Similarities & differences in upper GI cancer and bariatric surgery: nutrition & metabolic implications

CW le Roux[1,2]

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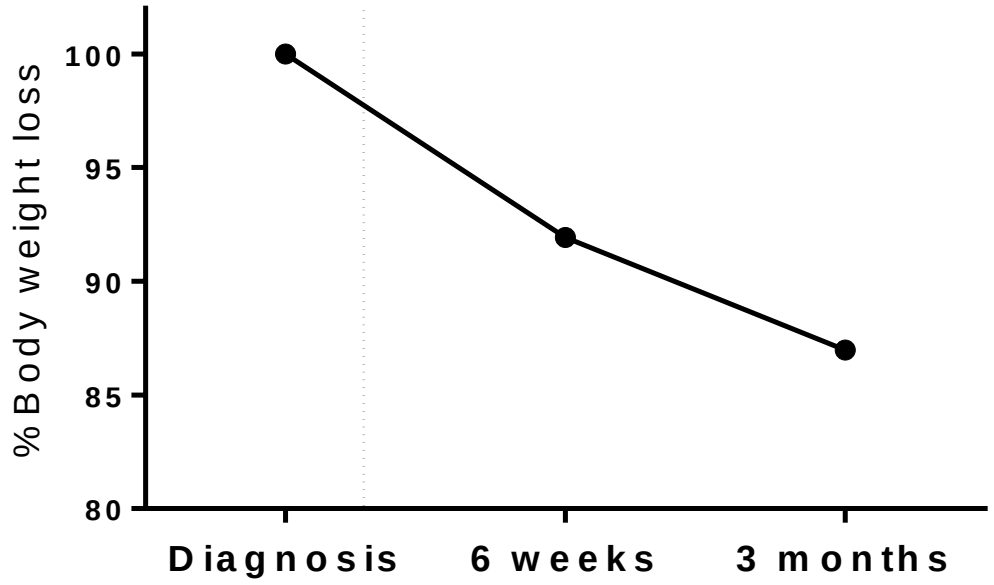
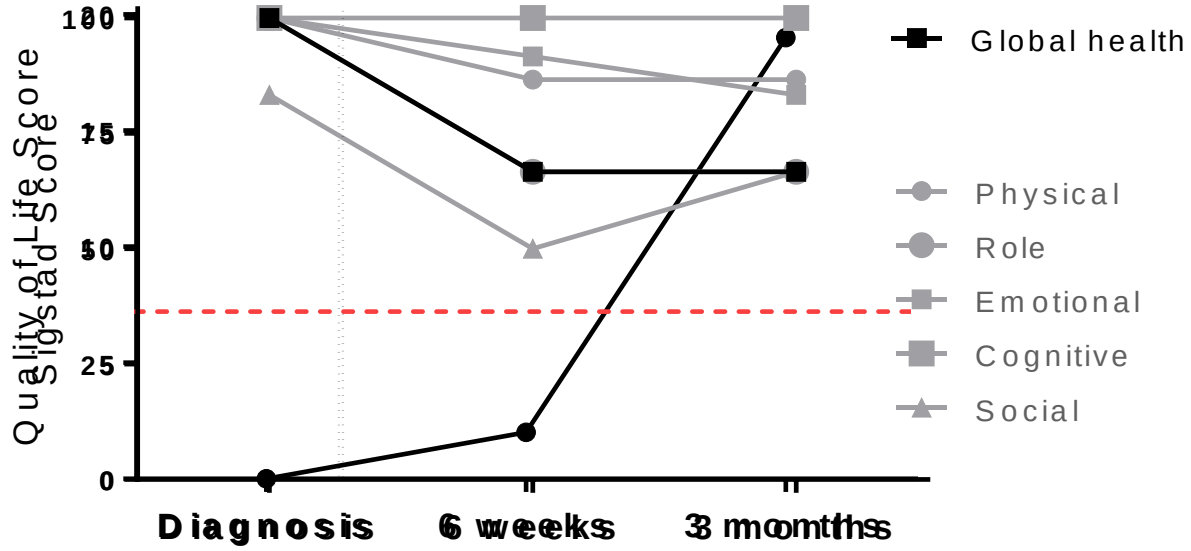
2. Gastrosurgical laboratory, Sahlgrenska Academy, University of Gothenburg

Department of Surgery, St. James's Hospital, Dublin, Ireland

Case presentation

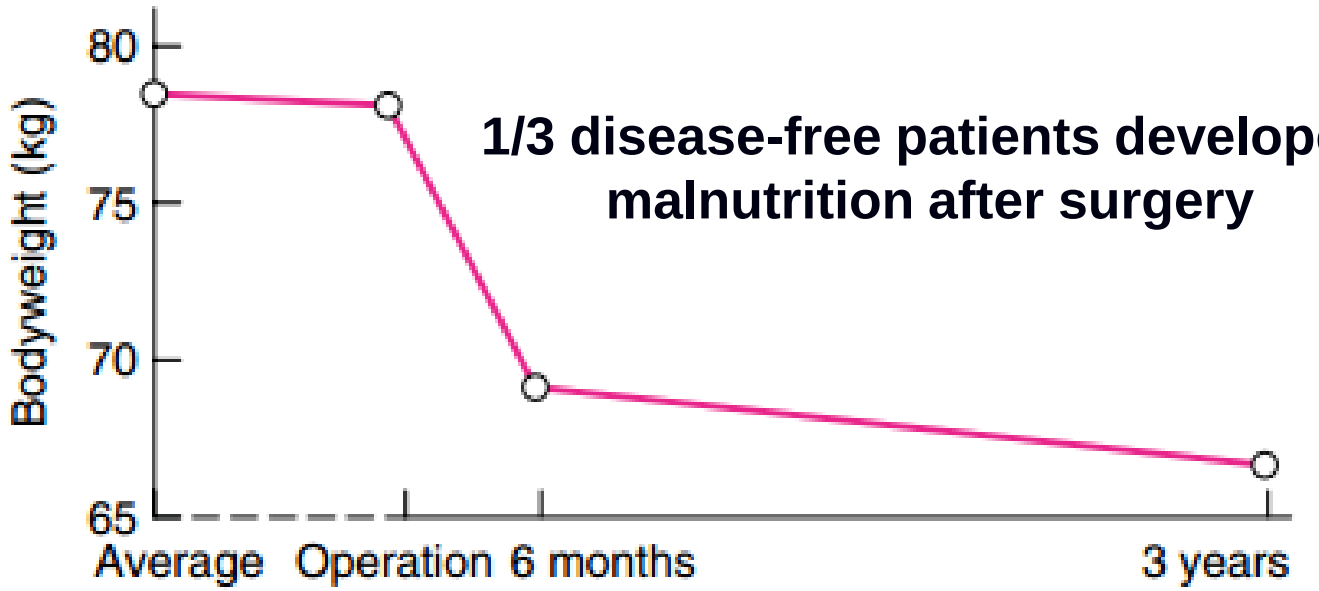
- 2-stage oesophagectomy, pT1bN0 R0, April 2015
- Uncomplicated, home POD 10
- Jejunostomy feeding x 6/52, clinical nutrition OPD





BJS

Long-term weight change after oesophageal cancer surgery

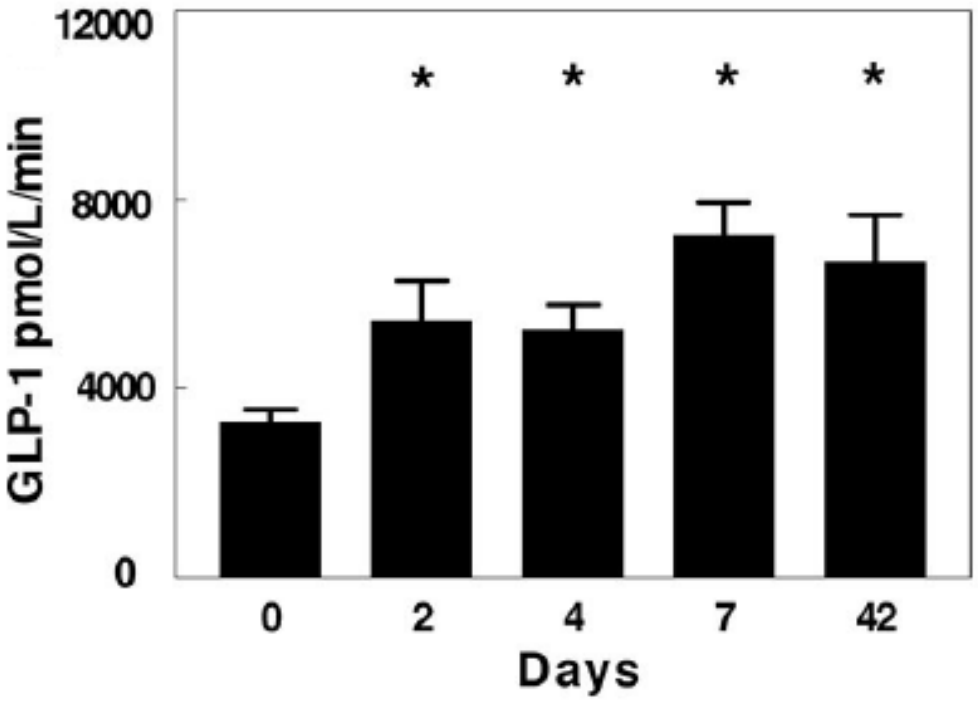


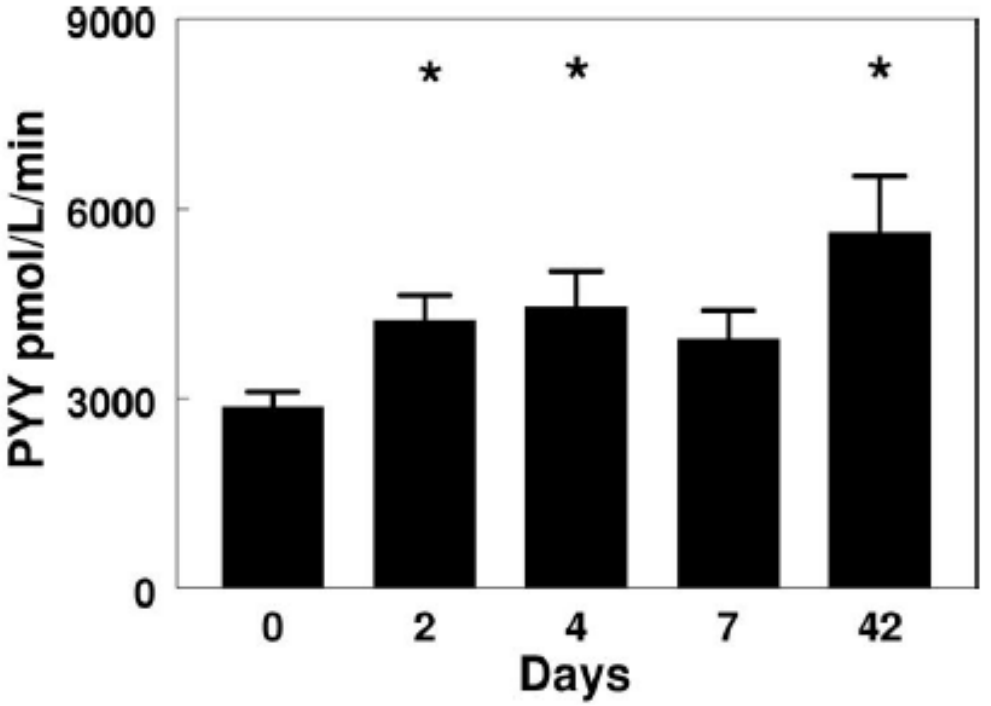
1/3 disease-free patients developed malnutrition after surgery

BMI change	No. of patients	Nausea or vomiting	Appetite loss
Stable or increased (reference)	33	17(17)	28(37)
Decrease (%)			
1–4	19	14(21)	17(24)
5–9	30	12(13)	30(32)
10–14	56	15(21)	23(29)
15–19	42	19(27)	33(35)
≥20	46	28(29)	54(34)*

Martin *et al.*
Br J Surg. 2007, 2009

Gut Hormones as Mediators of Appetite and Weight Loss After Roux-en-Y Gastric Bypass

