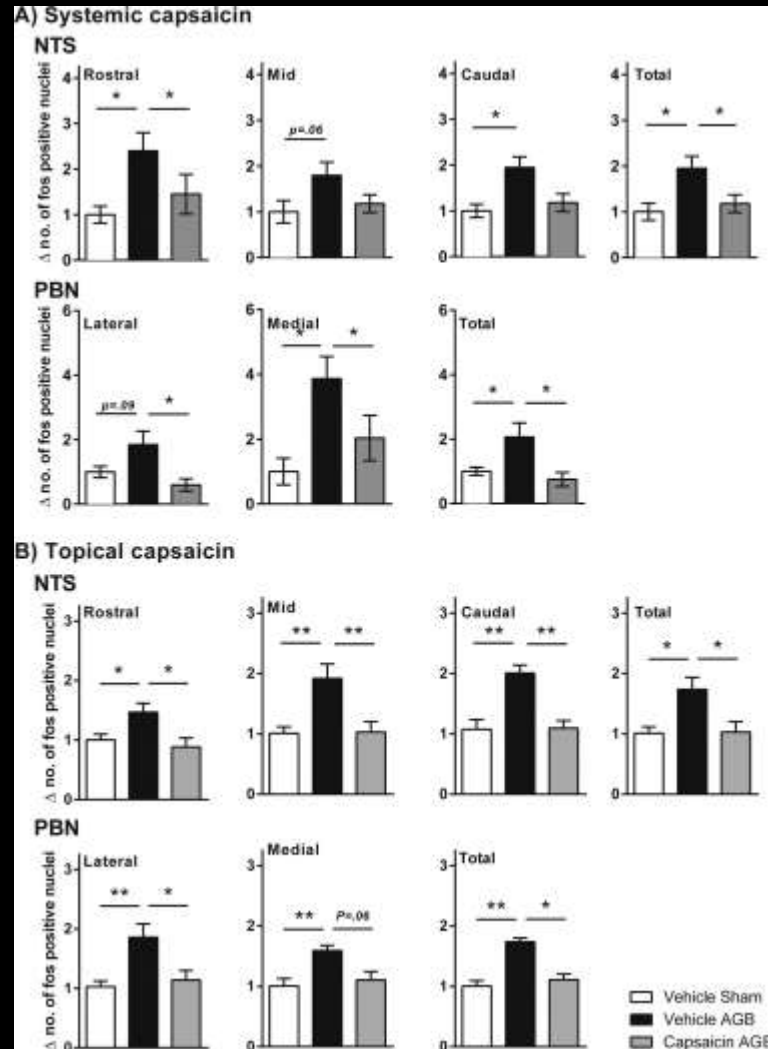
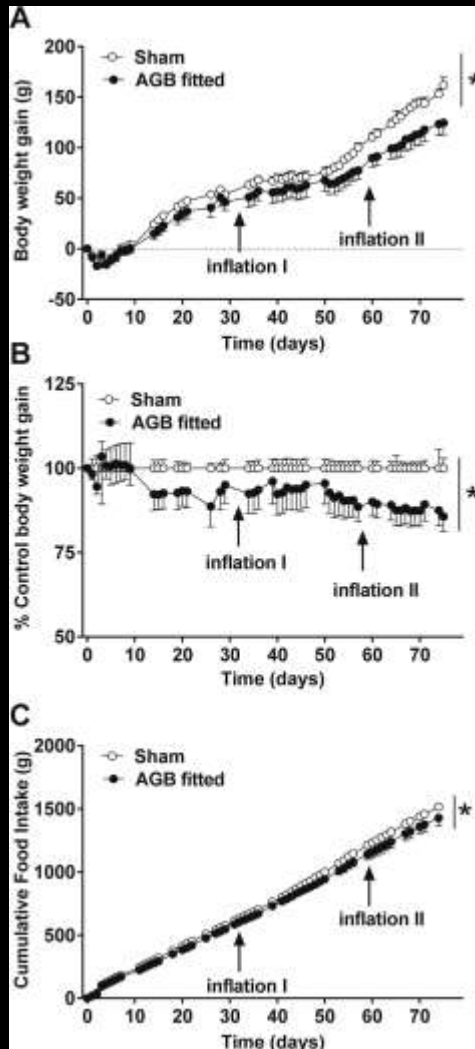
“ a low-calorie diet combined with RYGB surgery resulted in a greater reduction in 24-h EE and basal EE compared with diet alone, even after adjusting for differences in loss of fat and fat-free mass”

