Appetite, Glycemia and Entero-Insular Hormone Responses Differ Between Oral, Gastric-Remnant and Duodenal Administration of a Mixed Meal Test After Roux-en-Y Gastric Bypass

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Appetite, Glycemia, and Entero-Insular Hormone Responses Differ Between Oral, Gastric-Remnant, and Duodenal Administration of a Mixed-Meal Test After Roux-en-Y Gastric Bypass

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How a surgical complication provided an experimental model….

Baseline

37 years old male patient, non-diabetic

RYGB for severe obesity (BMI 43 kg/m^2) in a peripheral hospital

4 months

Reoperation for internal hernia, complicated by intestinal perforation

Postoperative septic shock -> transfer our tertiary bariatric referral center

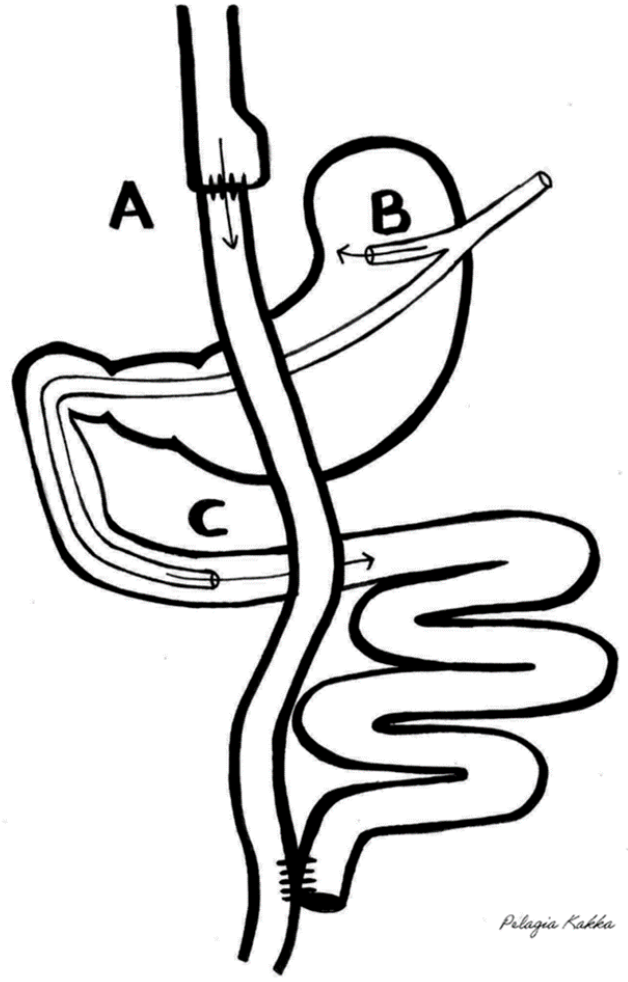
Upon arrival at USZ:

Laparotomy to repair intestinal perforations

Insertion of a double-lumen percutaneous gastrostomy to the remnant stomach

- gastric decompression
- post-pyloric enteral nutrition (tip of line: D3)

6 months -> weight stabilized (BMI = 35 kg/m^2), good general condition



Bariatric surgery's effect on Type 2 diabetes mellitus

American Diabetes Association. Diabetes Care

Metabolic Surgery in the Treatment Algorithm for Type 2 Diabetes: A Joint Statement by International Diabetes Organizations

*Francesco Rubino,[1] David M. Nathan,[2] Robert H. Eckel,[3] Philip R. Schauer,[4] K. George M.M. Alberti,[5] Paul Z. Zimmet,[6] Stefano Del Prato,[7] Linong Ji,[8] Shaukat M. Sadikot,[9] William H. Herman,[10] Stephanie A. Amiel,[1] Lee M. Kaplan,[2] Gaspar Taroncher-Oldenburg,[11] and David E. Cummings,[12] on behalf of the Delegates of the 2nd Diabetes Surgery Summit**

Diabetes Care 2016;39:861–877 | DOI: 10.2337/dc16-0236

IFSO

REVIEW ARTICLE

The Long-Term Effects of Bariatric Surgery on Type 2 Diabetes Remission, Microvascular and Macrovascular Complications, and Mortality: a Systematic Review and Meta-Analysis

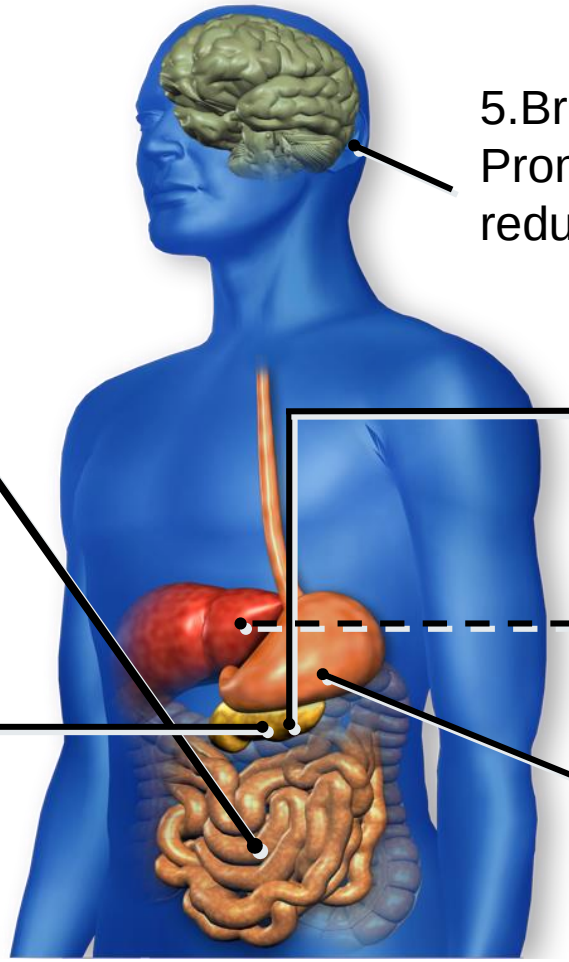
Binwu Sheng[1] · Khoa Truong[2] · Hugh Spitler[2] · Lu Zhang[2] · Xuetao Tong[3] · Liwei Chen[2]

Bariatric surgery's effect on Type 2 diabetes mellitus

1. Weight-loss independent improvement of T2DM
2. Different effect of different surgical procedures
3. Gut-hormones play a key role

GLP-1 effects in humans

GLP-1 secreted upon the ingestion of food
Half-life = 2-3 min



5.Brain:
Promotes satiety and reduces appetite[4,5]

2.α-cell:
Suppresses postprandial glucagon secretion[1]