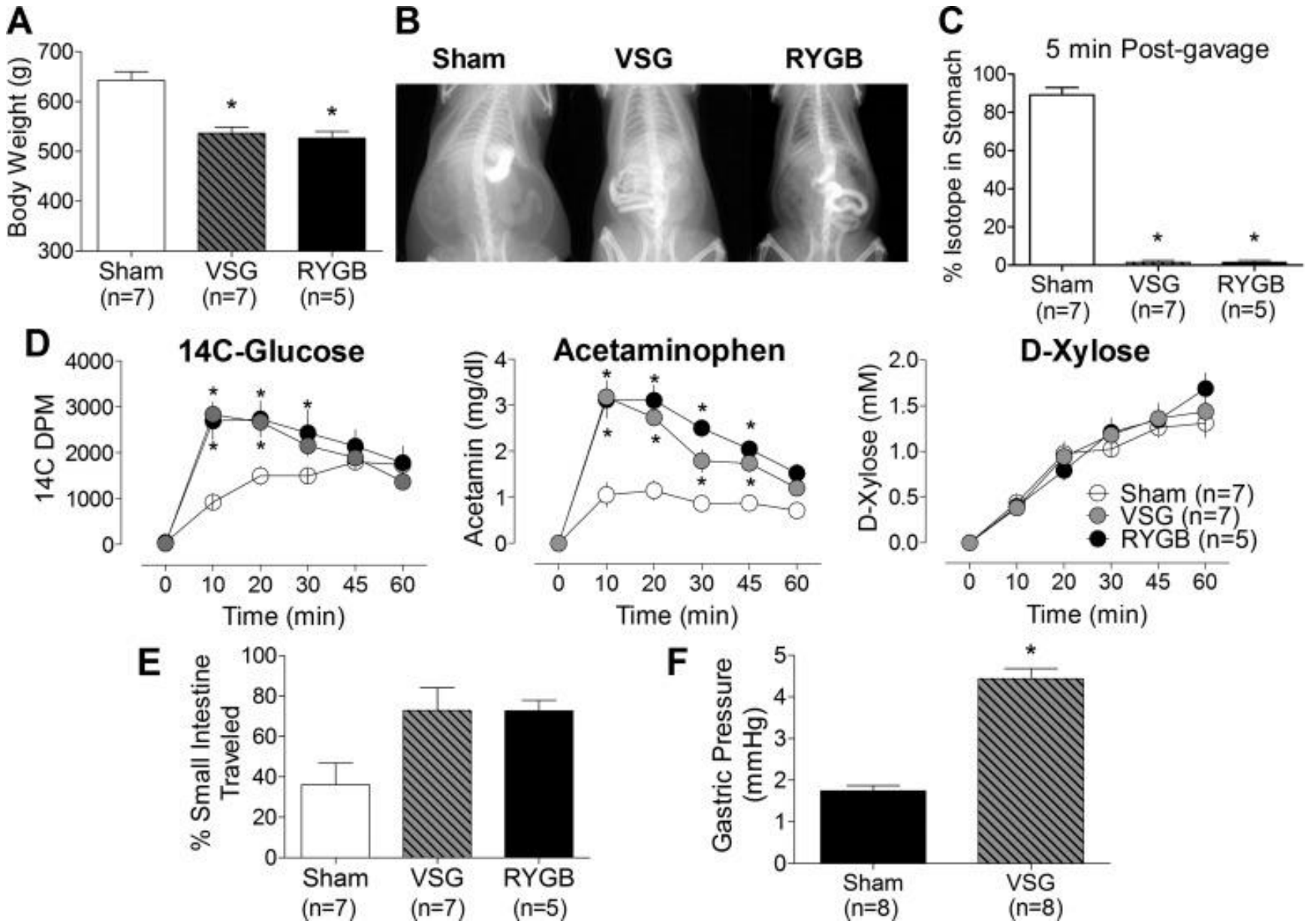




ANNALS OF SURGERY

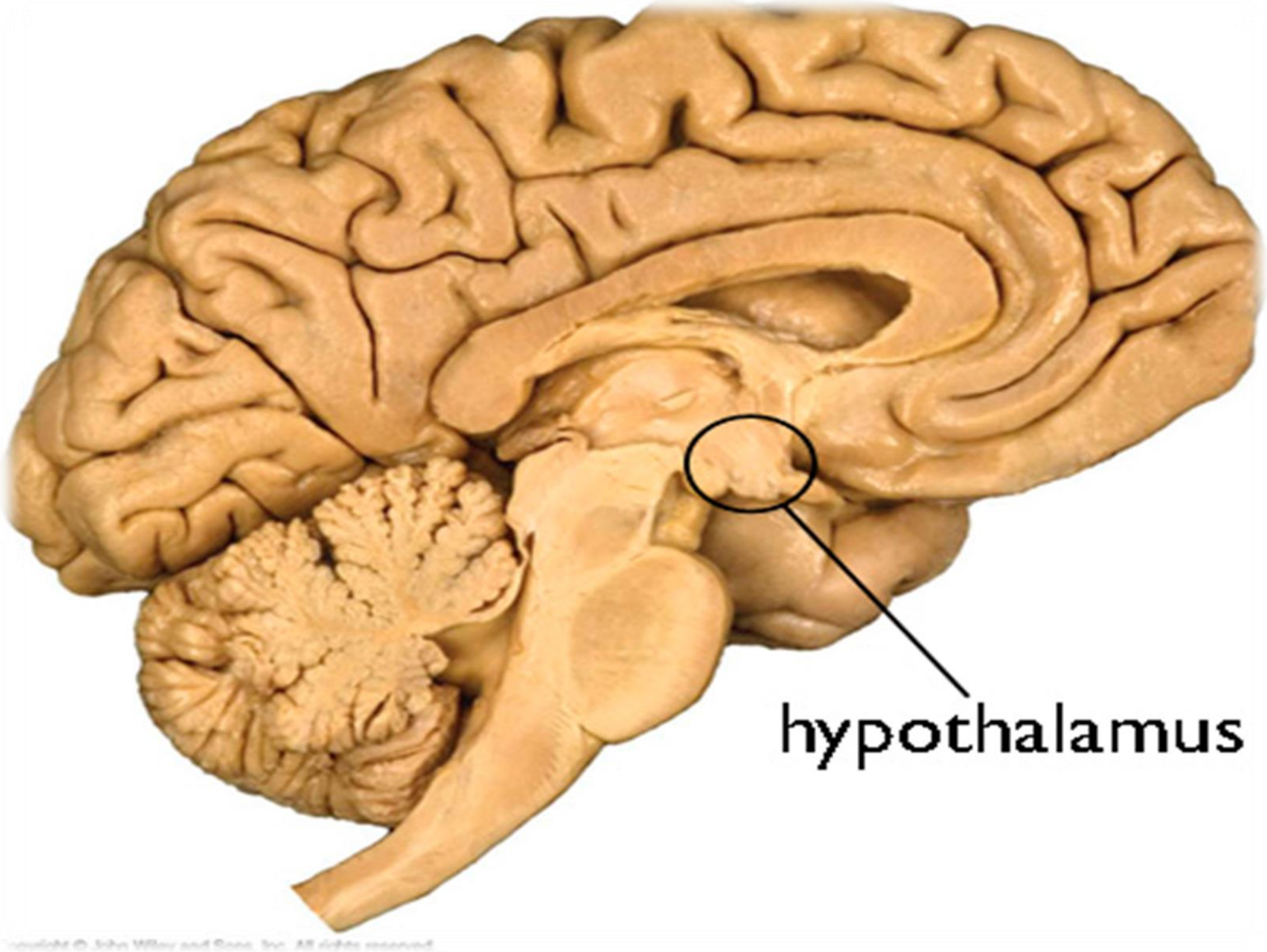
le Roux *et al.*
Annals of Surgery, 2007

Rapid nutrient transit after VSG



Subcortical areas of the brain

le Roux et al. Irish Medical Journal 2016



Hypothesis

Gut hormones are **pathophysiologic mediators** of altered appetite, post ingestive symptoms and weight loss after oesophagectomy.

Study Aims

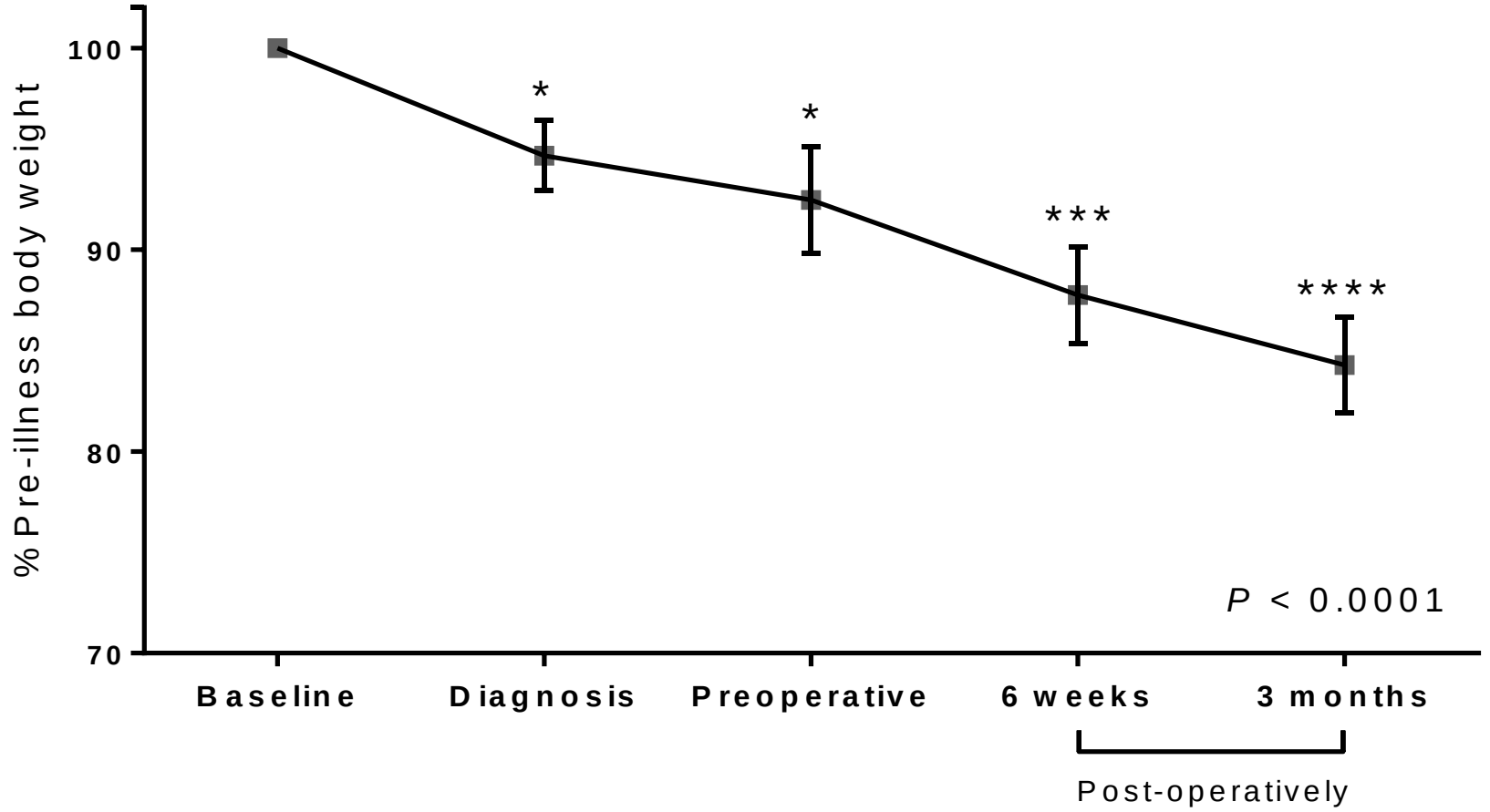
Among post-oesophagectomy patients:

Aim 1: Prospectively characterise the post-prandial **gut hormone profile** after surgery

Aim 2: Determine effect of **gut hormone blockade** on **food reward** and ***ad libitum* food intake**

Results: Aim 1

Significant body weight loss after oesophagectomy

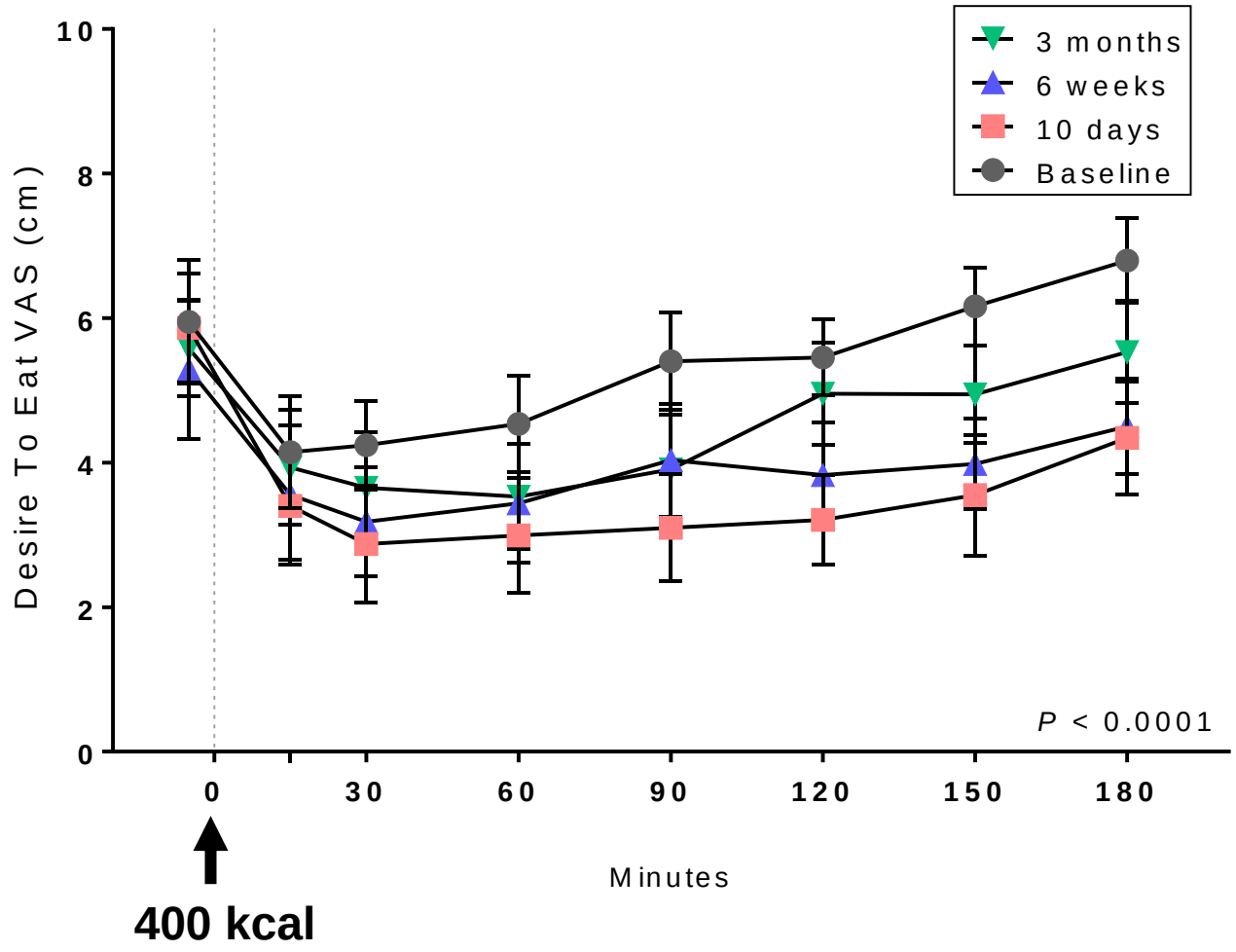


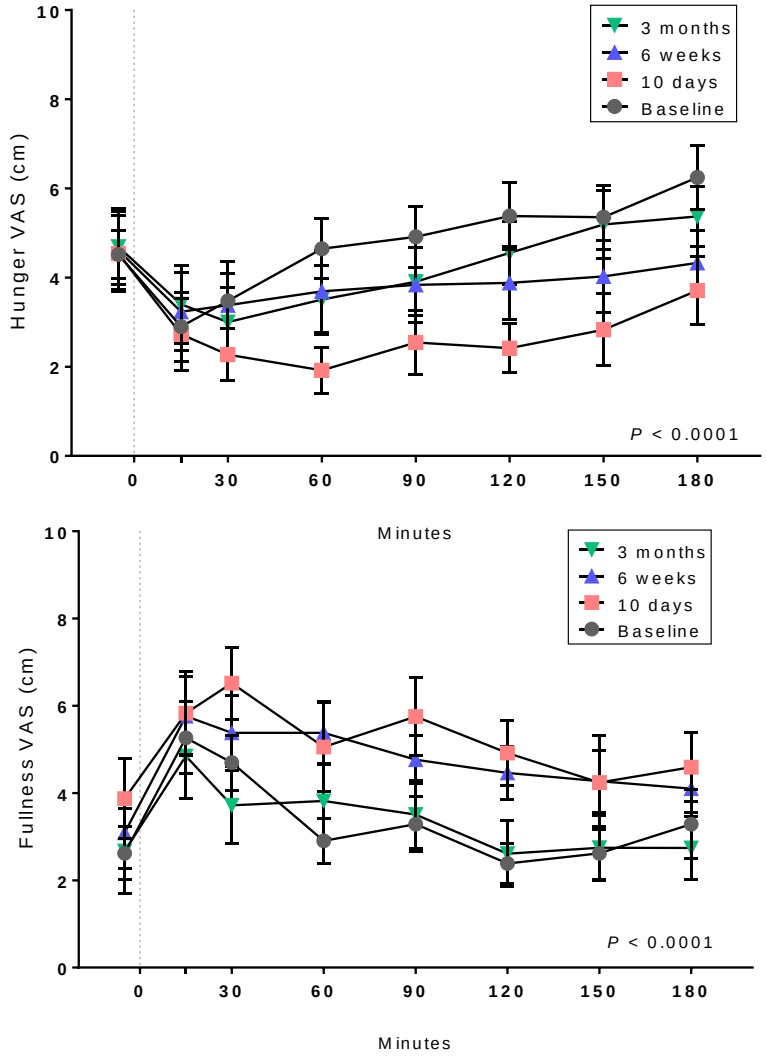
Weight, kg *Median (range)*	**88 (63–124)**	**79 (63-102)**	**81 (65-96)**	**76 (60-91)**	**72 (60-92)**