Mediators

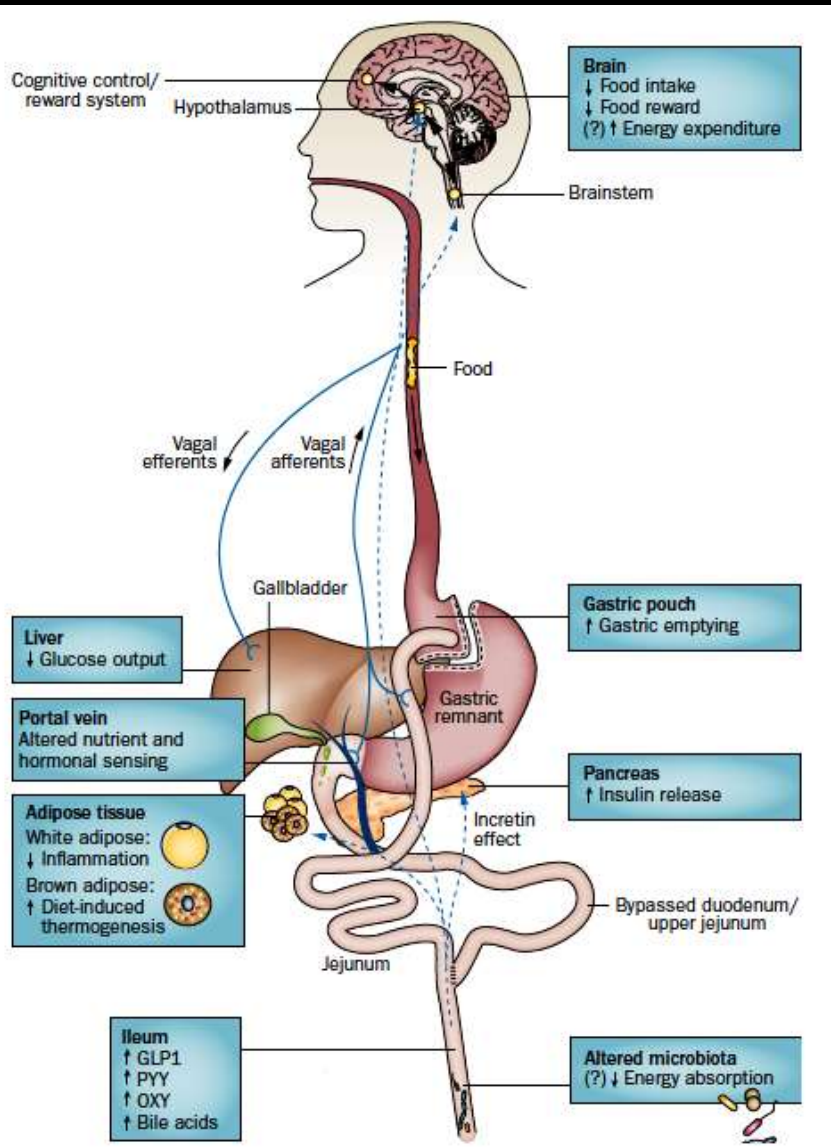
Gastric band - neural signalling



Gastric band - neural signalling

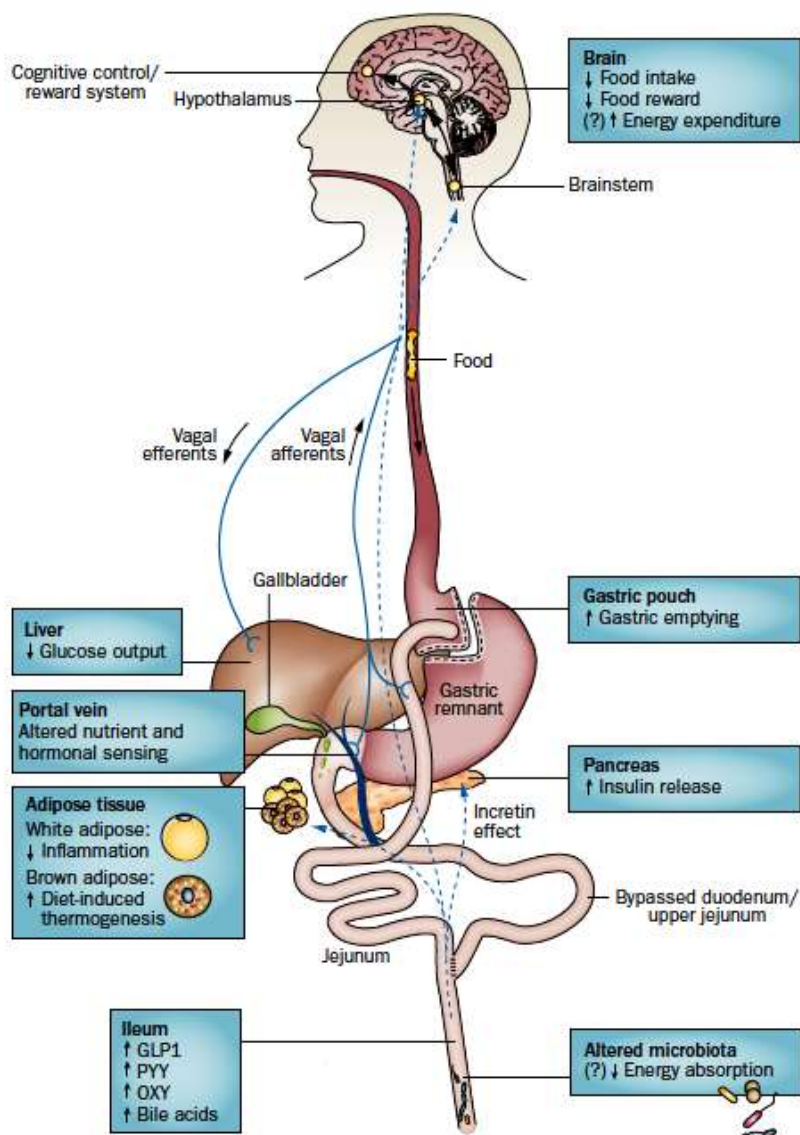


Mediators for RYGB and VSG



- Gut hormones
- Bile acids
- Microbiota

Conclusion



- Operations mainly work on food intake
- Discrepancies between humans and rodents
- Understanding of mechanisms important for weight regain and adjunctive medications

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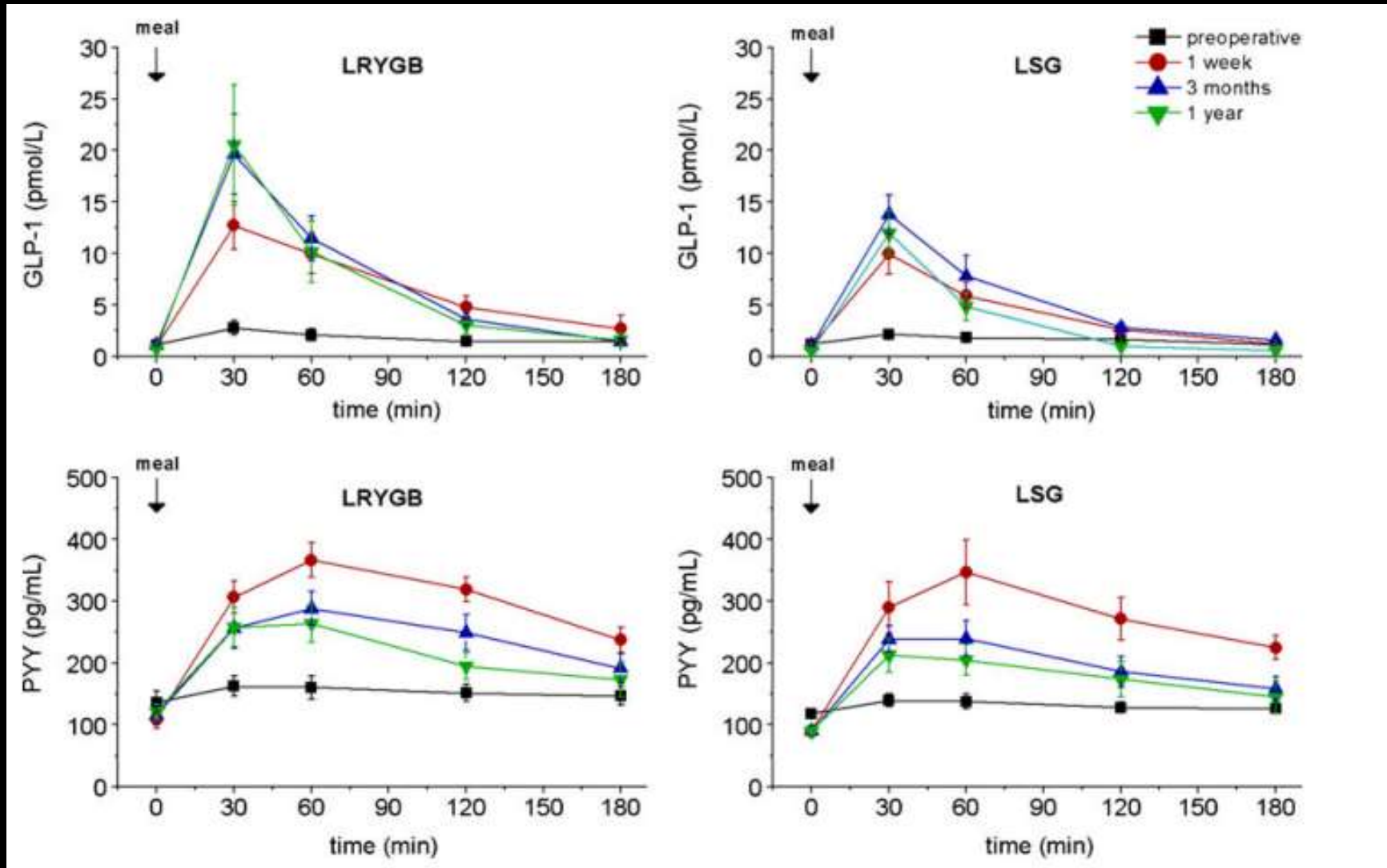
University of Wurzburg