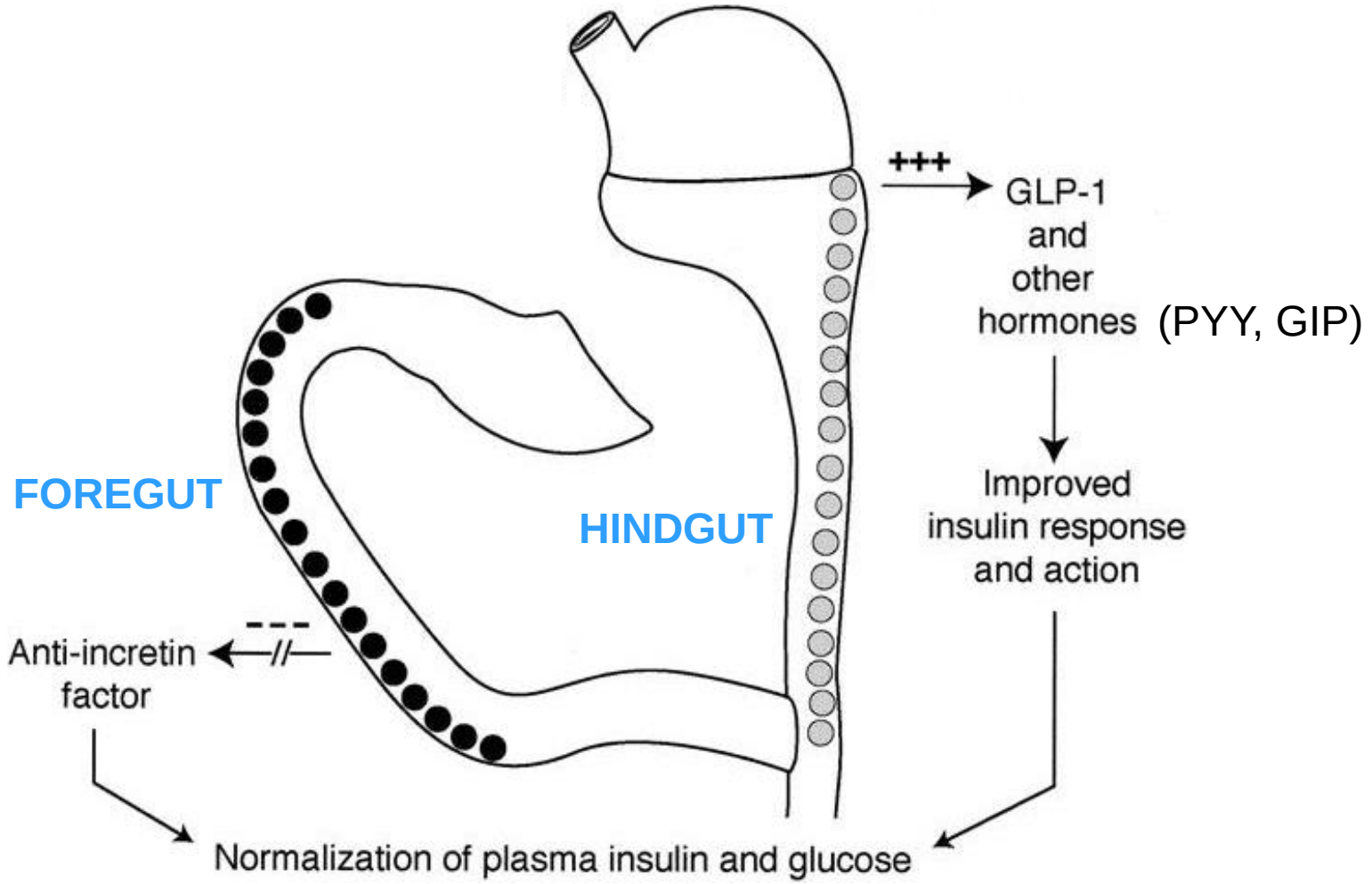
3.Liver:
reduces hepatic glucose output[2]

4.Stomach:
slows the rate of gastric emptying[3]

1.β-cell:
Enhances glucose-dependent insulin secretion in the pancreas
= **INCRETIN**[1]

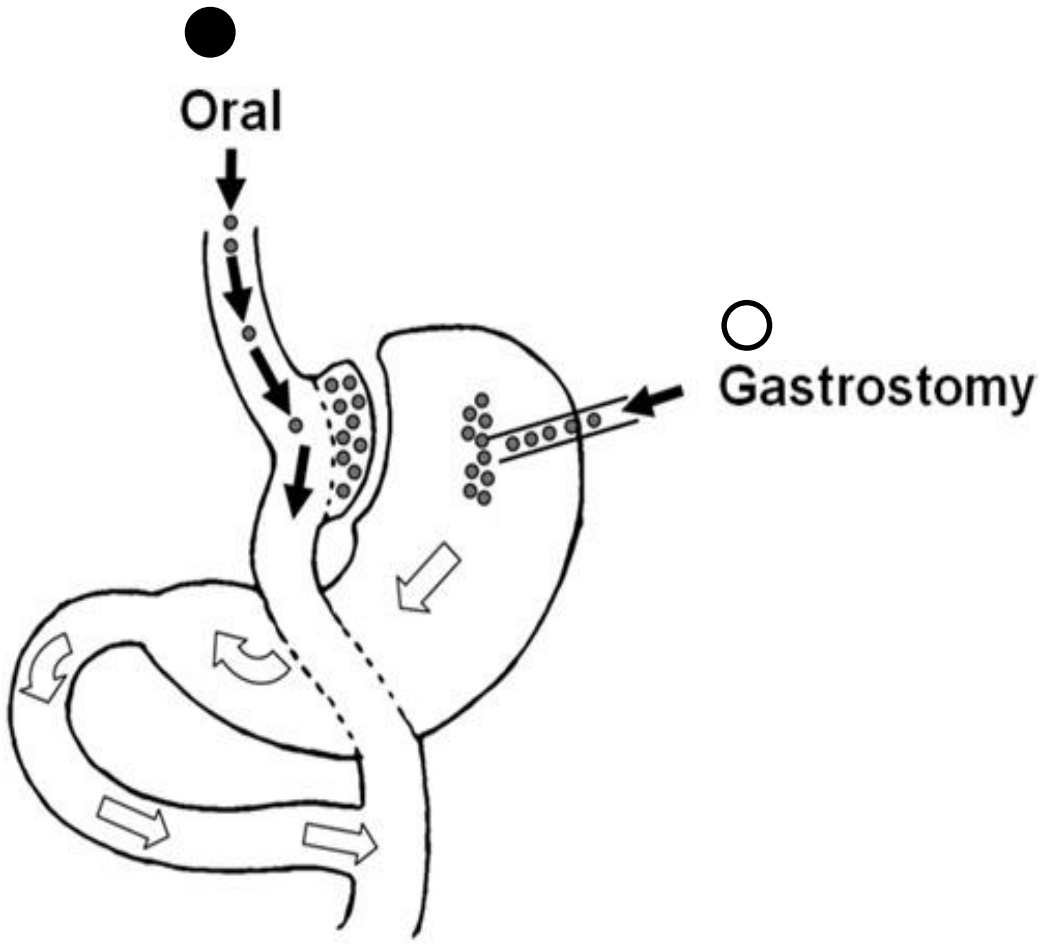
Adapted from [1]Nauck MA, et al. *Diabetologia* 1993;36:741–744; [2]Larsson H, et al. *Acta Physiol Scand* 1997;160:413–422; [3]Nauck MA, et al. *Diabetologia* 1996;39:1546–1553; [4]Flint A, et al. *J Clin Invest* 1998;101:515–520; [5]Zander et al. *Lancet* 2002;359:824–830.

Glycemic control after RYGB: Mechanism?