3 month %BWL = 14.3% (3.8 – 30.7%)

Results: Aim 1

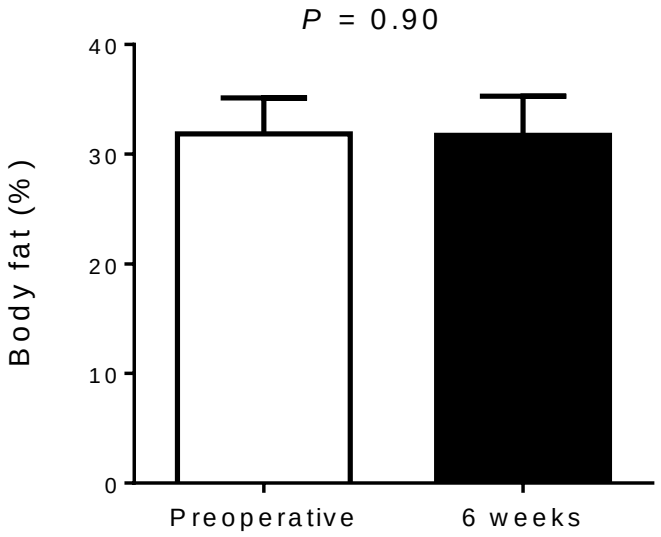
Self-reported desire to eat, hunger, fullness

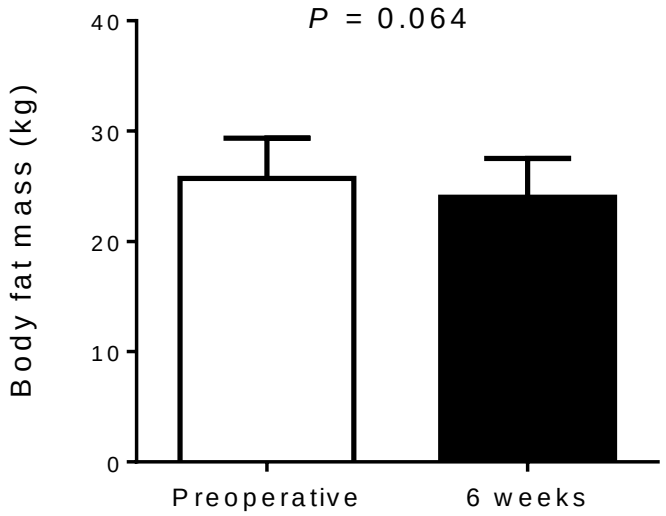


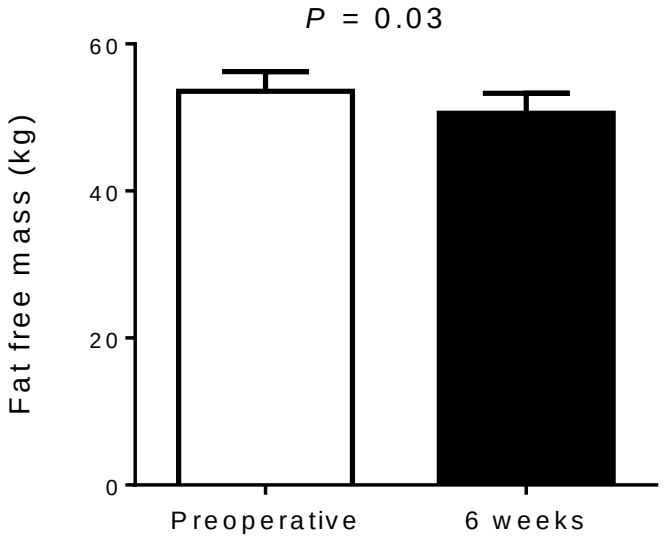


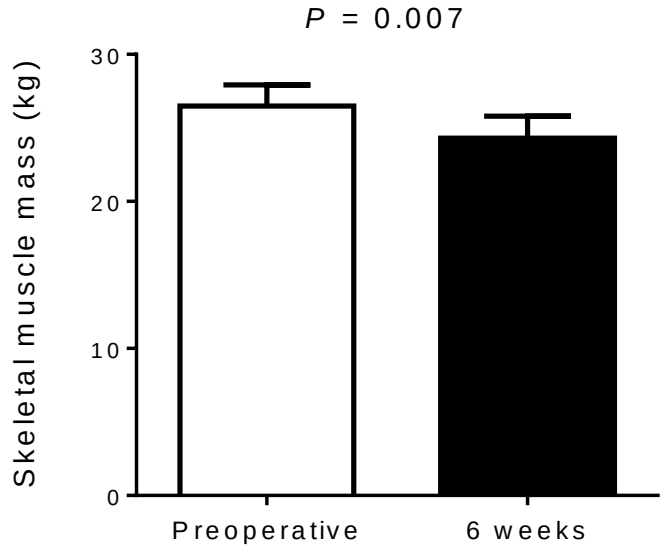
Results: Aim 1

Changes in body composition after oesophagectomy

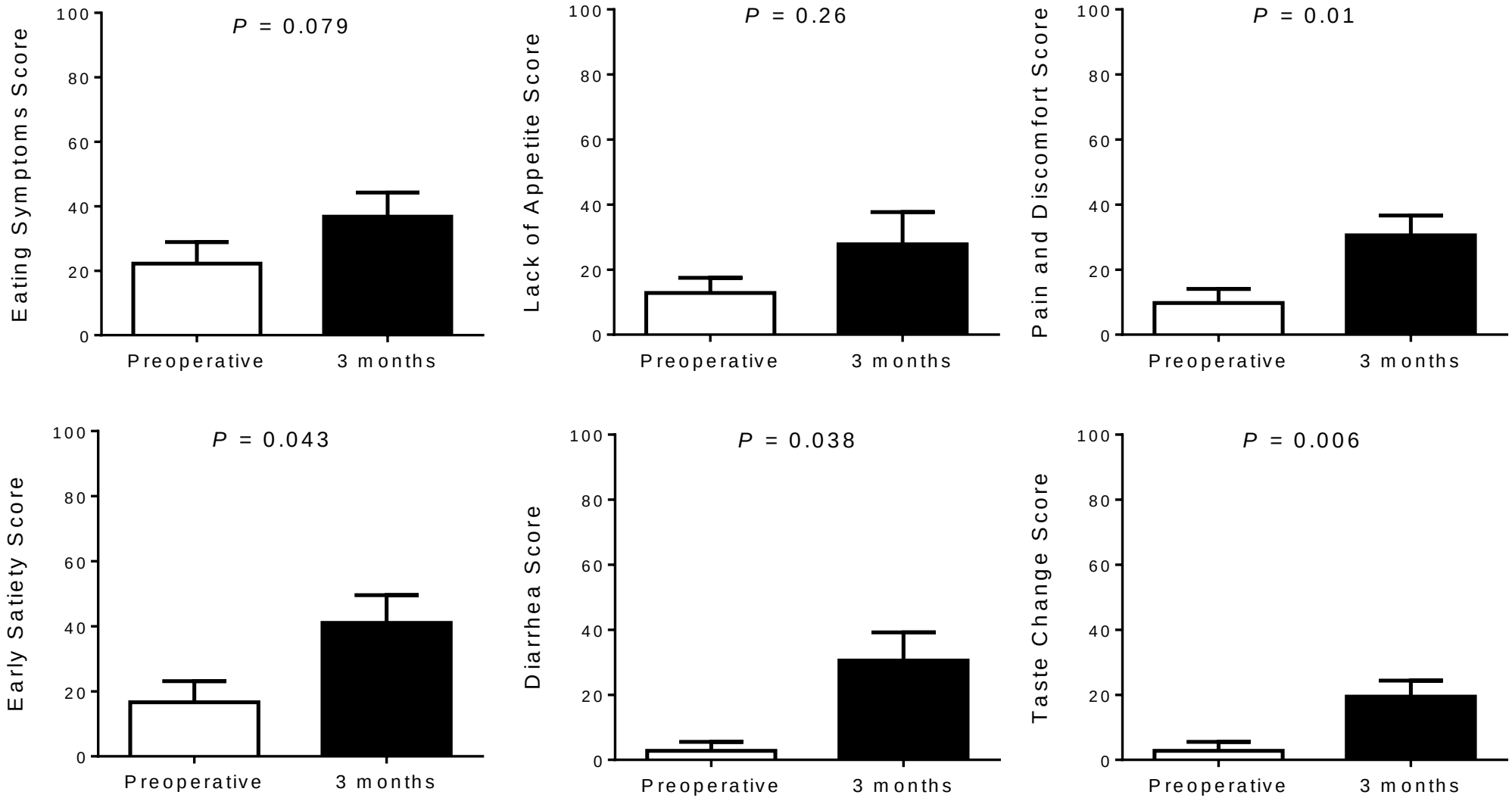






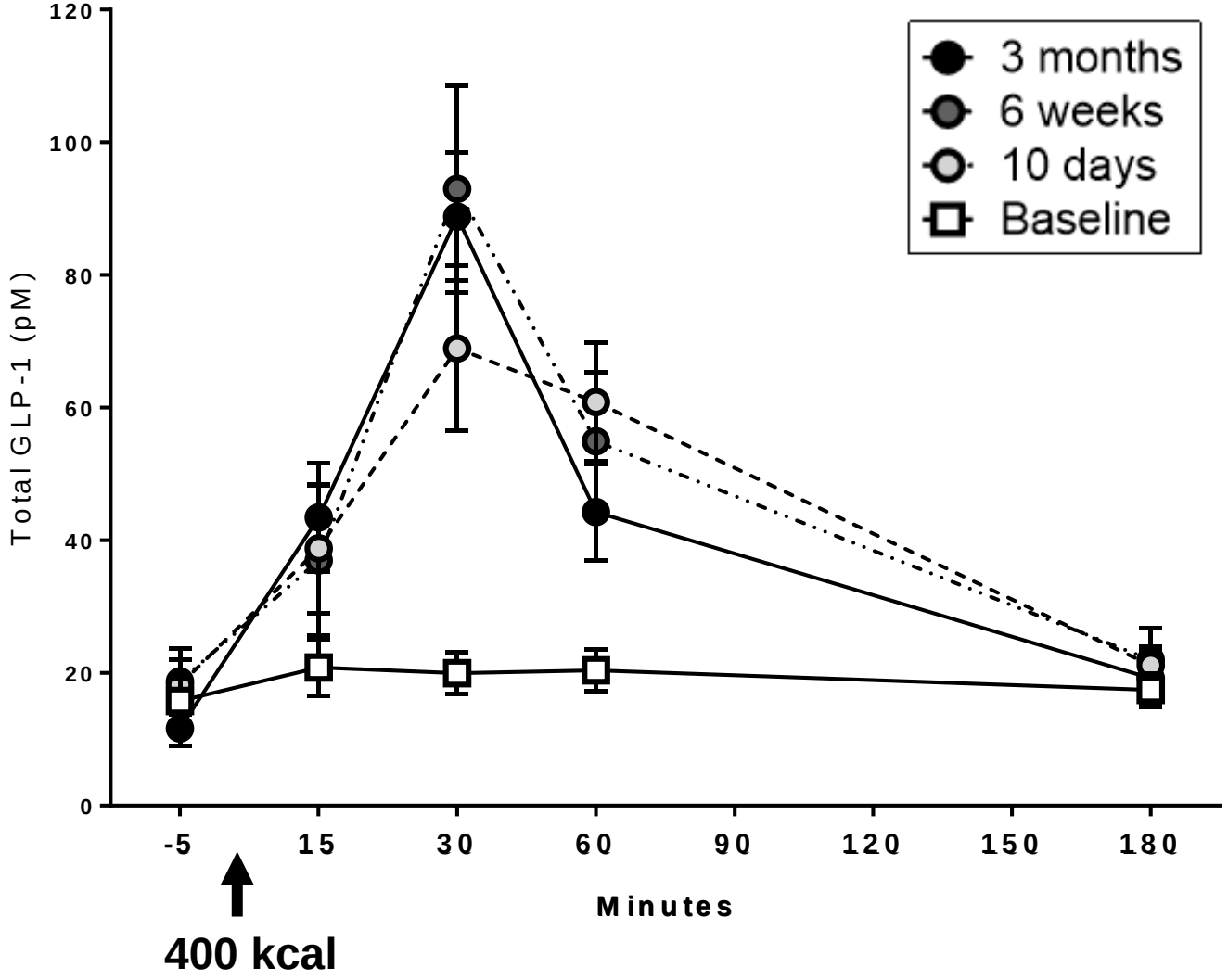


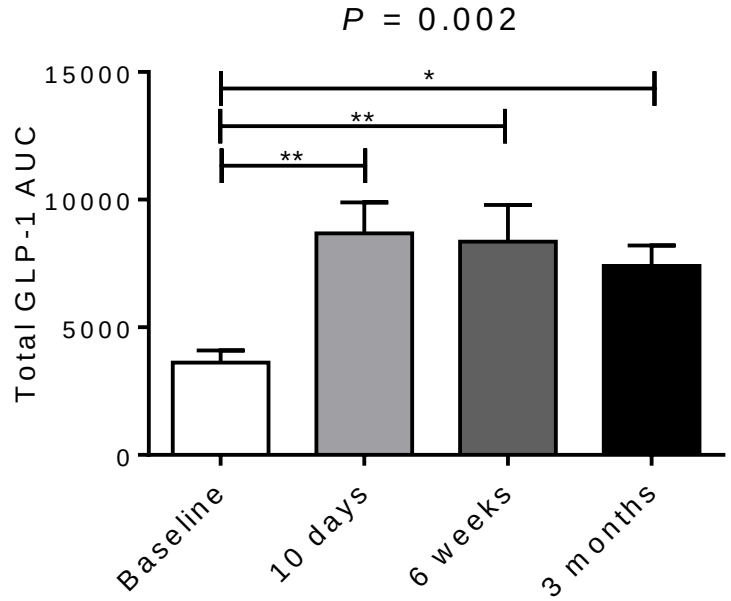
Results: Aim 1
Gastrointestinal QoL scores