Florian Seyfried

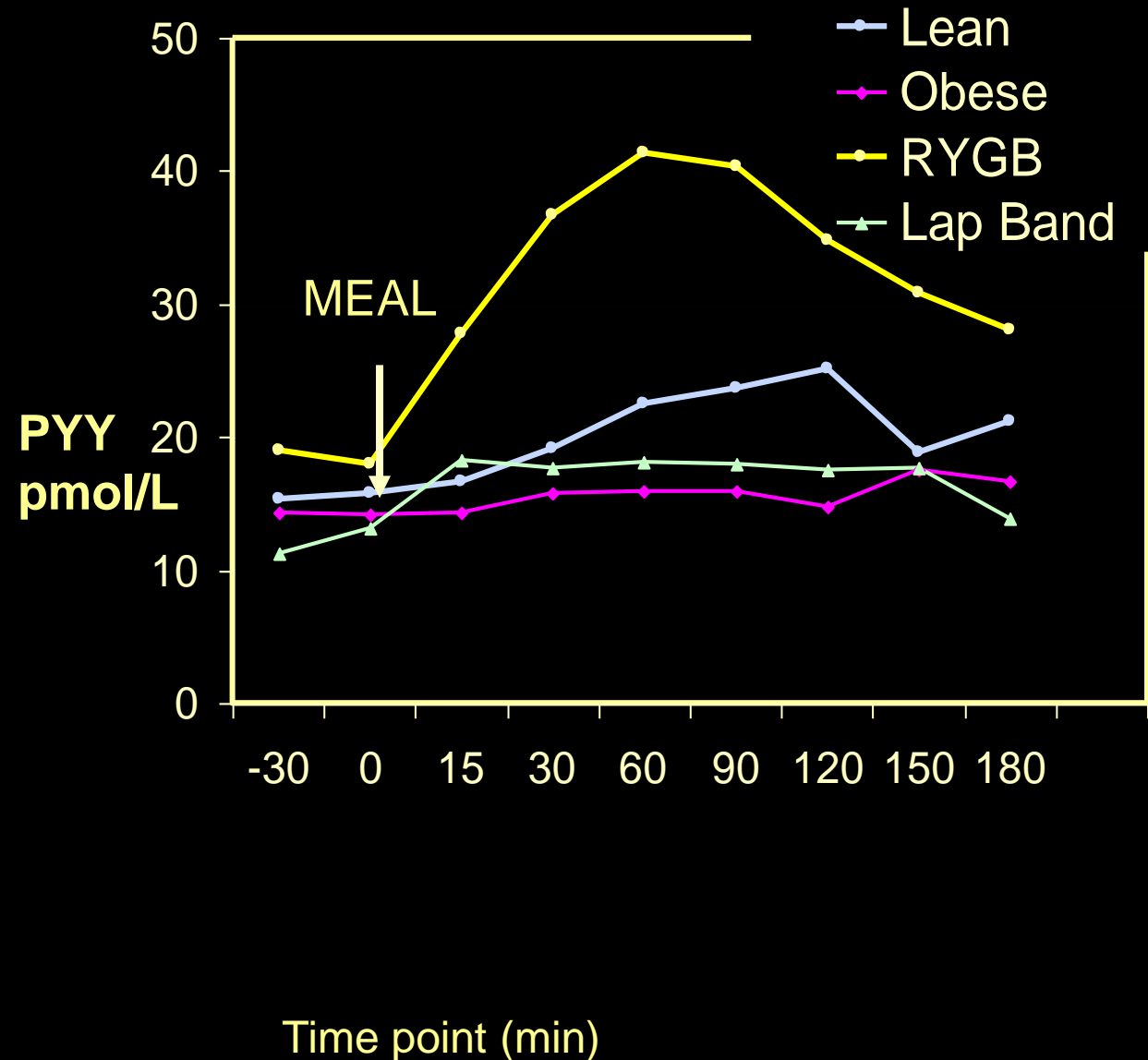
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Margot Umpleby
Barbara Fielding
Nicola Jackson