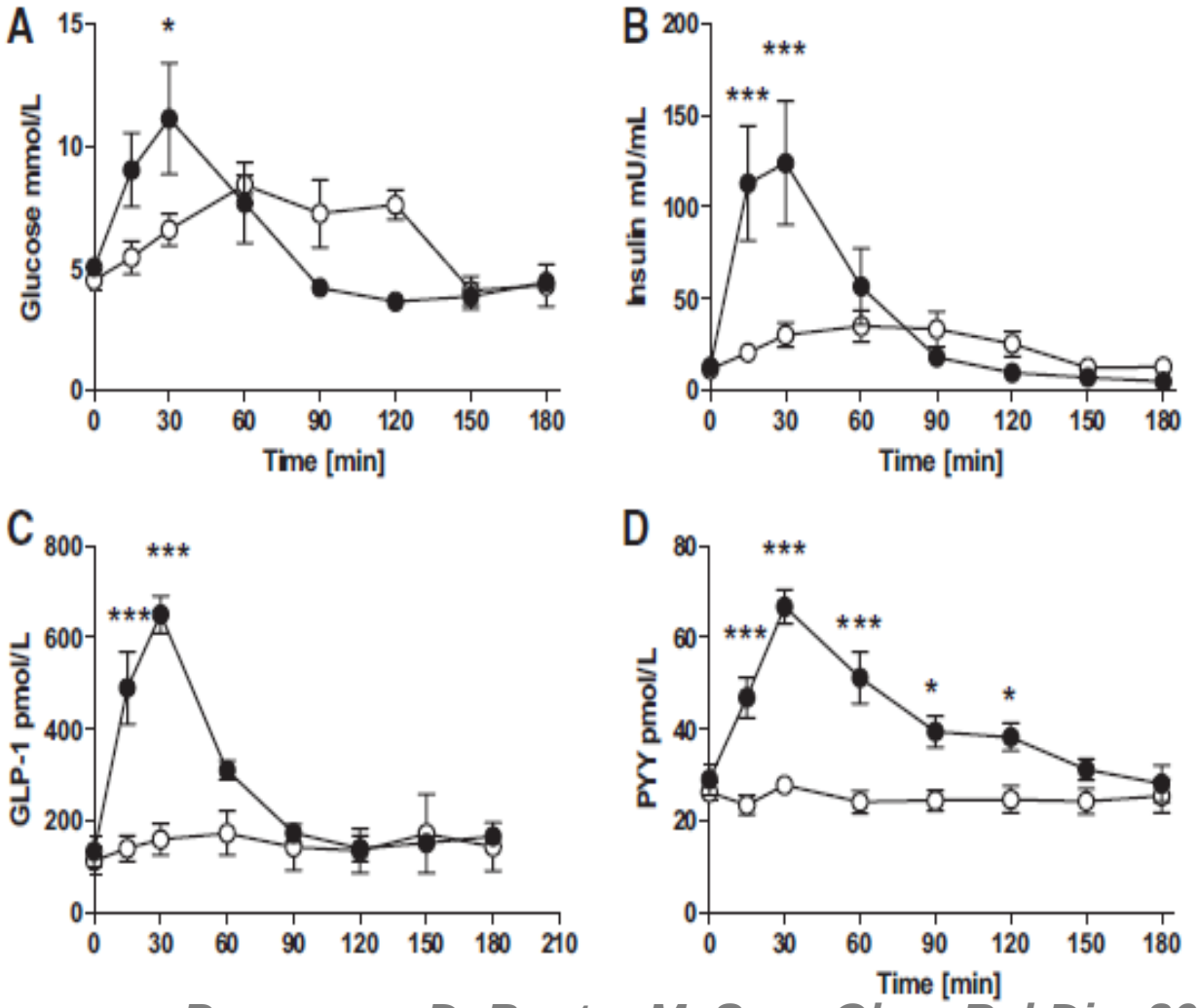


Rubino. Ann Surg. 2002

Post-bariatric gut hormone response in humans
Switching on/off the RYGB

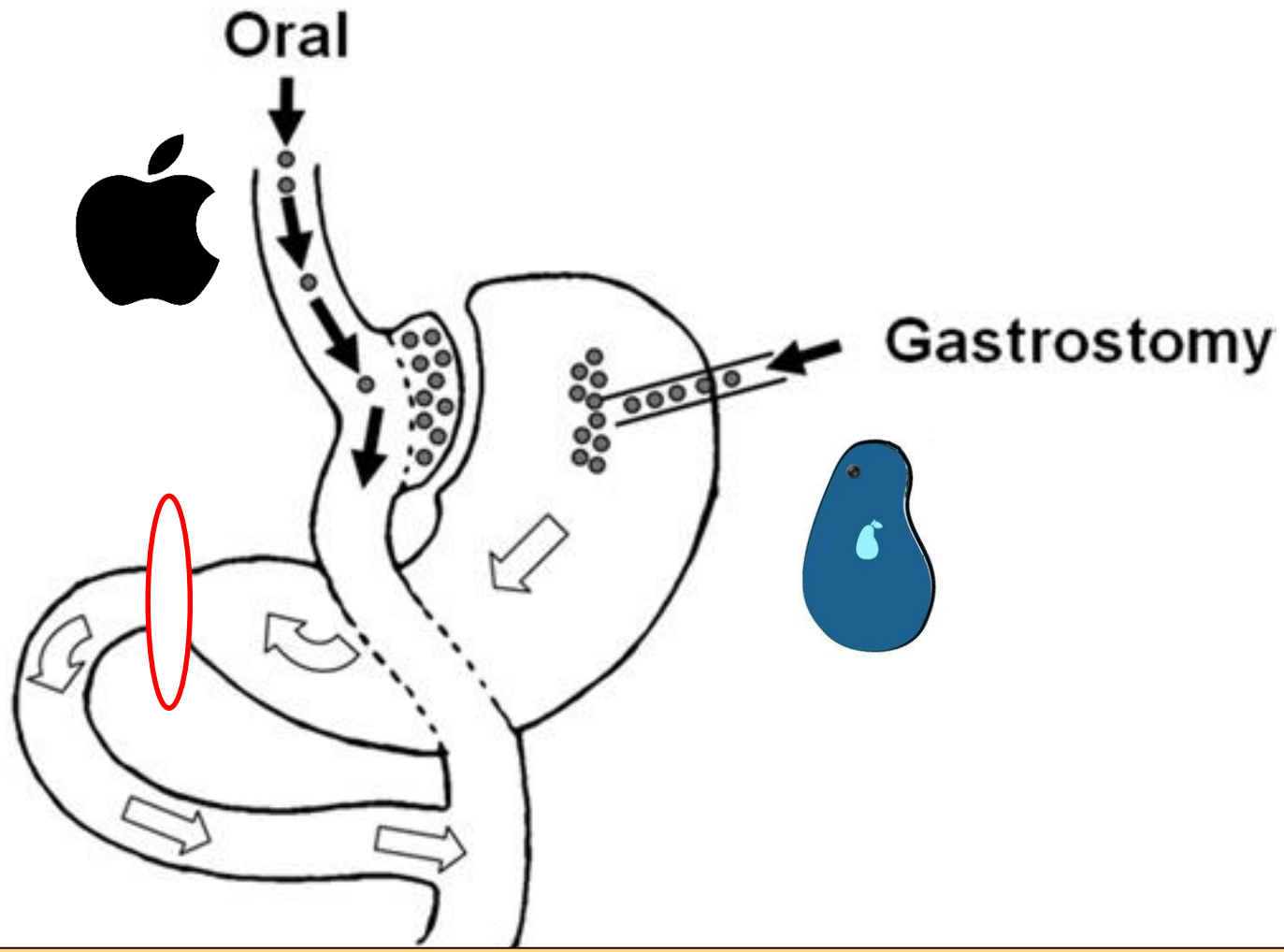


ClinicalTrials.gov Identifier: NCT01025999



Pournaras D, Bueter M, Surg Obes Rel Dis. 2012
Dirksen C, Diab Care. 2010

Systemic bias in study design



Speed of food arrival into the intestines might matter

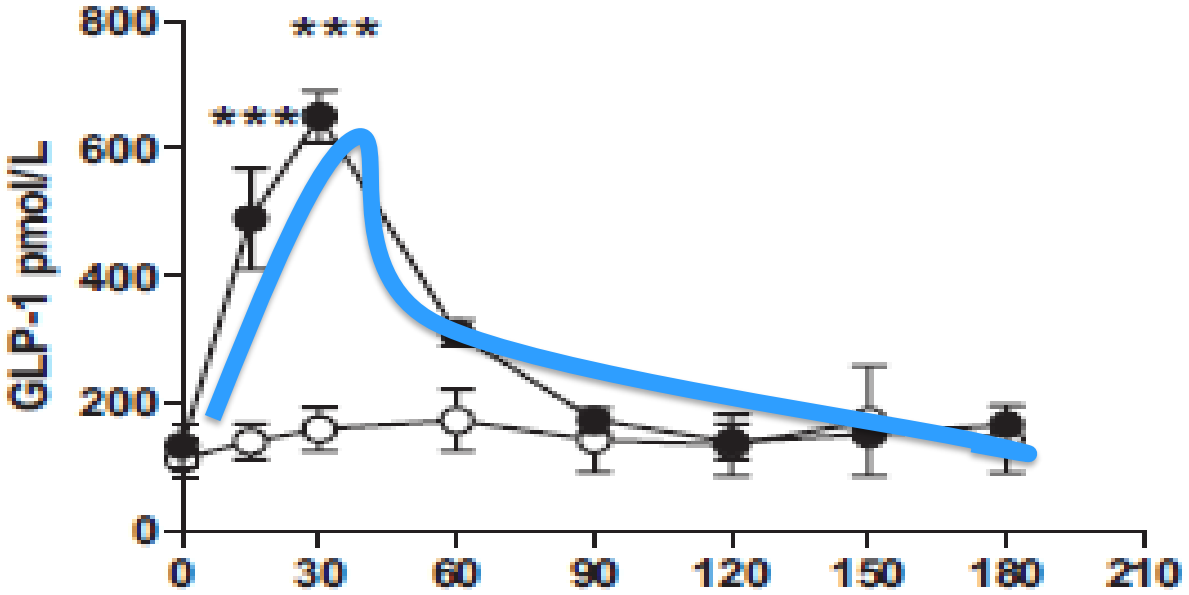