Results: Aim 1

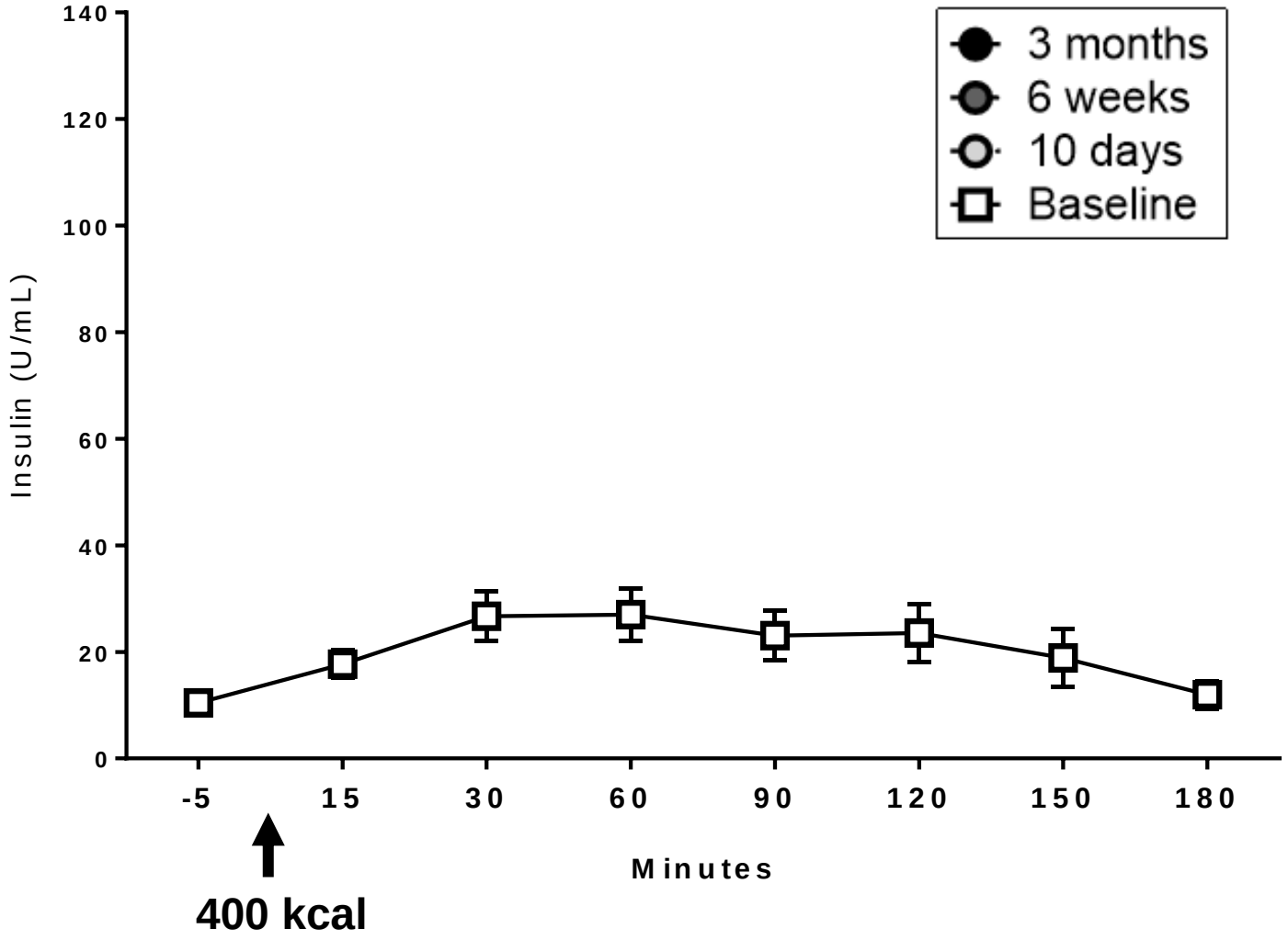
Post-prandial GLP-1 after oesophagectomy