GLP-1: RYGB vs. Vertical Sleeve gastrectomy

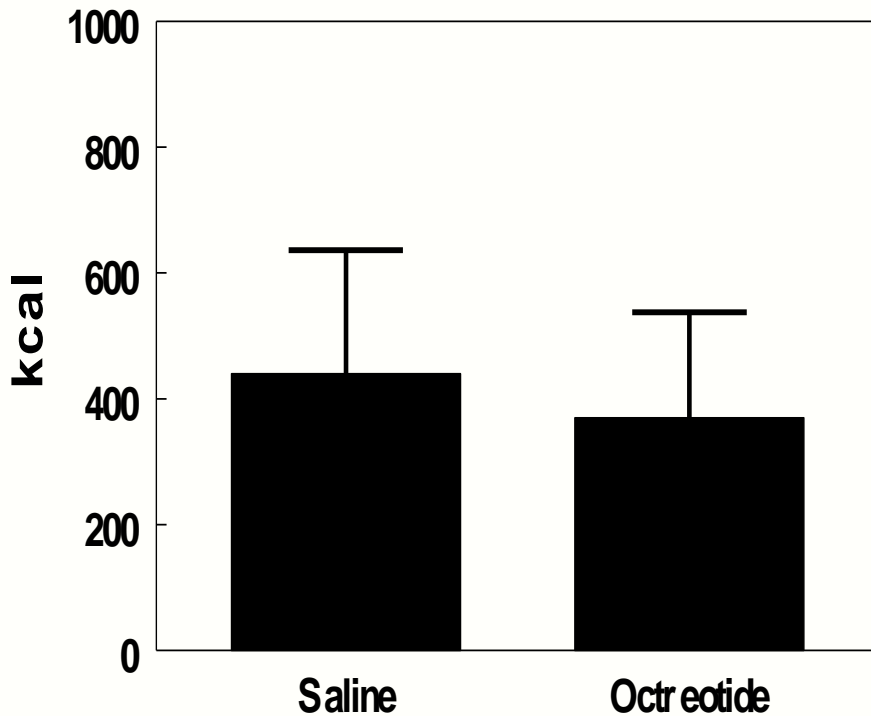


PYY response after obesity surgery

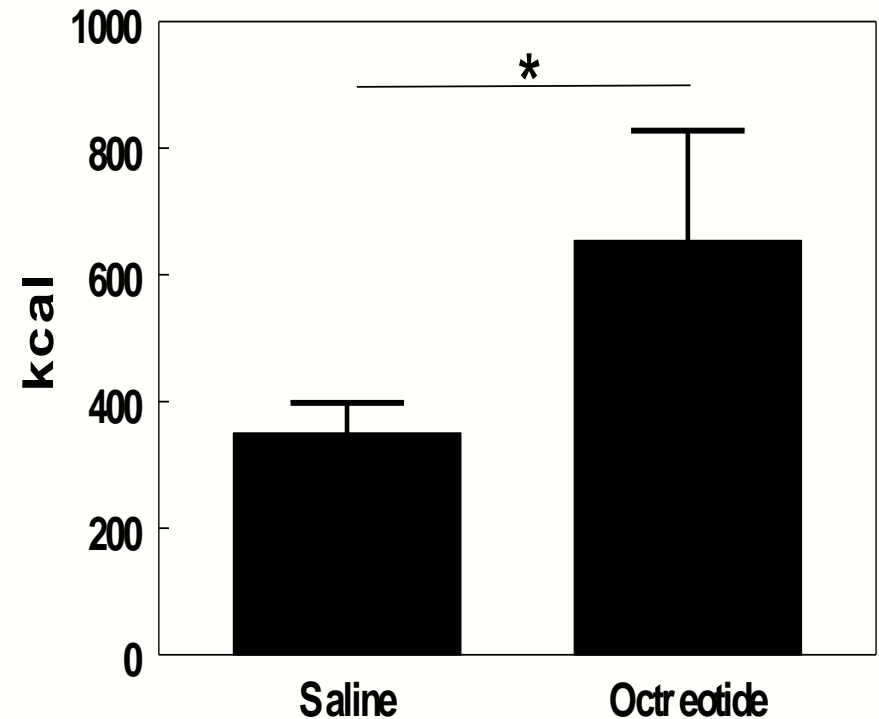


Blocking gut hormones with octreotide

Gastric banding



Gastric bypass



Blocking GLP-1 and PYY actions after RYGB

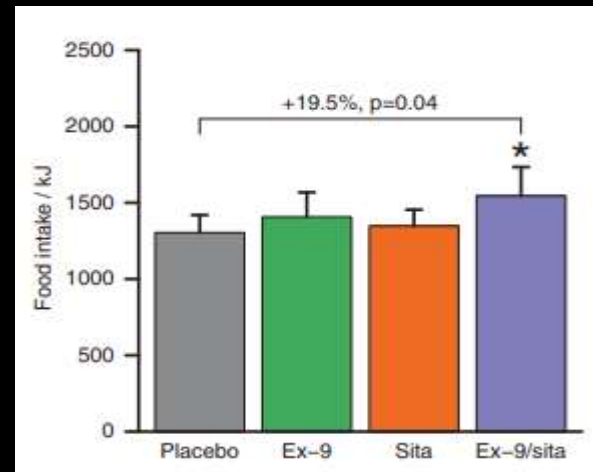
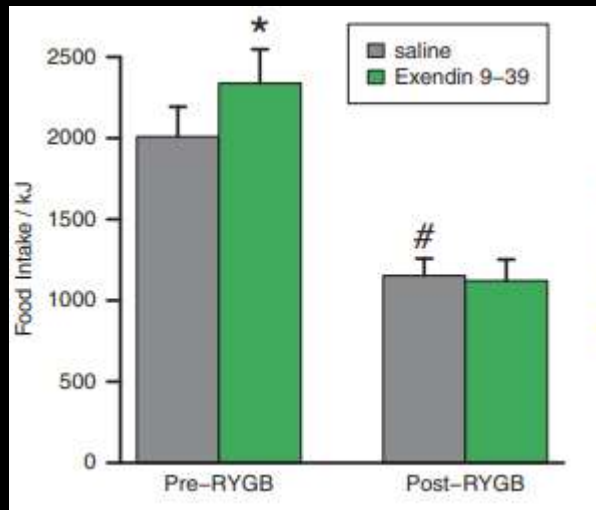
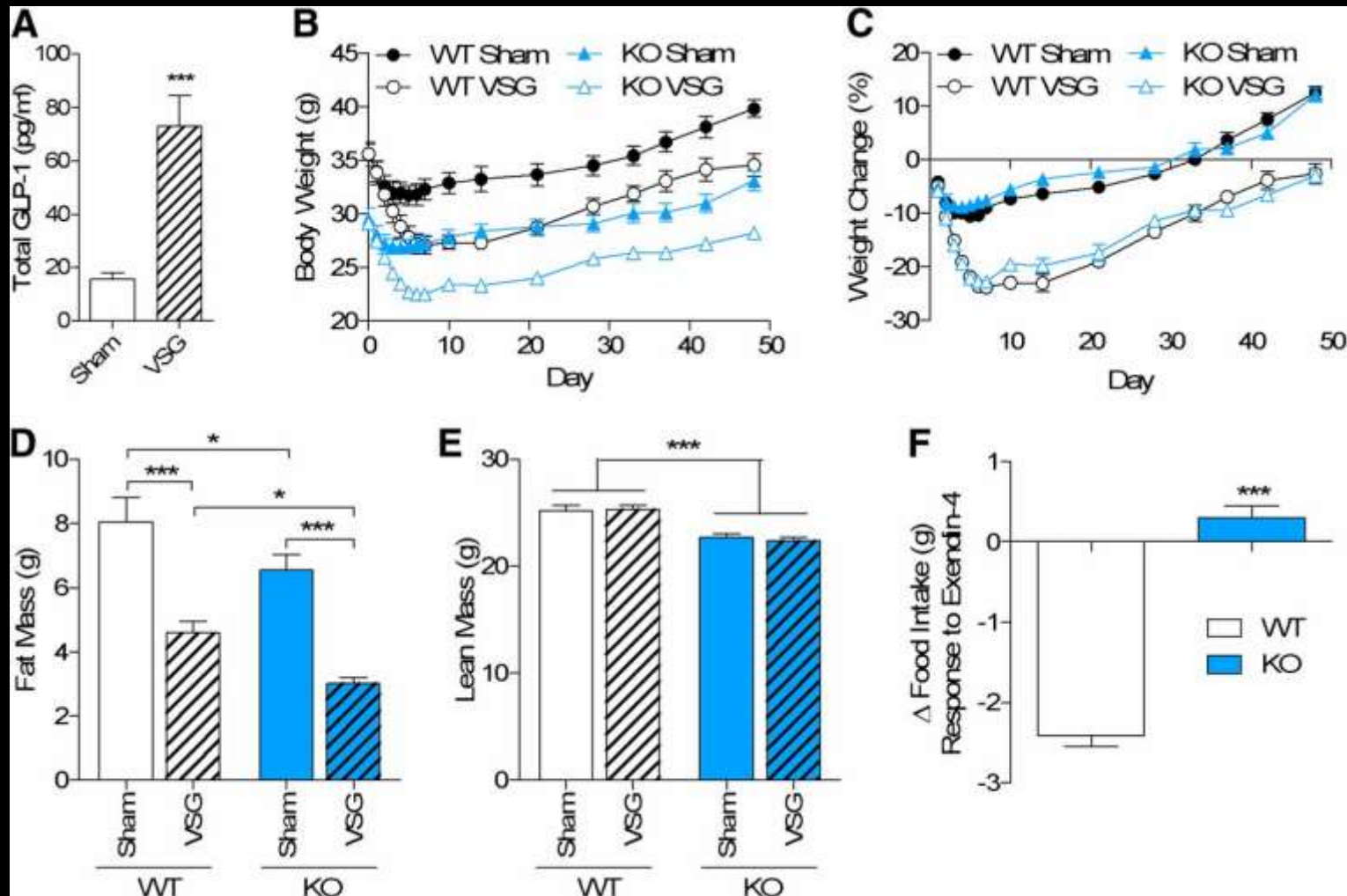
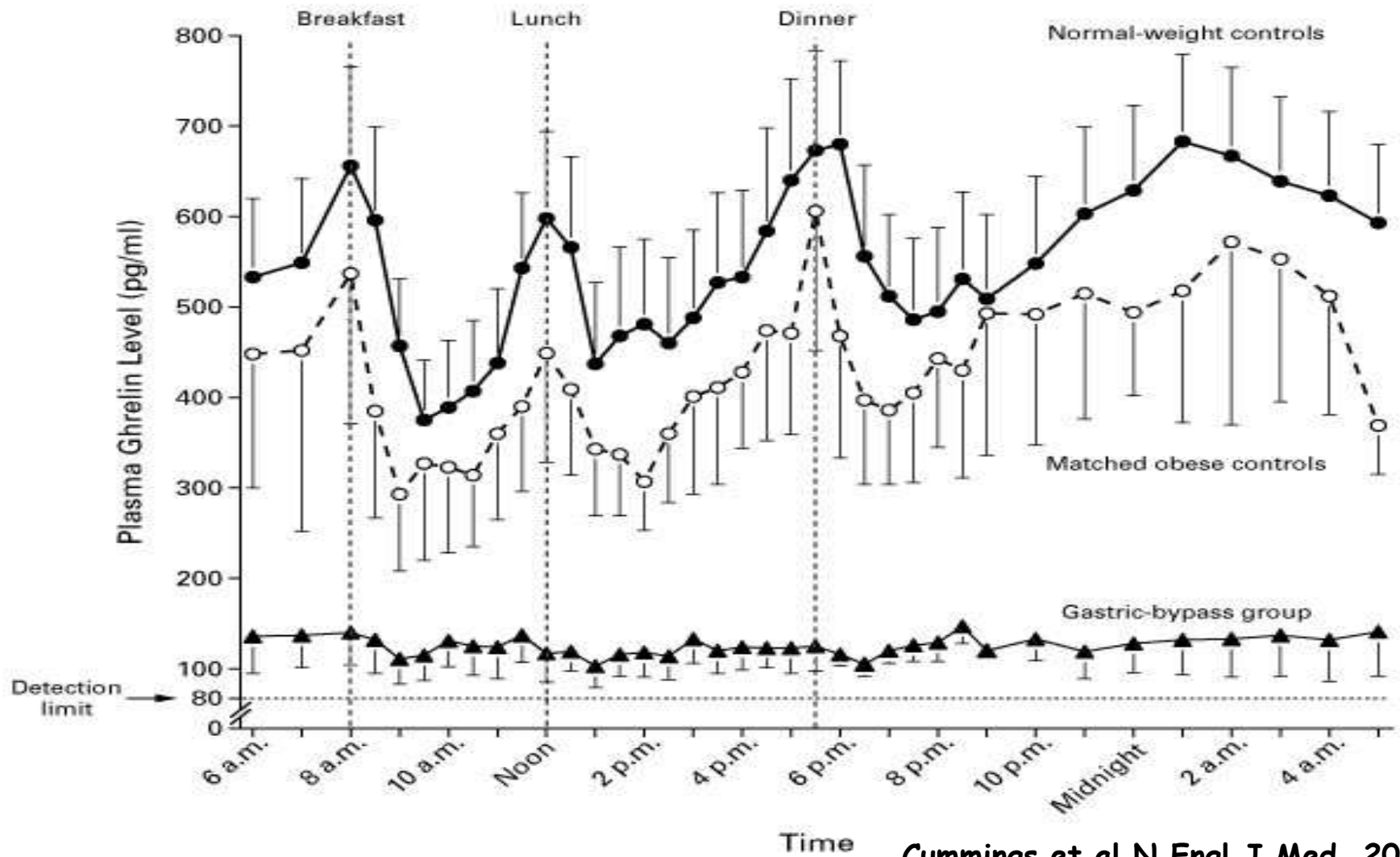


Figure 1. Food intake during an *ad libitum* meal test (served at $t = 240$) preceded by a 4-h standard mixed-meal test (at $t = 0$) in two different studies: (a) Study 1: Nine patients with type 2 diabetes examined before (pre) and after (post) RYGB on 2 days with and without infusion of the GLP-1R antagonist Ex-9 and (b) Study 2: 12 RYGB-operated patients examined on 4 days with placebo, Ex-9, the DPP-4 inhibitor Sita or Ex-9/Sita. Data are means \pm s.e.m.; * $P < 0.05$ vs placebo; # $P < 0.05$ vs preoperatively.