Ma. Diabet Med. 2012

Our hypothesis

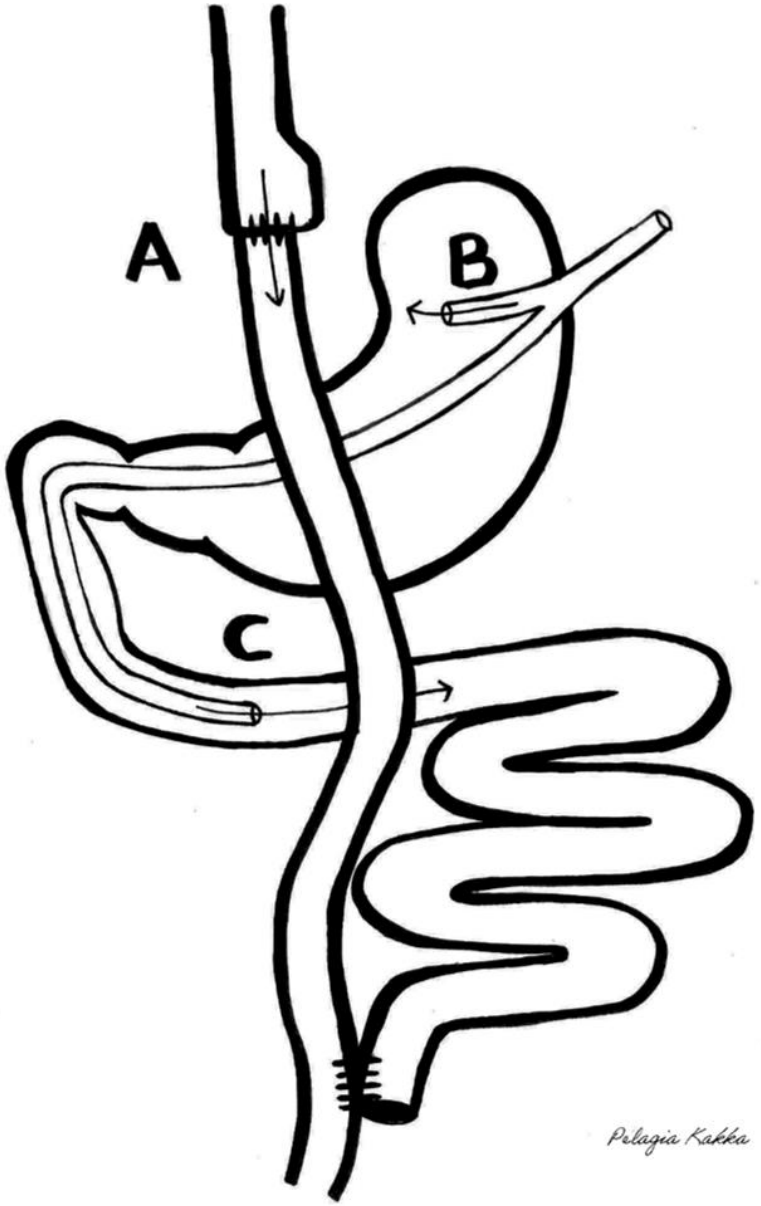
Nutrients delivered into the <u>duodenum</u> lead to

a. comparable changes in **Gut hormones**, **Glucose metabolism** & **Appetite** as <u>orally</u>

b. but different to the <u>gastrostomy</u>



New concept



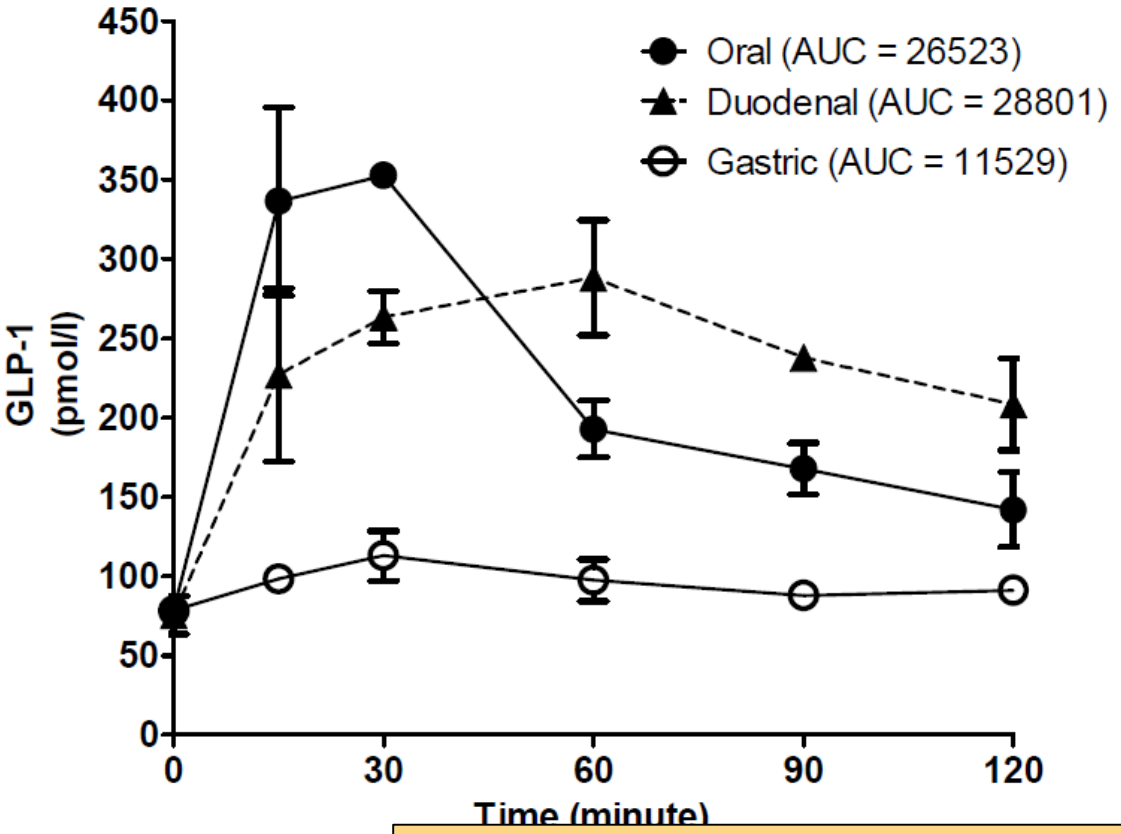
<u>Design</u>
Resource 200 ml test meal in 4min
Baseline to 120 min blood tests
2x each route