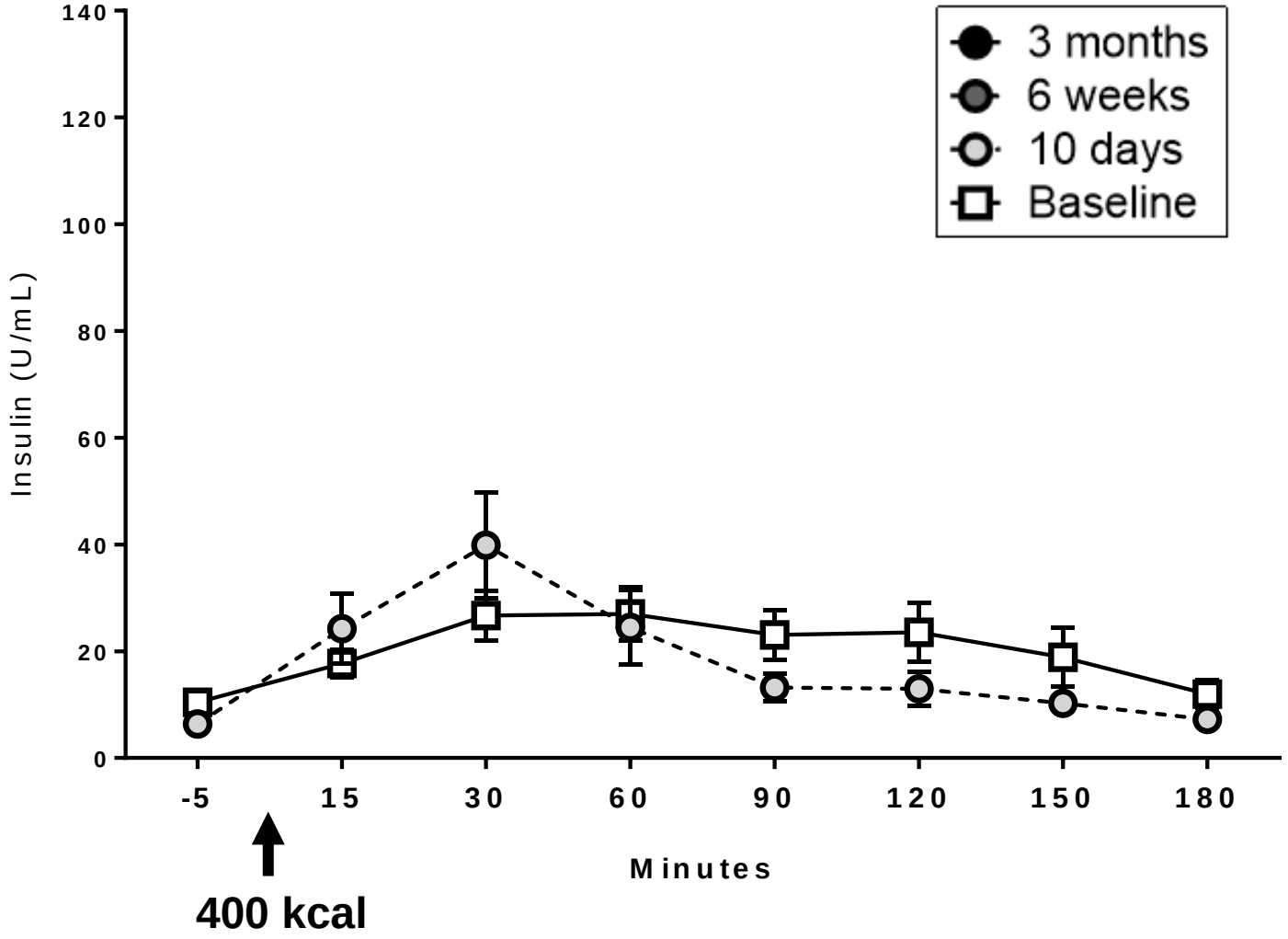
Results: Aim 1

Post-prandial insulin after oesophagectomy



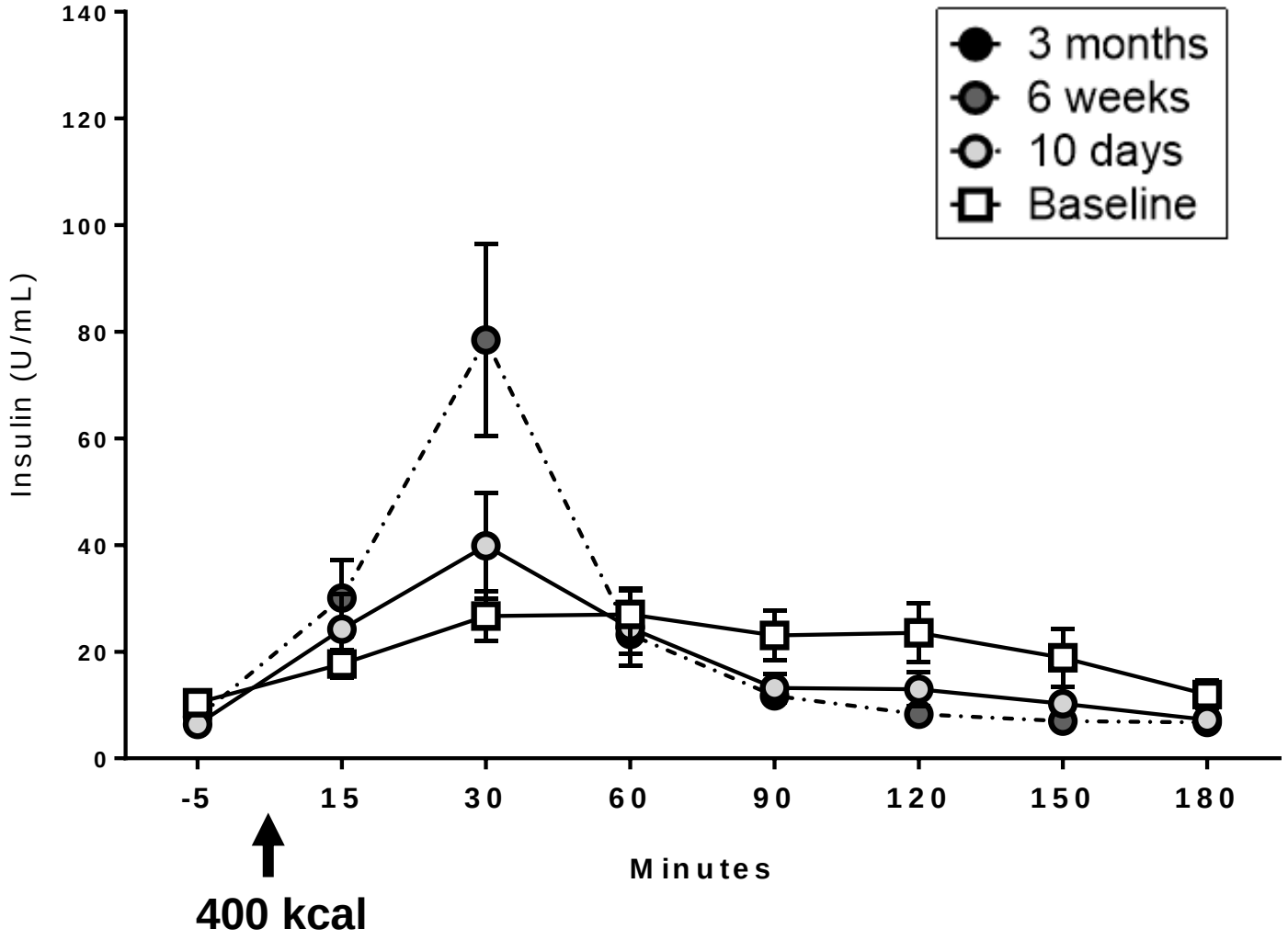
Results: Aim 1

Post-prandial insulin after oesophagectomy



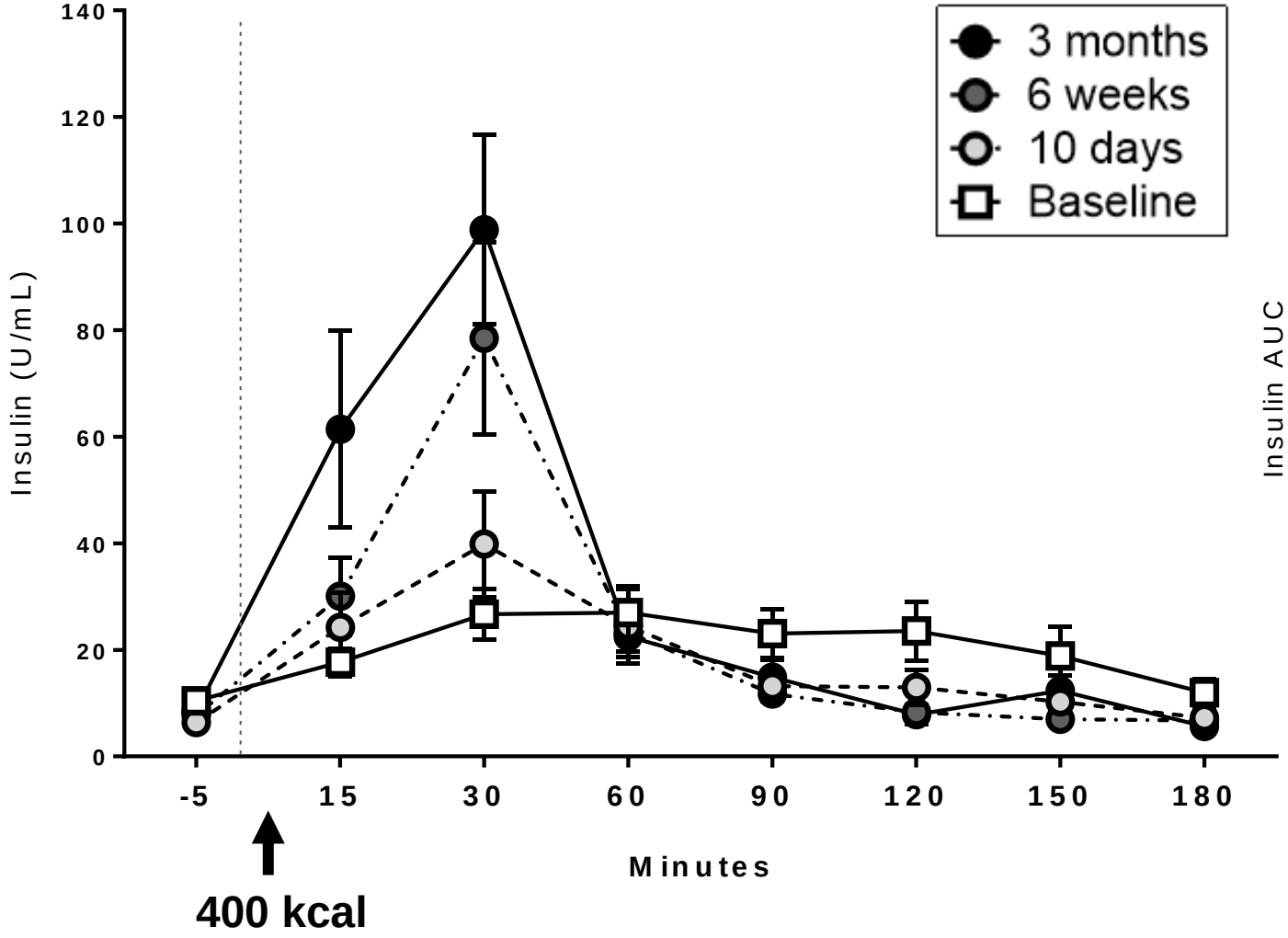
Results: Aim 1

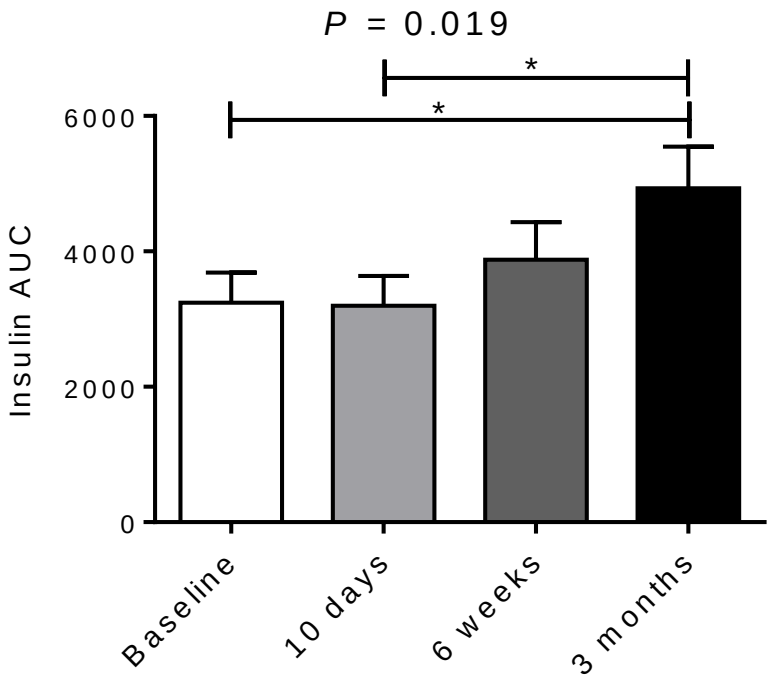
Post-prandial insulin after oesophagectomy



Results: Aim 1

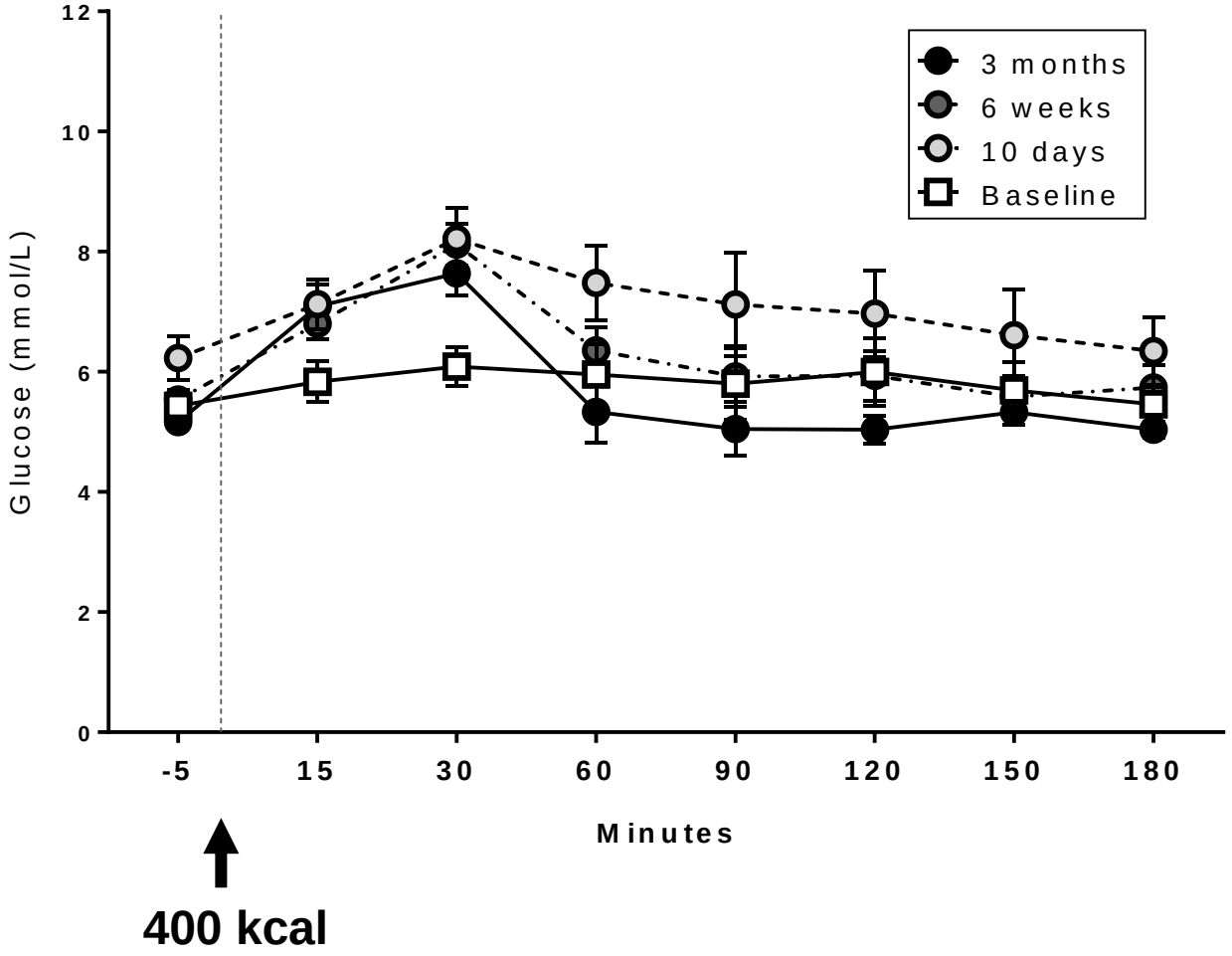
Post-prandial insulin after oesophagectomy

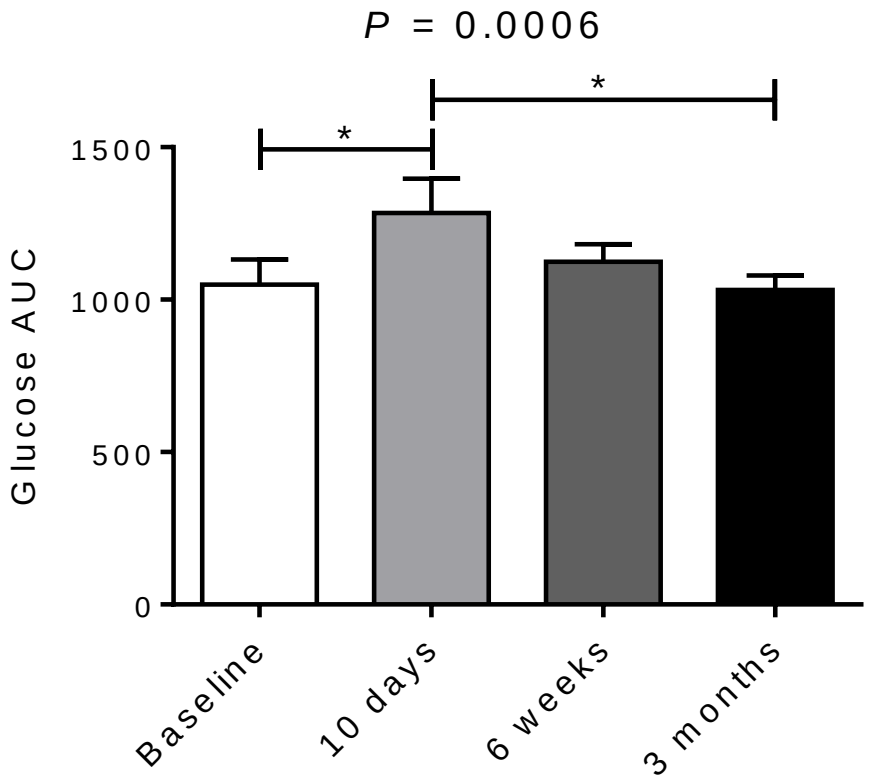




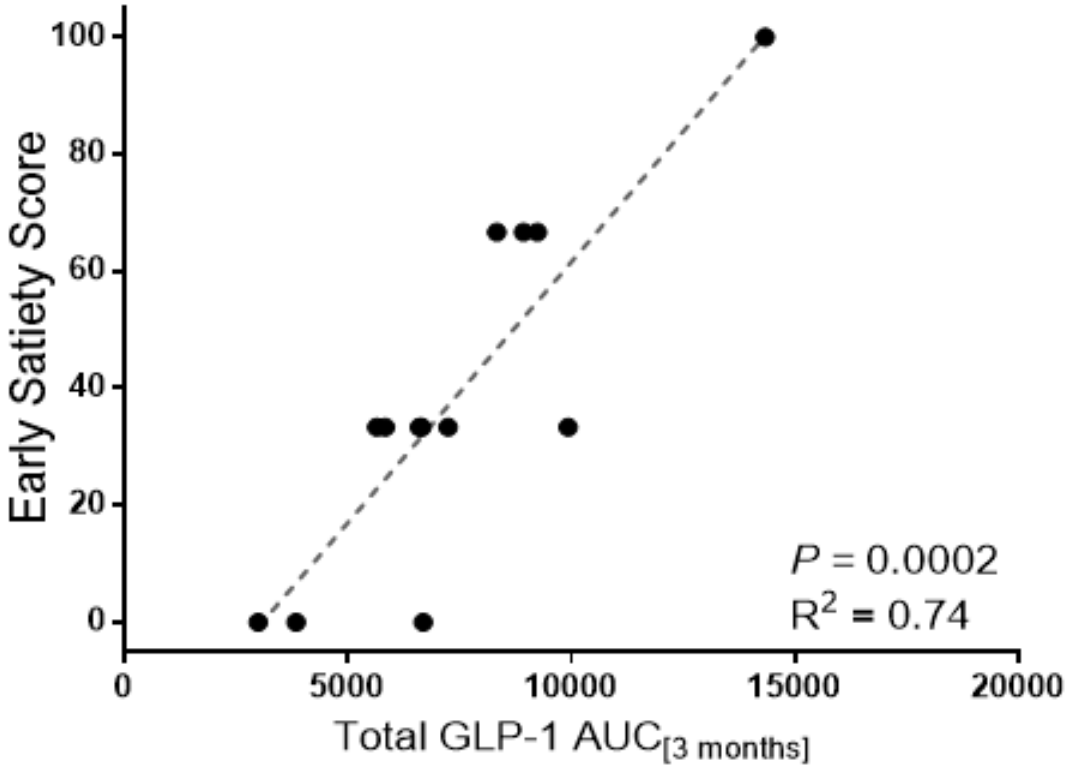
Results: Aim 1

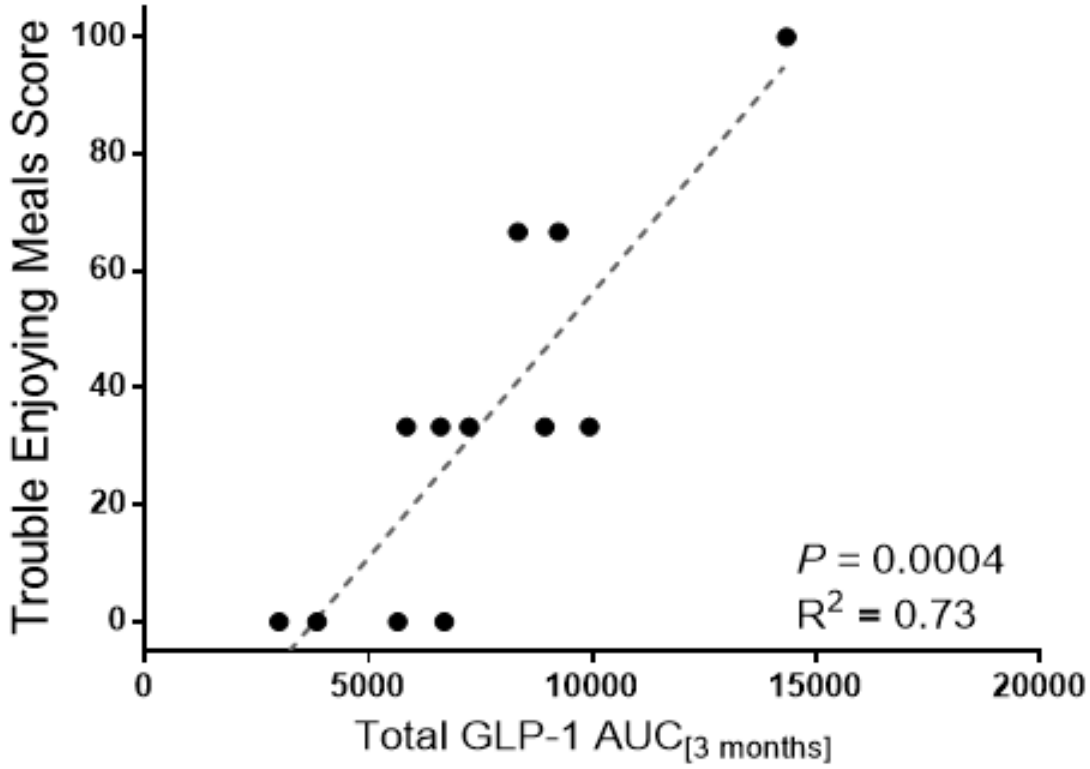
Post-prandial blood glucose after oesophagectomy