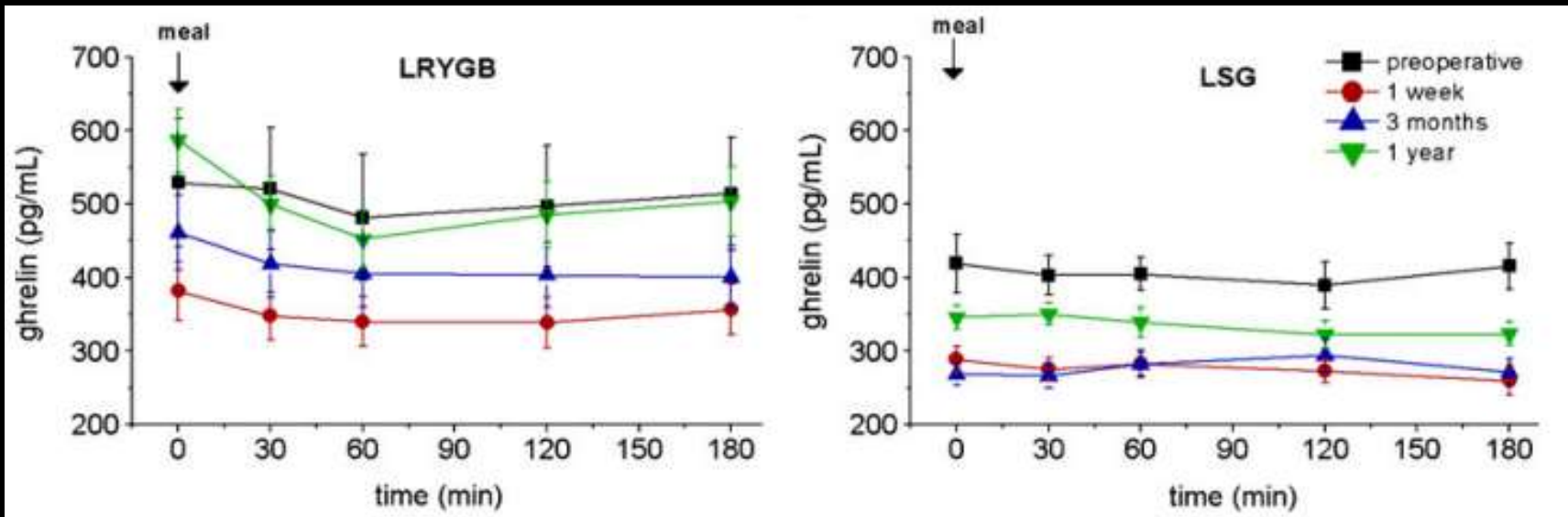
Role of GLP-1 after VSG



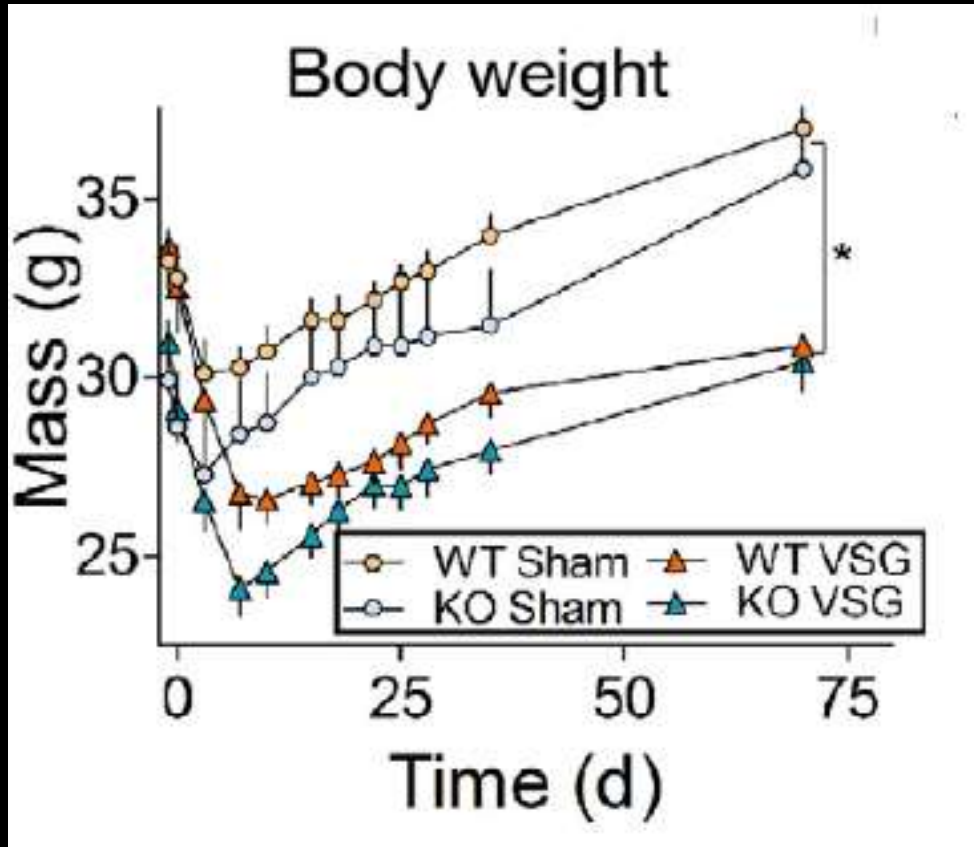
Ghrelin after RYGB



RYGB vs. Vertical Sleeve gastrectomy

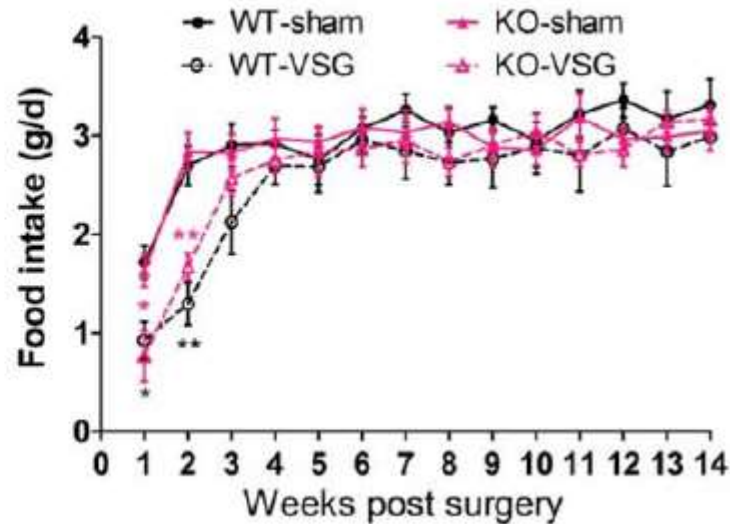
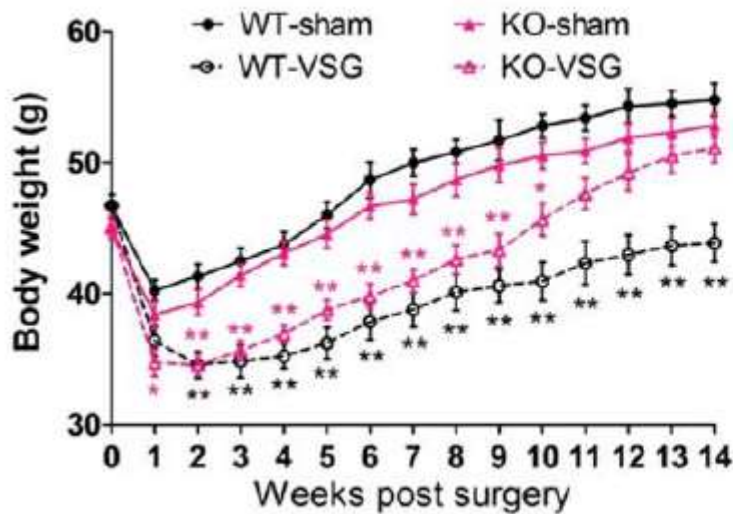