<u>Gastric emptying assessment</u>
Gastrografin with X-ray 30min later

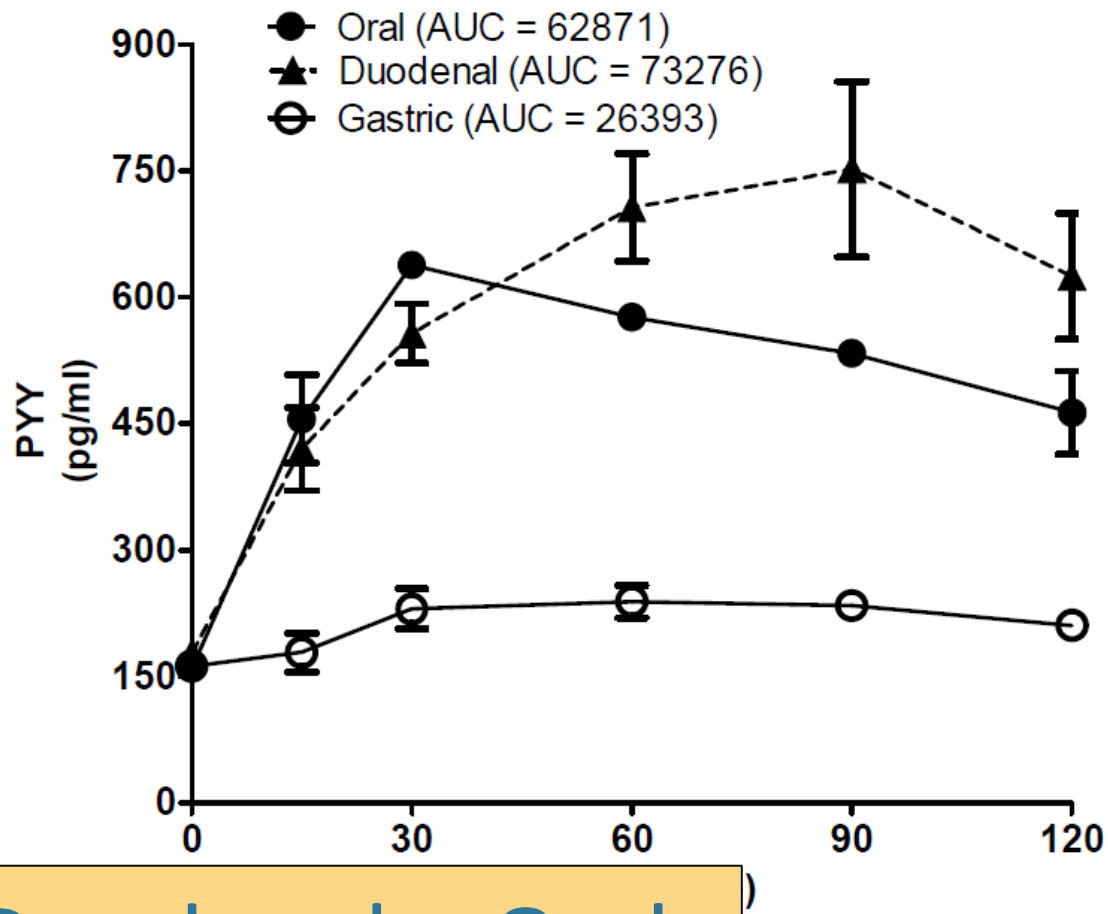
<u>Ethical approval</u>
Cantonal Ethics Committee of Zürich
BASEC-Nr. Req-2017-0616