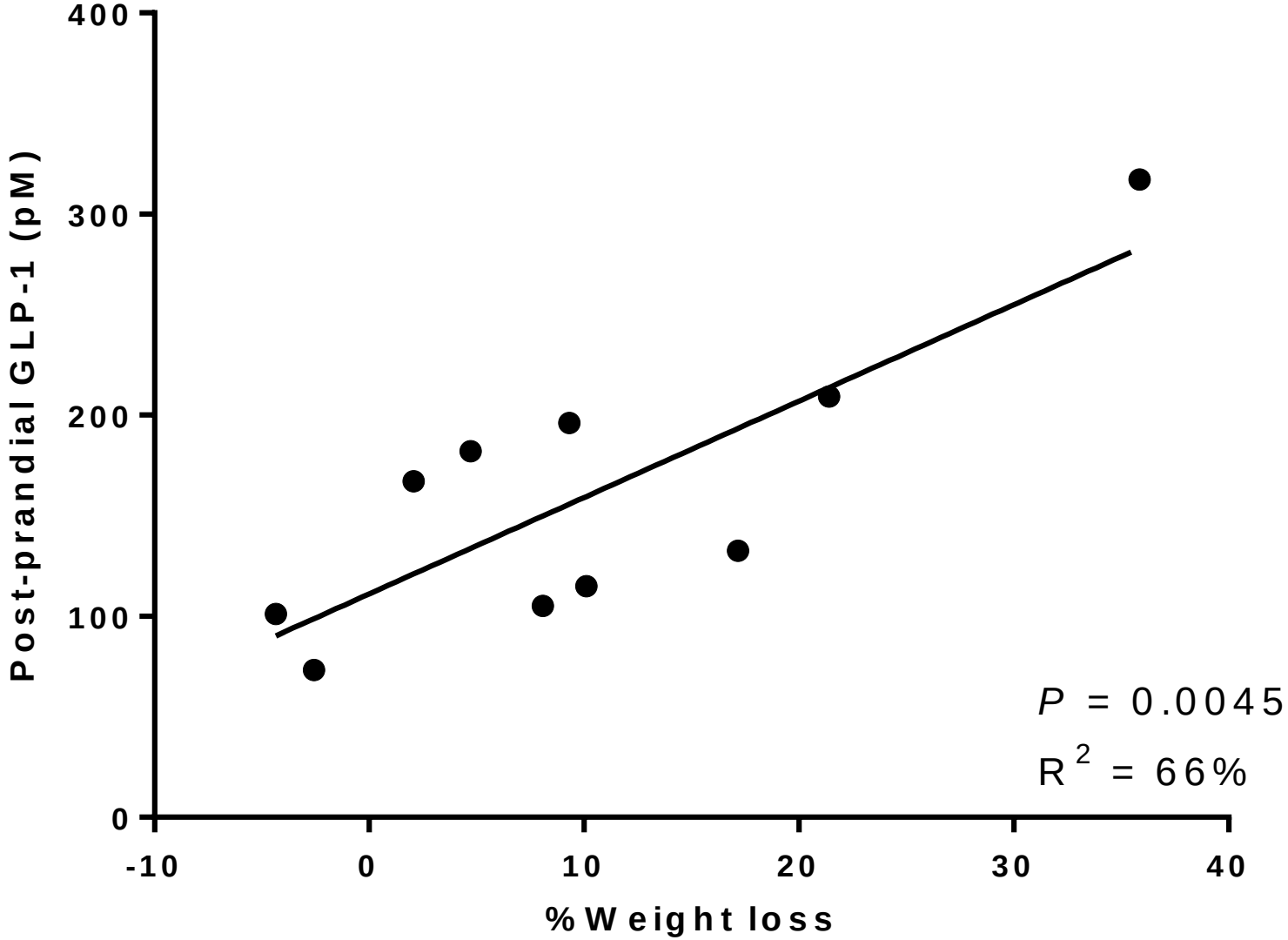
Results:
Gastrointestinal QoL and GLP-1





Aim 1: Results

Post-prandial GLP-1 levels significantly correlated with %weight loss post-oesophagectomy



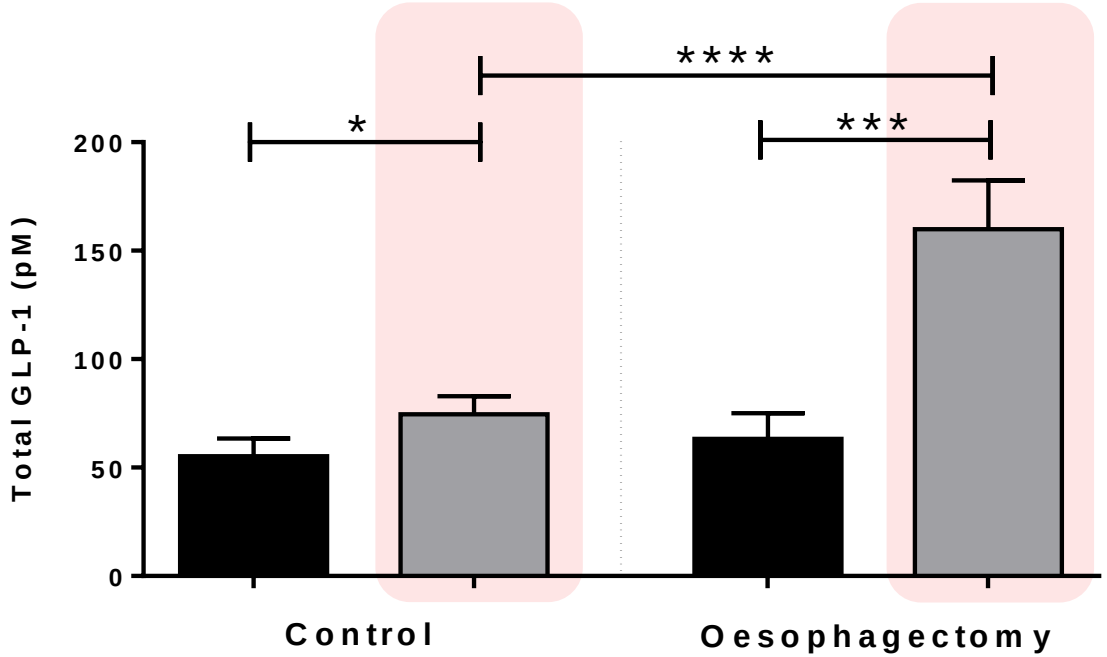
Summary: Aim 1

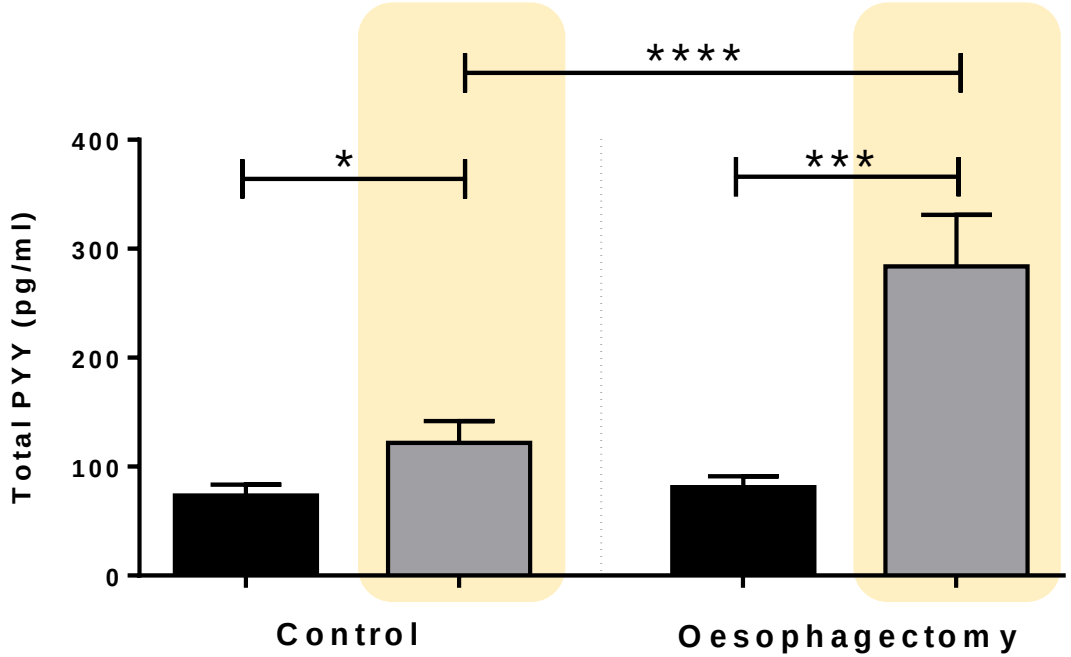
The **post-prandial satiety gut hormone response** is **significantly exaggerated** early after oesophagectomy, in association with **body weight loss** and increasing **post-ingestive symptoms**

Aim 2: Determine effect of **gut hormone blockade** on **food reward** and ***ad libitum* food intake**

Aim 2: Results

Oesophagectomy is associated with an exaggerated post-prandial satiety gut hormone response



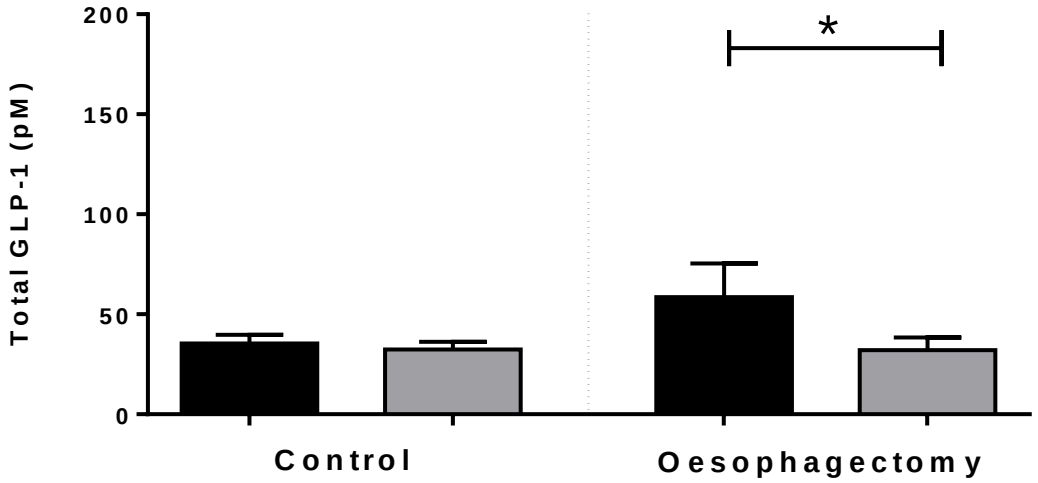


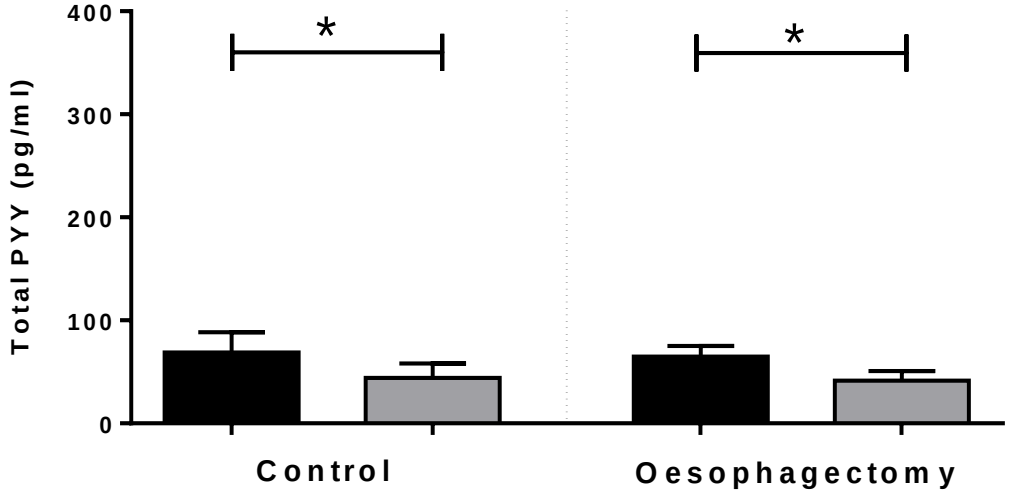
Saline day fasting [■] and post-prandial [▒] plasma GLP-1 and PYY concentrations

JA Elliott *et al*. Ann Surg, 2015

Aim 2: Results

Octreotide attenuates the post-prandial satiety gut hormone (GLP-1 and PYY) response



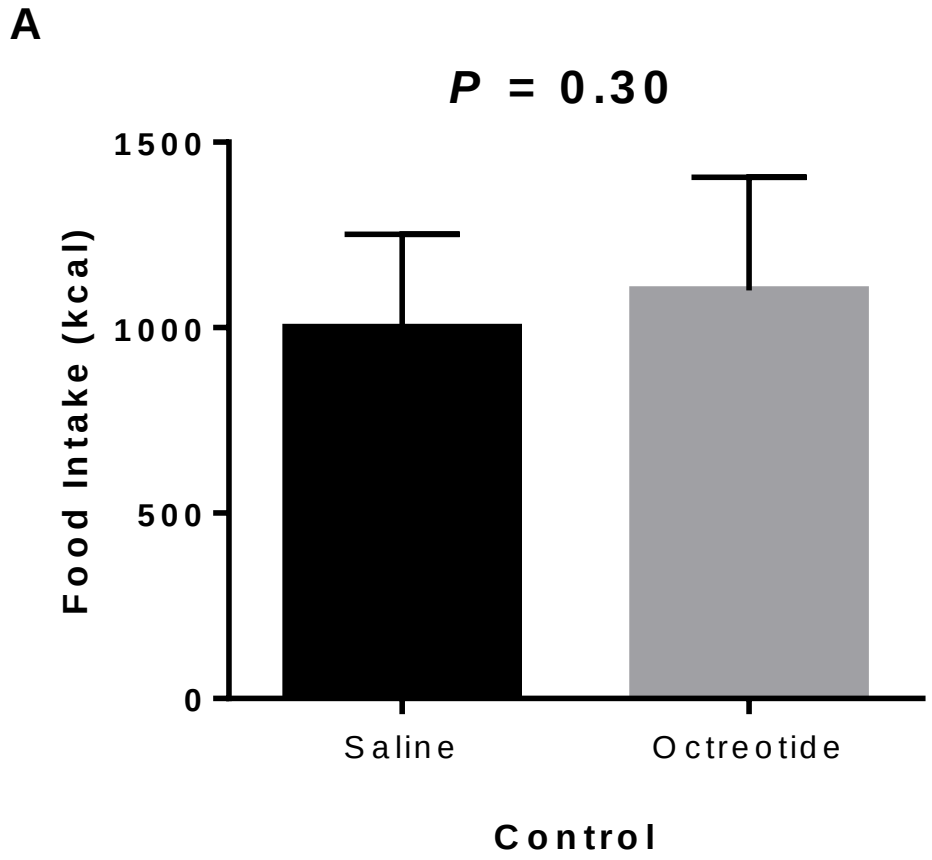


Octreotide day fasting [■] and post-prandial [□] plasma GLP-1 and PYY concentrations