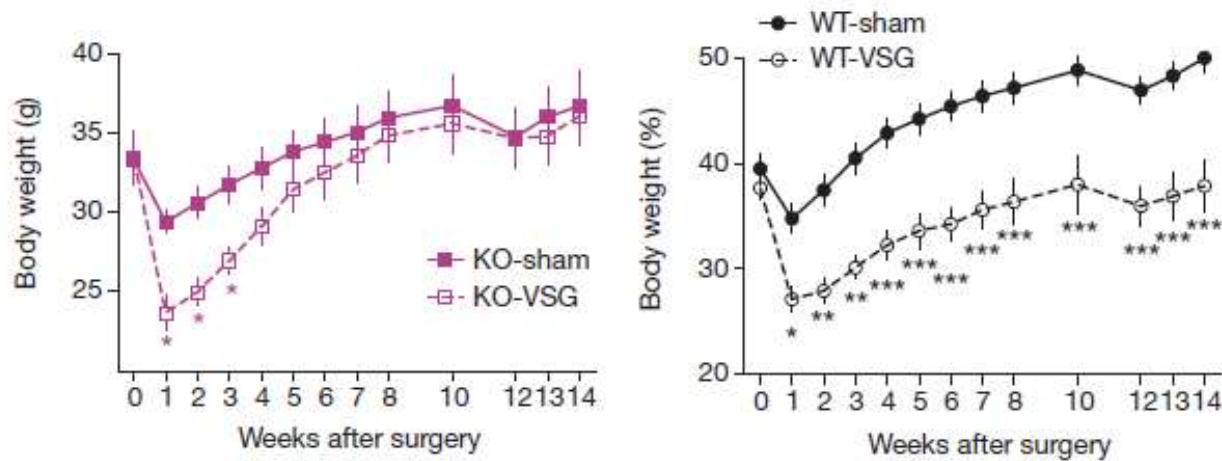


Ghrelin role after VSG



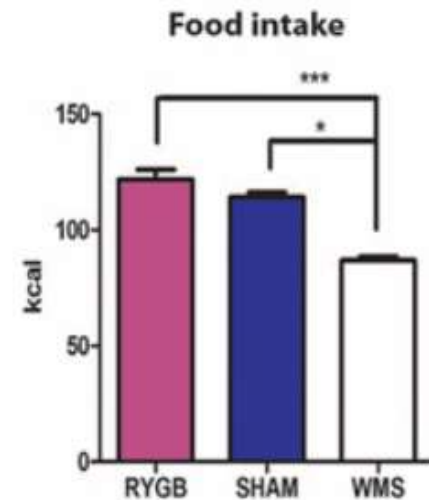
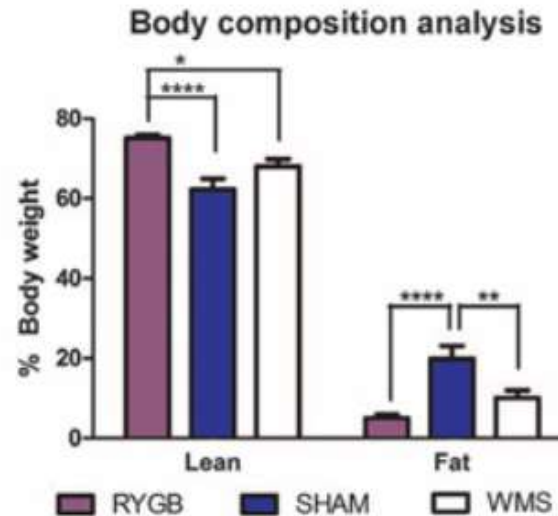
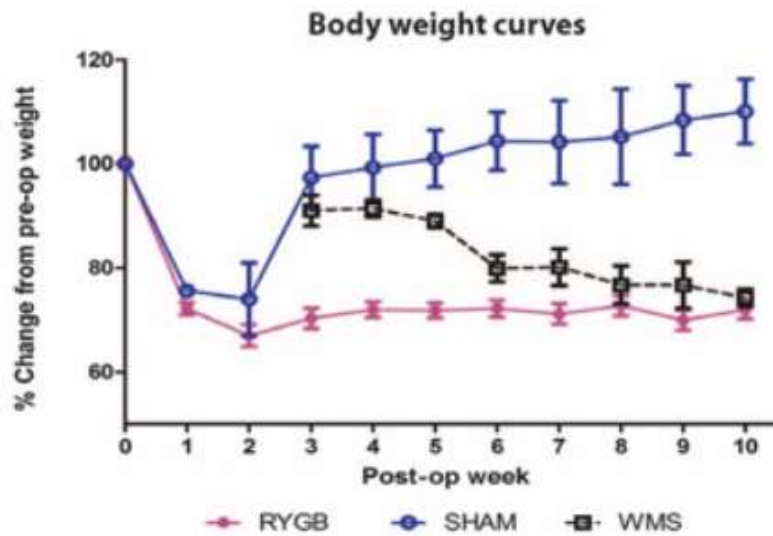
Bile acid signalling in weight loss maintenance after VSG - FXR and TGR5 knock outs