Gut hormone response

GLP-1

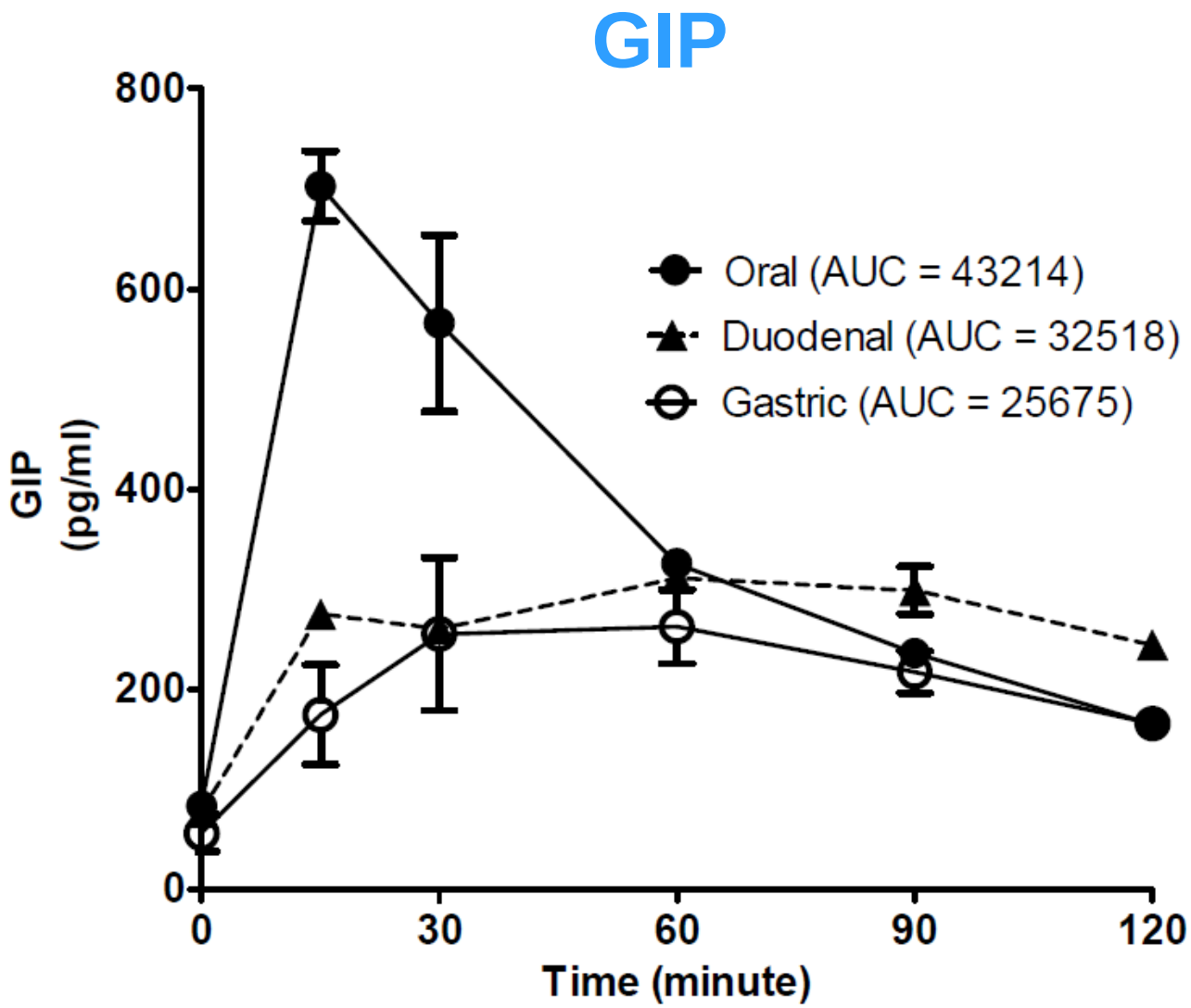


PYY



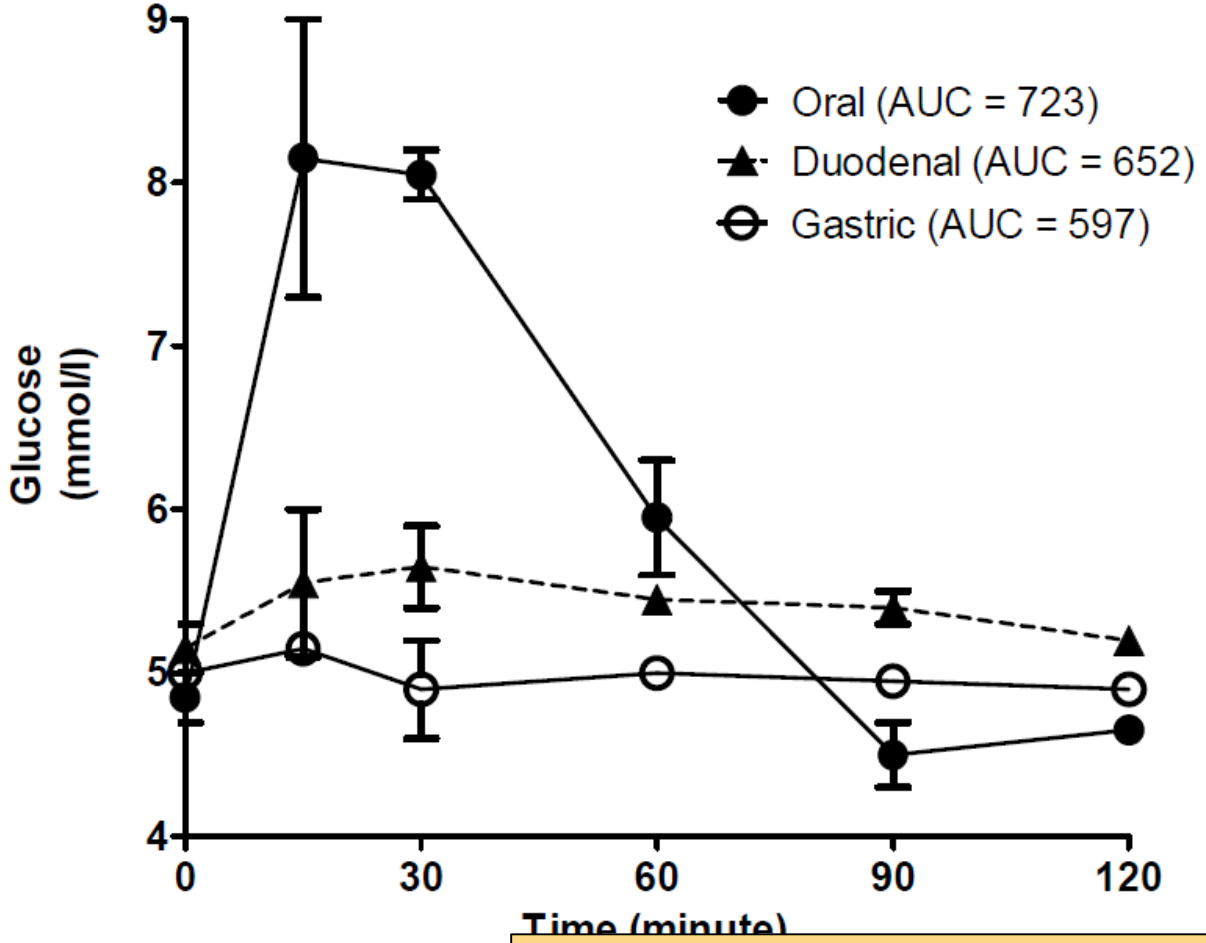
Hypothesis: Correct! Duodenal = Oral

Gut hormone response

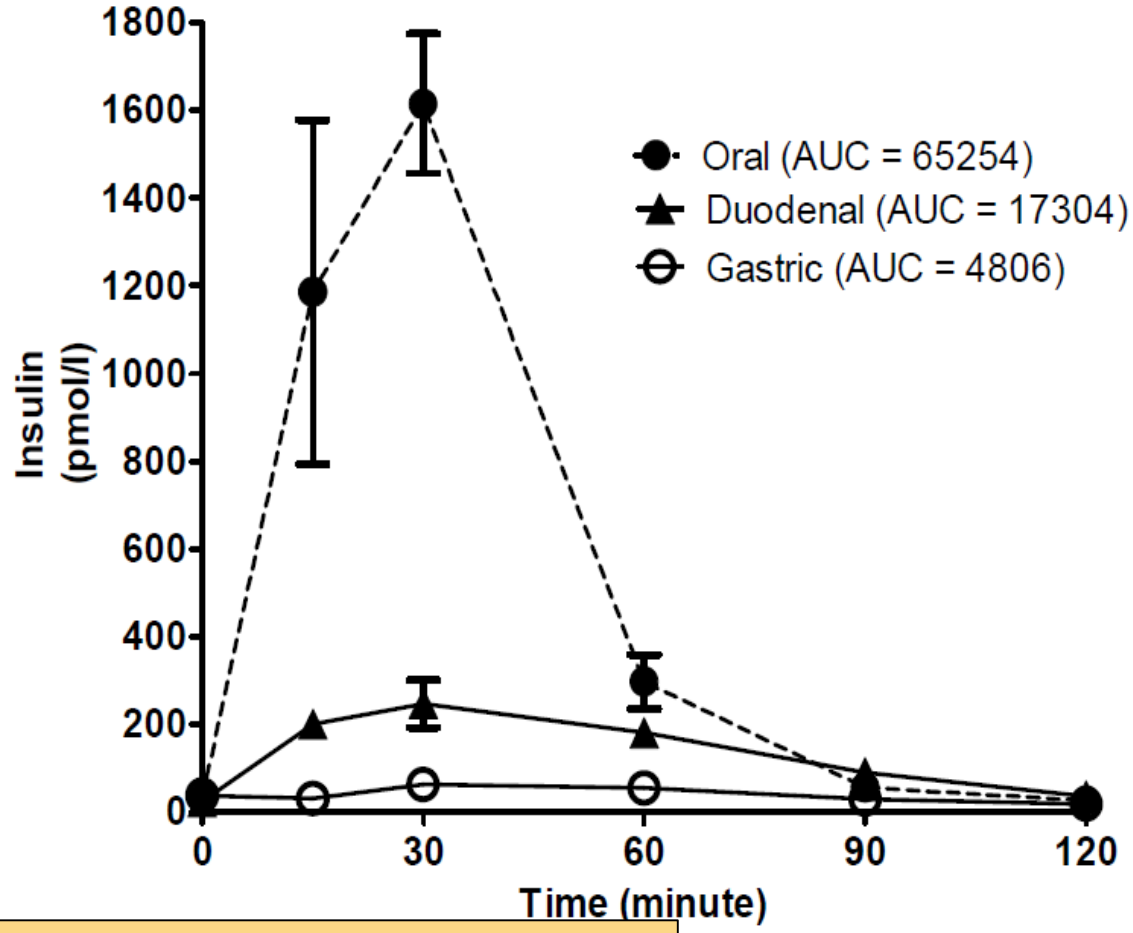