JA Elliott *et al*. Ann Surg, 2015

Aim 2: Results

Single dose octreotide is associated with increased *ad libitum* calorie intake among post-oesophagectomy subjects, but not controls

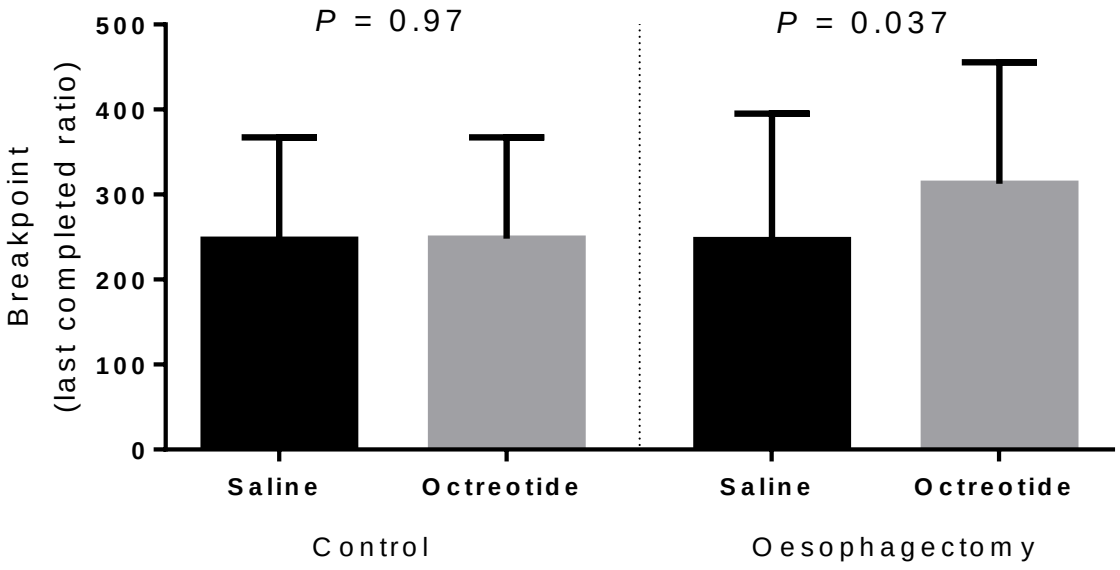


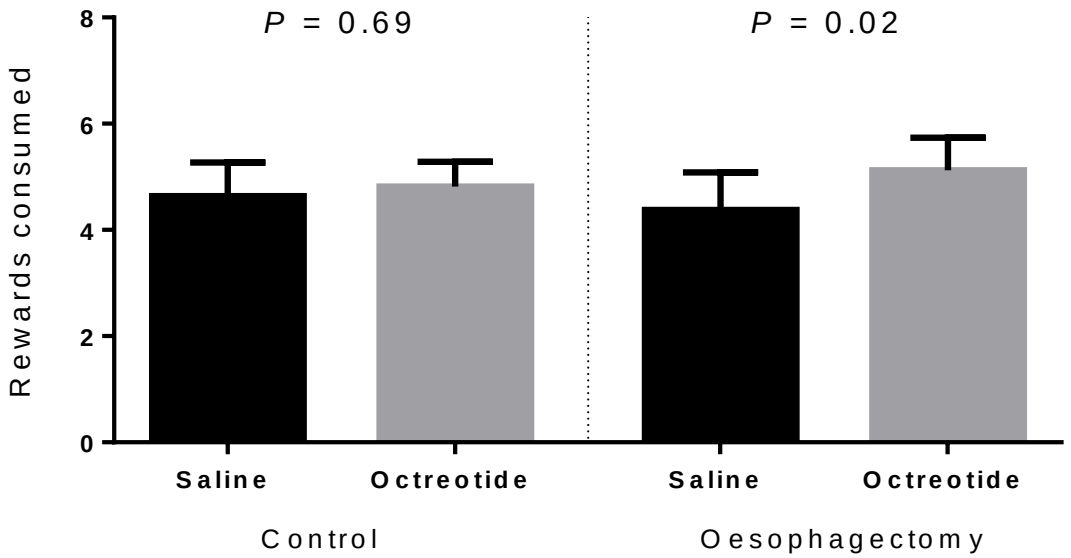
Trend towards lower calorie intake in OES group on saline day ($P = 0.085$)
No difference in calorie intake between groups on octreotide day ($P = 0.51$)

JA Elliott *et al*.
Ann Surg, 2015

Aim 2: Results

Satiety gut hormone blockade is associated with increased appetitive behaviour among post-oesophagectomy subjects, but not controls





Breakpoint ≈ Reward value of stimulus

Summary

After oesophagectomy…

1. Patients experience **significant** and **sustained body weight loss**

2. Weight loss and post-ingestive symptoms are associated with an **exaggerated post-prandial satiety gut hormone response**

3. Pharmacologic **blockade** of the **gut hormone response** increases *ad libitum* **food intake** and **food reward**

Conclusion

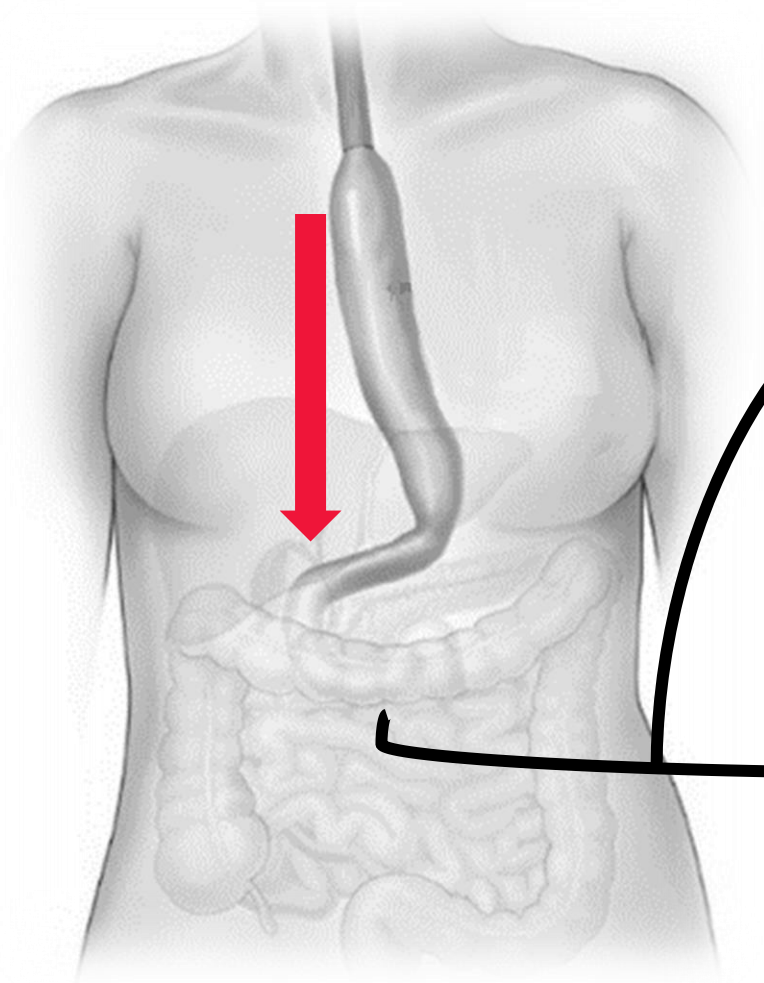
↓ Body weight
↓ GI QoL

↑Satiety
↓Food intake

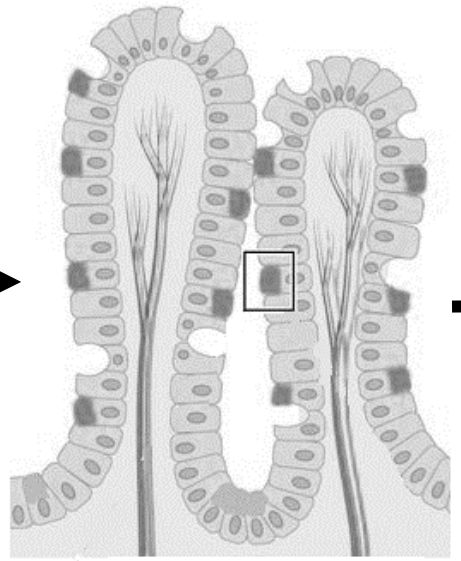
Arcuate Nucleus

Post-ingestive symptoms

GLP-1
PYY
OXM



Rapid nutrient transit



Enteroendocrine L-cell

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- Catherine Godson, Donal O'Shea,

University College Dublin

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Trinity College Dublin

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- Steve Bloom, Mohammad Ghatei, Alex Miras, Andrew Frankel, Julian Teare

King's College London

- Francesco Rubino, Stephanie Amiel, Simon Aylwin, Ameet Patel, Cynthia Borg

University of Zurich

- Thomas Lutz, Marco Bueter

Musgrove Hospital, Taunton

- Richard Welbourn, Rob Andrews, Dimitri Pournaras, Alan Osborn

Florida State University

- Prof Alan Spector

Oswaldo Hospital, Soa Paulo

- Ricardo Cohen

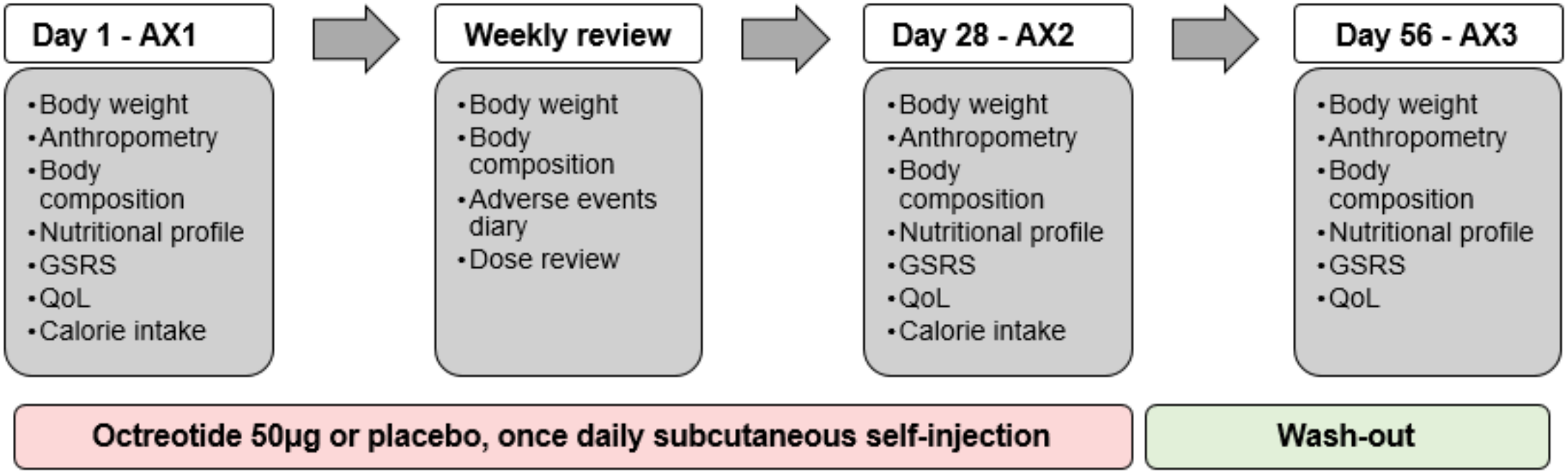
Catholic University of Chile

- Camilo Boza

Saudi Arabia

- Al-Qahtani, Ghalia Abdeen

Next steps
RCT design



Additional slides

Original article

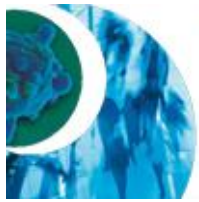
Malnutrition after oesophageal cancer surgery in Sweden

BJS

Cancer

Health-related Quality of Life Among Patients Cured by Surgery for Esophageal Cancer

Quality of life and **persisting symptoms** after oesophageal cancer surgery



EJC

EUROPEAN JOURNAL OF CANCER

cnr

CLINICAL NUTRITION RESEARCH

Comparison of **Quality of Life** and **Nutritional Status** in Gastric Cancer Patients Undergoing Gastrectomies

Remapping the Body: Learning to Eat Again After Surgery for Esophageal Cancer

Long-term effect of **radical gastrectomy** on **nutrition** and immunity

SURGERY TODAY

Mechanisms of increased gut nutrient sensing post-bariatric surgery – parallels in upper GI/HPB?