Ryan et al., Nature 2014

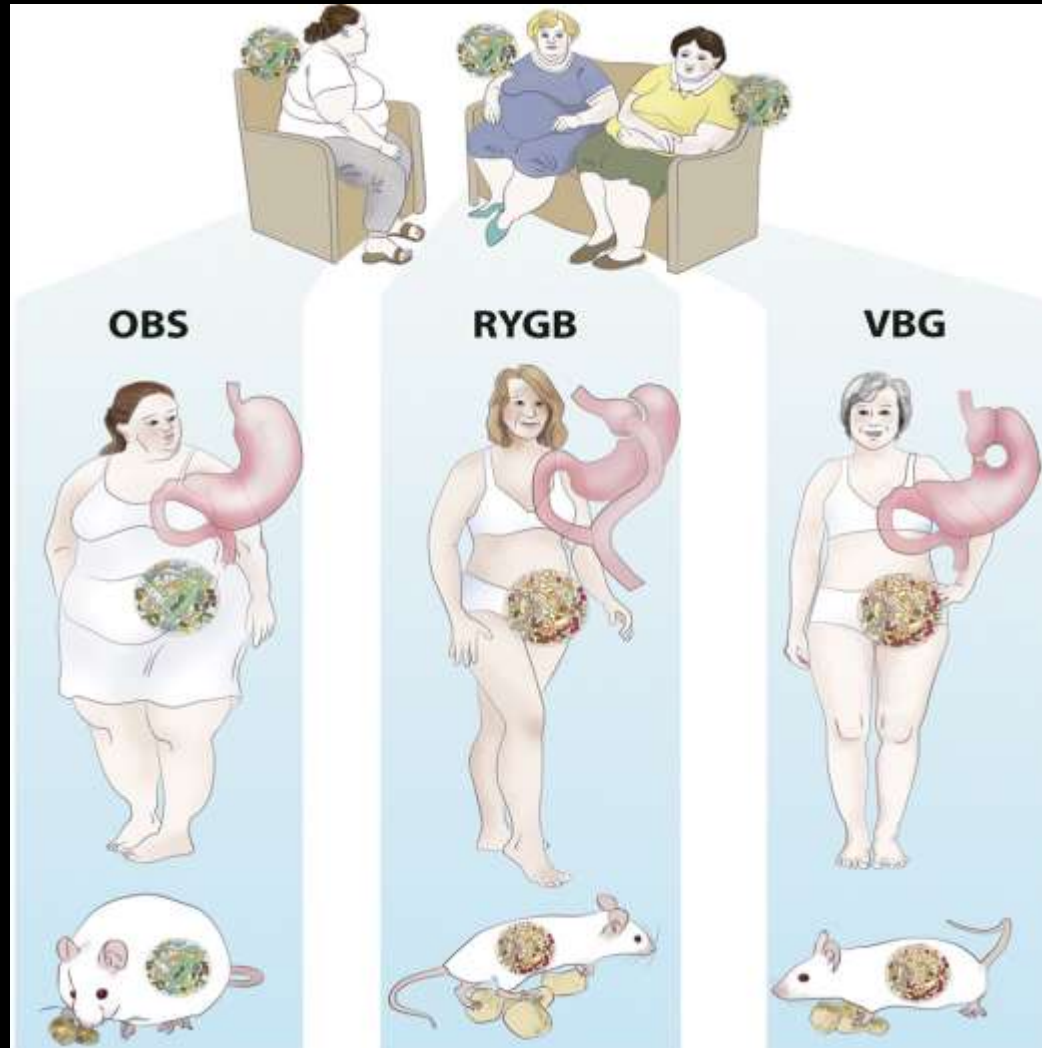


Ding et al., Hepatology 2016

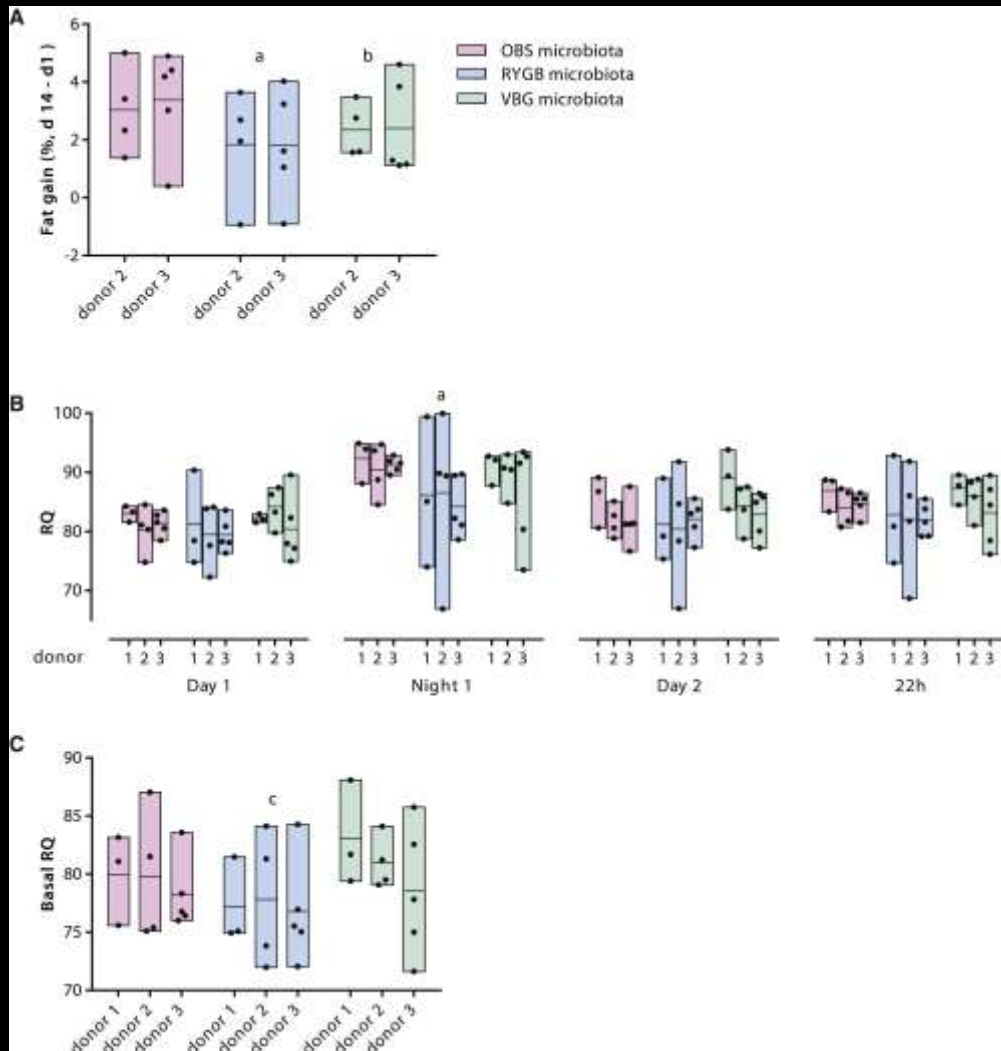
Gut microbiota - mice to mice transfer



Gut microbiota - human to mice transfer



Gut microbiota



“thus indicating decreased utilization of carbohydrates and increased utilization of lipids as fuel in recipients of RYGB microbiota.”