Glucose metabolism

Glucose



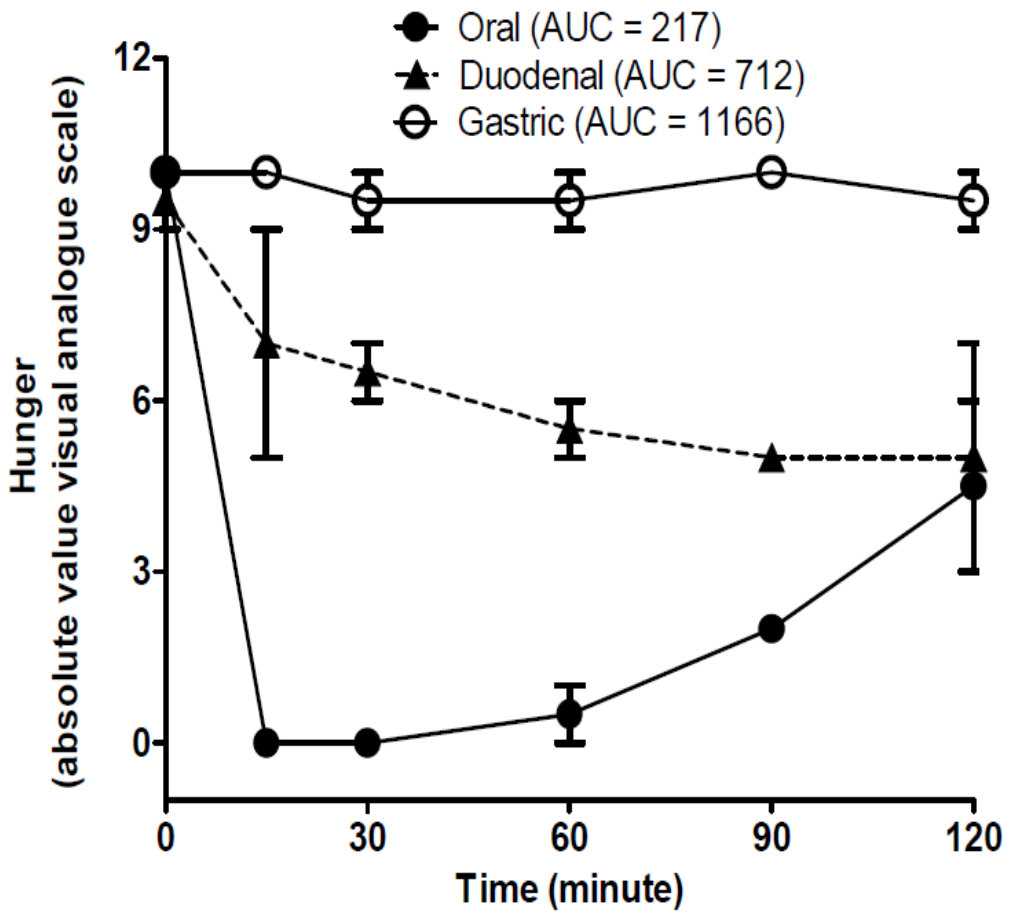
Insulin



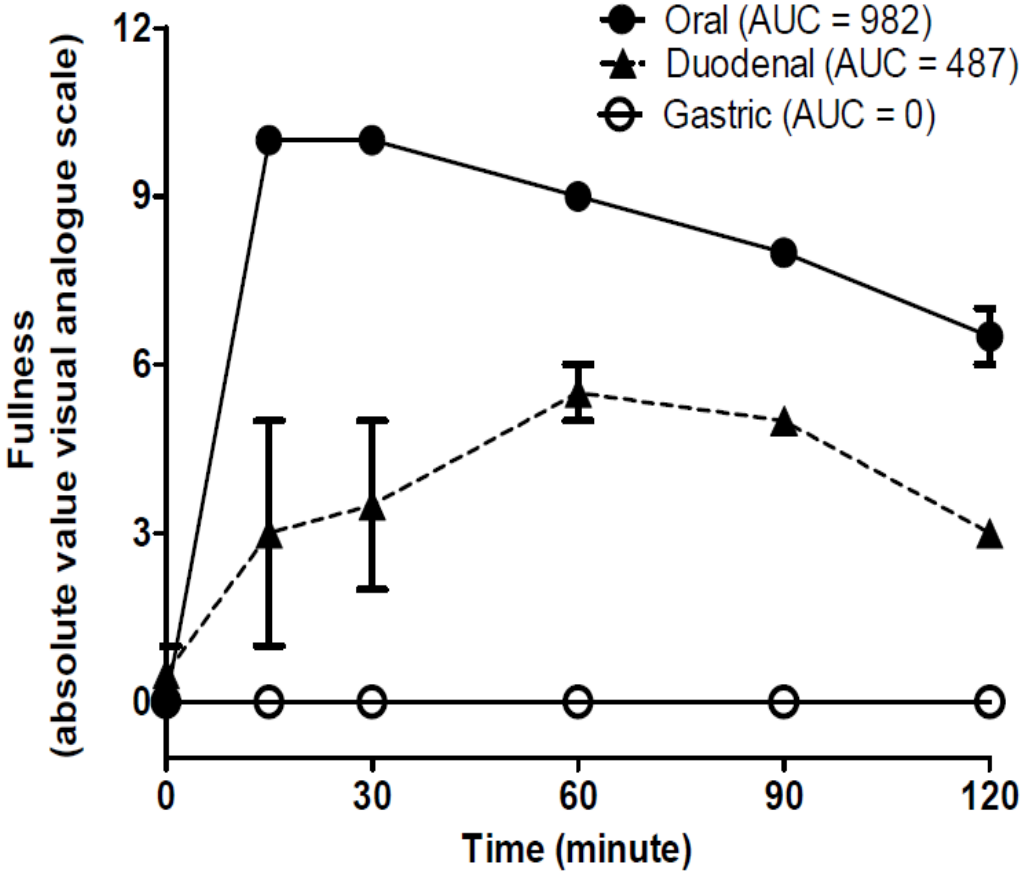
Other factors may play a role…

Appetite (Visual analogue scale)