OPEN ACCESS Freely available online

PLOS | ONE

Hypertrophy Dependent Doubling of L-Cells in Roux-en-Y Gastric Bypass Operated Rats

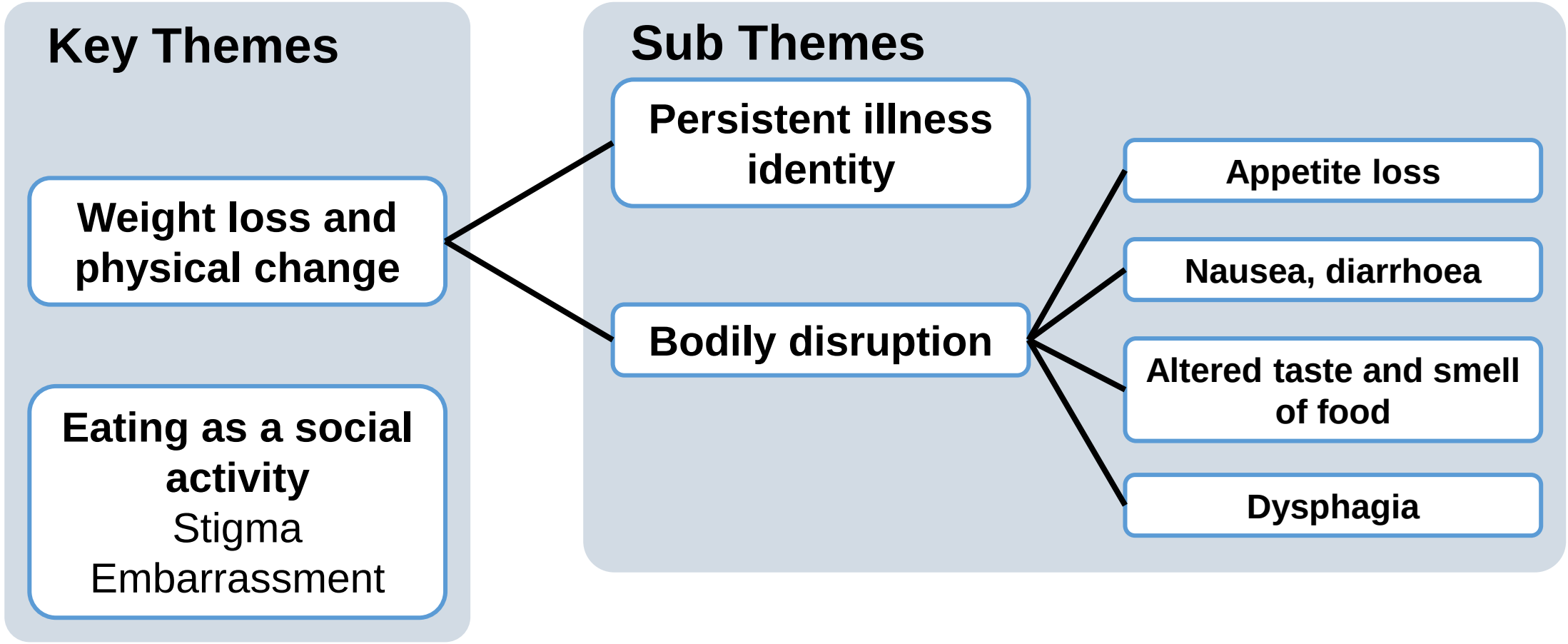
Carl Frederik Hansen[1,2], Marco Bueter[3,4], Nadine Theis[5], Thomas Lutz[4,5], Sarah Paulsen[1], Louise S. Dalbøge[1], Niels Vrang[1], Jacob Jelsing[1]*

ANNALS OF SURGERY

Gut Hypertrophy After Gastric Bypass Is Associated With Increased Glucagon-Like Peptide 2 and Intestinal Crypt Cell Proliferation

Carel W. le Roux, MRCP, PhD, Cynthia Borg, FRCS,† Katharina Wallis, MRCP,* Royce P. Vincent, MBChB,* Marco Bueter, MD,* Robert Goodlad, PhD,‡ Mohammed A. Ghatei, PhD,* Ameet Patel, FRCS,† Stephen R. Bloom, FRCP, DSc,* and Simon J. B. Aylwin, FRCP, PhD§*

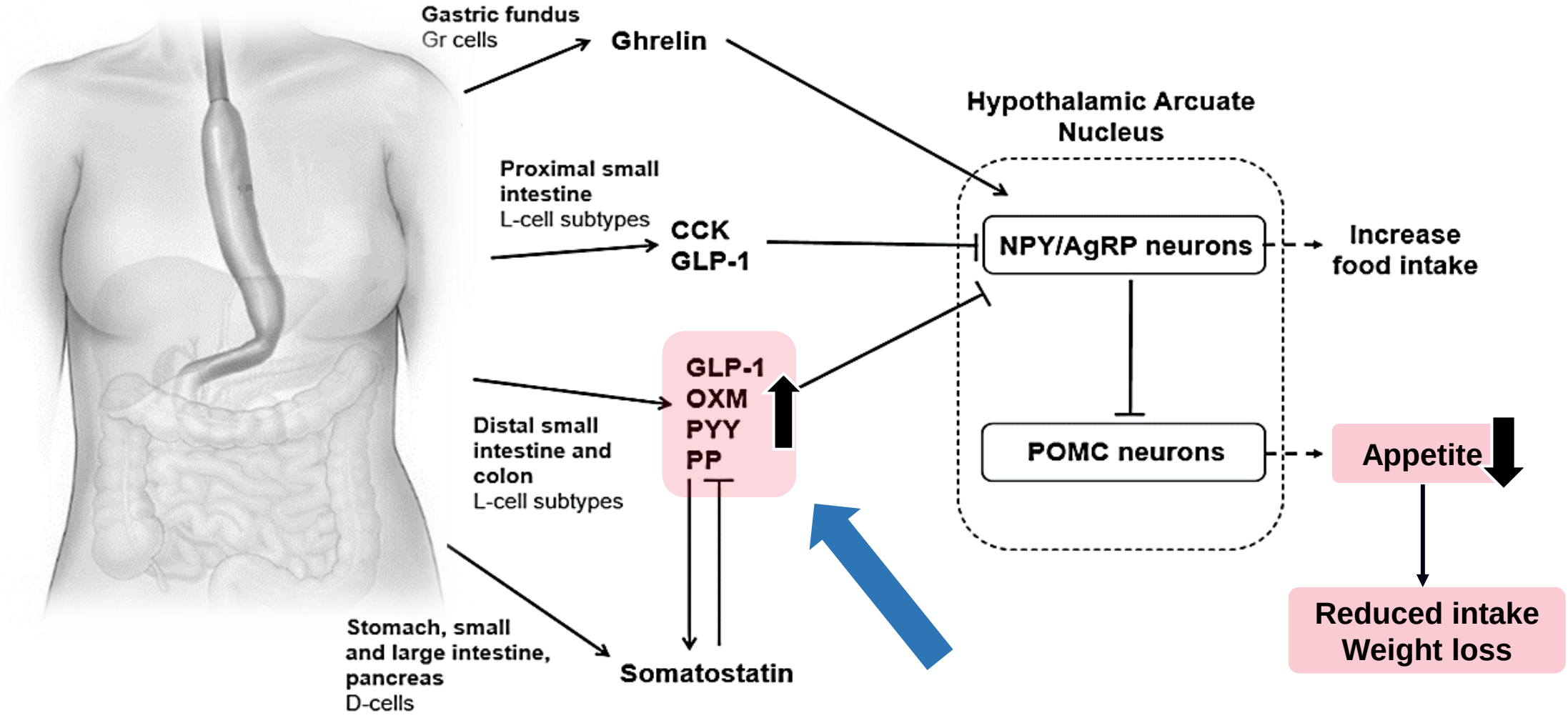
Appetite, post-ingestive symptoms and quality of life after oesophagectomy



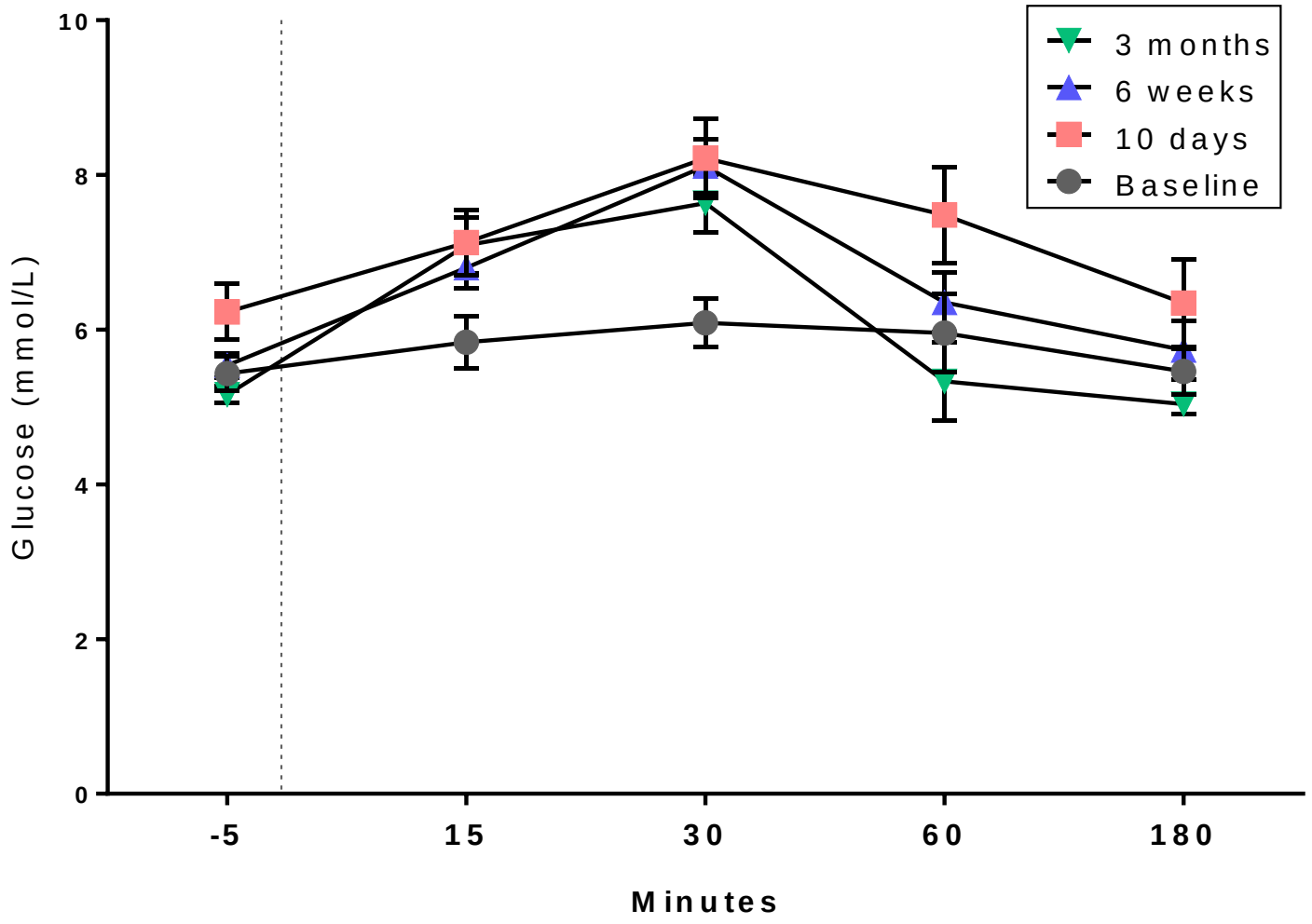
Adapted from Wainwright, Blazeby *et al*.
Qualitative Health Research, 2007

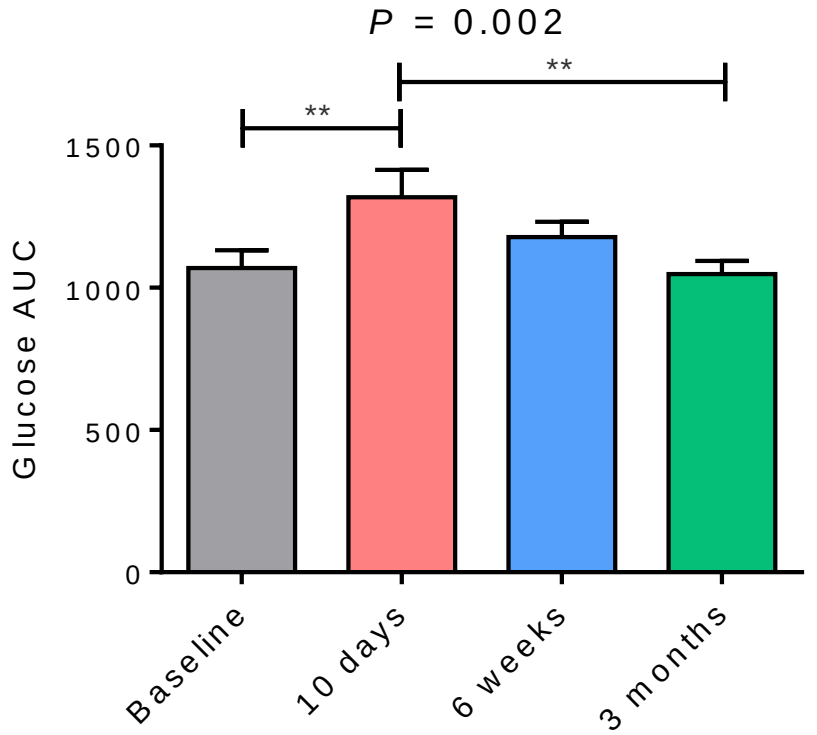
Conclusion

Exaggerated post-prandial gut hormone responses mediate appetite changes post-oesophagectomy**,** offering a **novel target** for **appetite modulation** in this cohort



Post-prandial blood glucose after oesophagectomy





Ghrelin and body weight loss after oesophagectomy

Author	Year	N	Surgery	DF	Time-points	Outcome
Doki	2006	9, 26	• 2SE • WS (28), GCC (7) • Digital pyloric bougie	Yes	• 3 and 7 days (n=9) • 25 (3-67) months (n=26)	• 51.4% and 49.8% of baseline at days 3 and 7 • 107.4% of baseline at 25 (5-67) months • Ghrelin levels negatively correlated with ΔBMI at <36 months • Ghrelin levels positively correlated with time since surgery • No difference between WS or GCC reconstruction
Koizumi	2011	22	• 2SE/3SE • GCC • Digital pyloric bougie	No	• Pre-operative • 1, 3, 6, 12 months post	• Ghrelin reduction at 1 month (63.9%) recovered to 75.8%, 99.7% at 3, 6 months post • Appropriate rebound at 12 months (125.0%) but continued BWL • Appetite score increases over time from surgery • Correlation between appetite score and ghrelin
Miyazaki	2012	25	• 2SE/3SE • GCC	No	• Pre-operative • 7 days • 6-24 months • >36 months	• 38.7% of baseline at day 7 ($P < 0.01$) • 56.0% of baseline at 22.1 (6-24) months ($P < 0.05$) • 111.6% of baseline at 53.4 (39–80) months • %ΔGhrelin correlated with %BWL at 6-24 months, but not at >36 months
Yamamoto	2013	20	• 3SE • GCC	Yes	• Pre-operative • Day 0, 1, 3, 10	• 33% (15-90%) baseline at day 1 • 50% baseline at day 3-10

DF, disease-free; 2SE, 2-stage oesophagectomy; 3SE, 3-stage oesophagectomy; WS, whole stomach; GCC, greater curvature conduit; BMI, body mass index; BWL, body weight loss