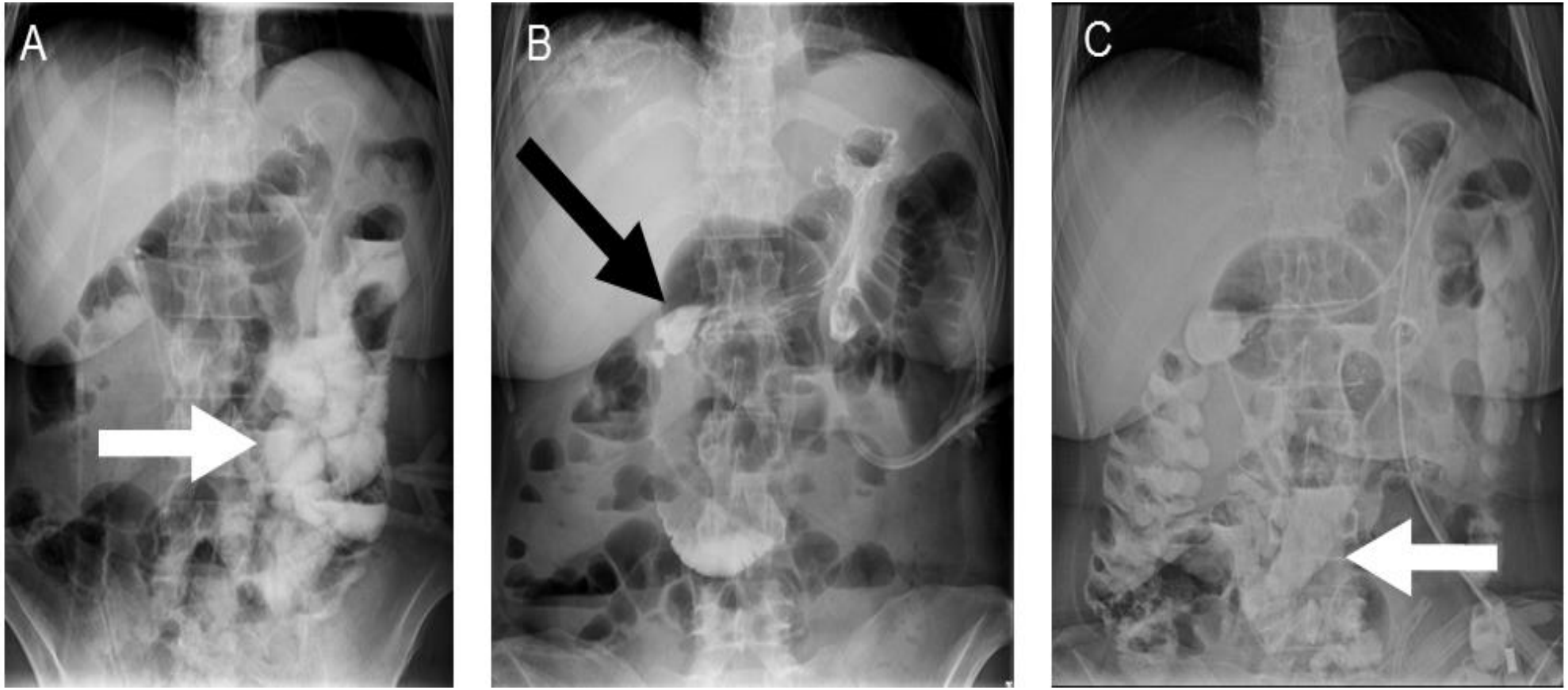
Hunger



Fullness



Gastric emptying at 20 minutes



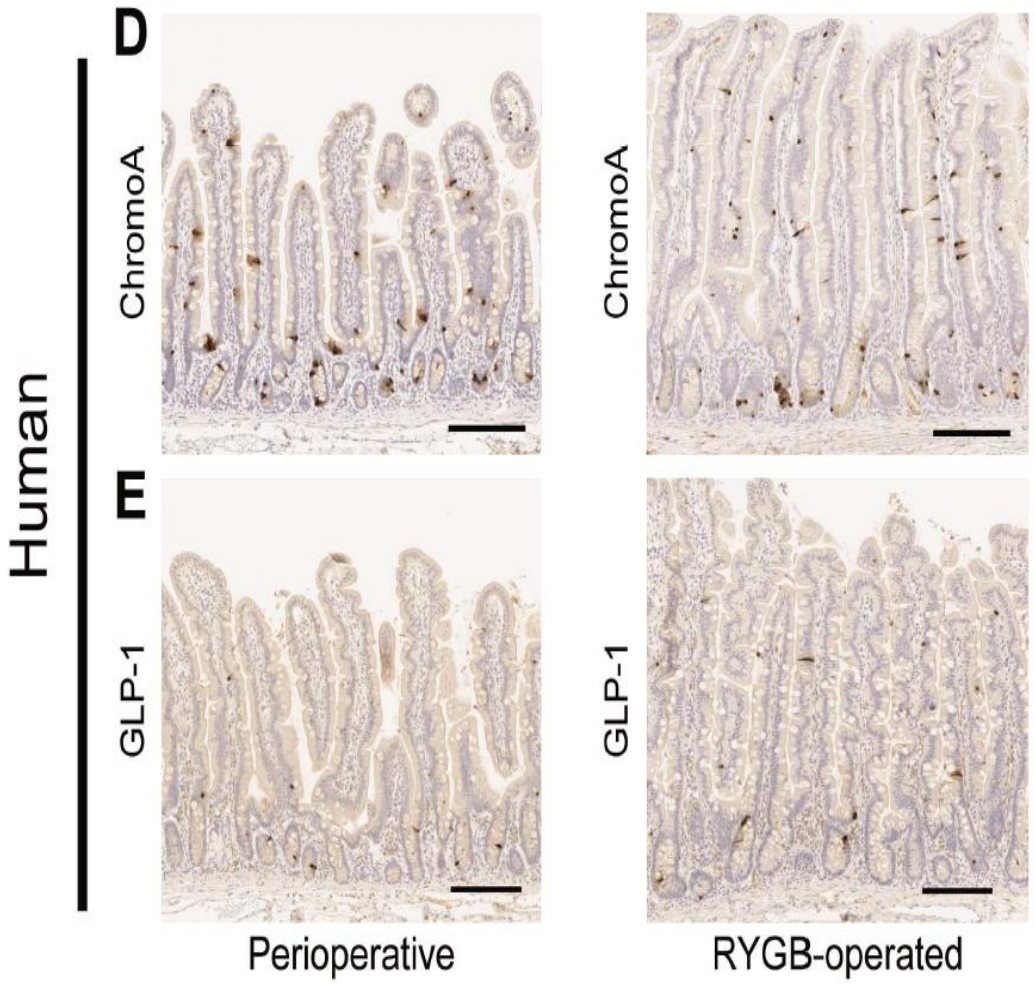
Main limitation

n = 1 (ethical obstacles to reproduce the model)

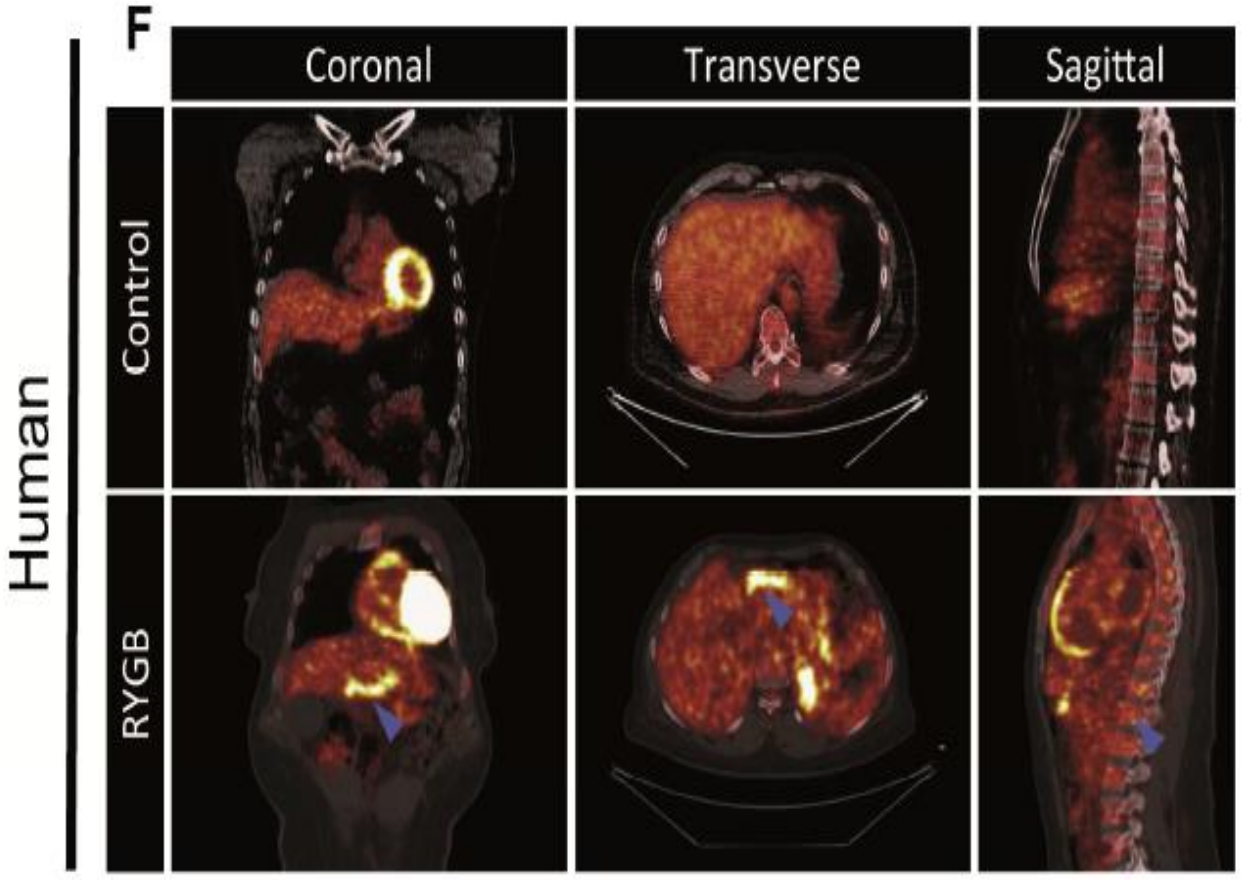
Discussion

1. Adaptation of Roux-limb «Enteroplasticity»

GLP1-cell (L) hyperplasia after RYGB



GLUT1 upregulation



Cavin. Gastroenterology. 2016
Hansen,Bueter. Plos One. 2013

2. Fast gastric-pouch emptying

Gastric pouch emptying rate of glucose drink
extremely rapid -> $T_{1/2}$ of 3 min
(Scintigraphic measurement)

Supraphysiologic intestinal **nutrient delivery of 107 kcal/min**
= x 25 increase

Nguyen. Obesity. 2014
Salehi. Diabetes Obes Metab. 2017

Take home message

Post-RYGB physiology seems to be more complex than initially thought

Forgut/hindgut theory needs to be challenged in future trials

For example, by testing the role of

- intestinal food arrival velocity
- Roux-limb adaptation

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Thomas Lutz, Dr. med. vet. (physiology of eating)

David E. Cummings, MD, PhD (diabetologist)

Pelagia Kakka (line art figure)