

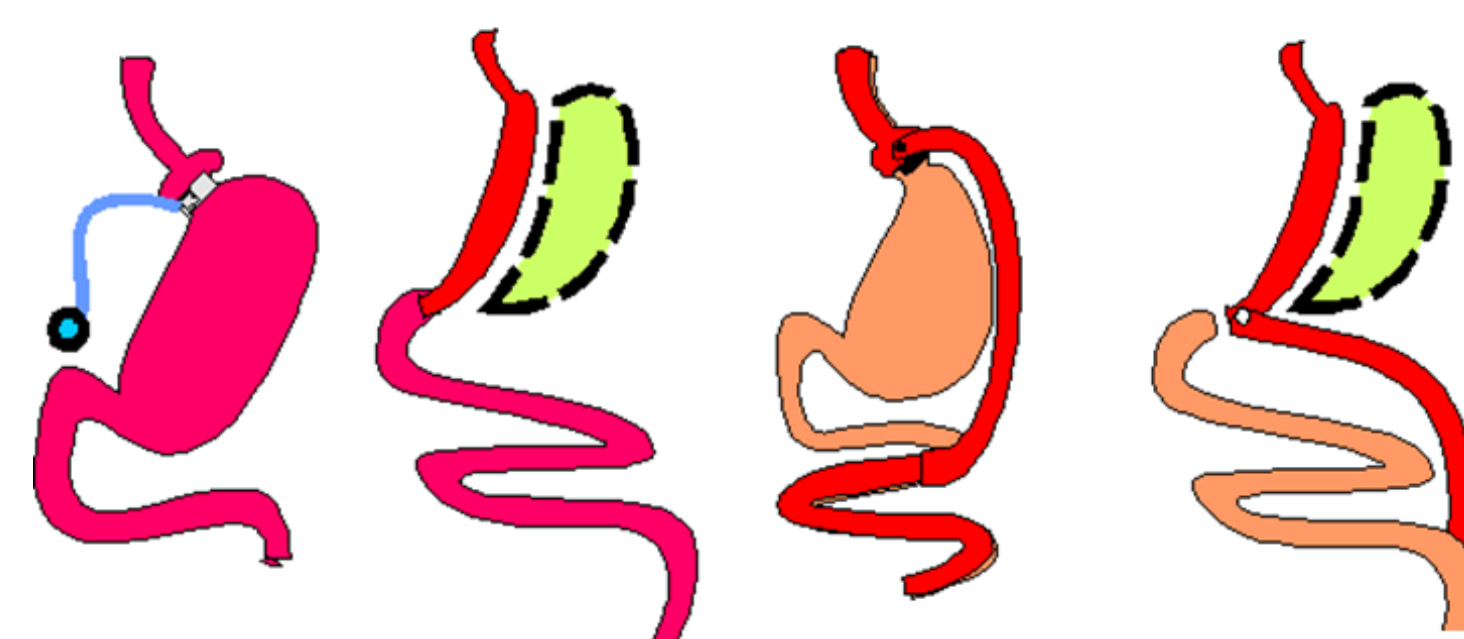
## ABSTRACT

- For decades it has become accepted and taught in medical schools that insulin resistance (IR) is the cause of type 2 diabetes mellitus.
- Longitudinal studies, which followed 488 bariatric patients for 7 years, have shown that hyperglycemia disappears within 1 week while IR remains (Pories et al, 2021).

## INTRODUCTION/BACKGROUND

- Type 2 diabetes (T2D) is a leading cause of death. Not only that, T2D causes a multitude of comorbid diseases that lead to poor prognosis, higher healthcare costs, and poor quality of life.
- This research is uncovering new ways to look at the disease process of T2D.
- By looking at T2D the proper way more treatment methods and preventative methods could potentially be invented, which in turn will drive the cost of healthcare down.

## MATERIALS & METHODS



	Gastric Band	Gastric Sleeve	Gastric Bypass	Duodenal Switch
Weight Loss %XS	46	55	58	64
Remission T2DM	57%	70%	80%	95%

Above is an illustration and table of the different variations of Gastric bypass surgery and their effectiveness in weight loss and the remission of Type 2 Diabetes.

## RESULTS

The findings suggest that not only was the original idea that IR causes type 2 diabetes mellitus faulty, but that the opposite seems to be true according to the data:

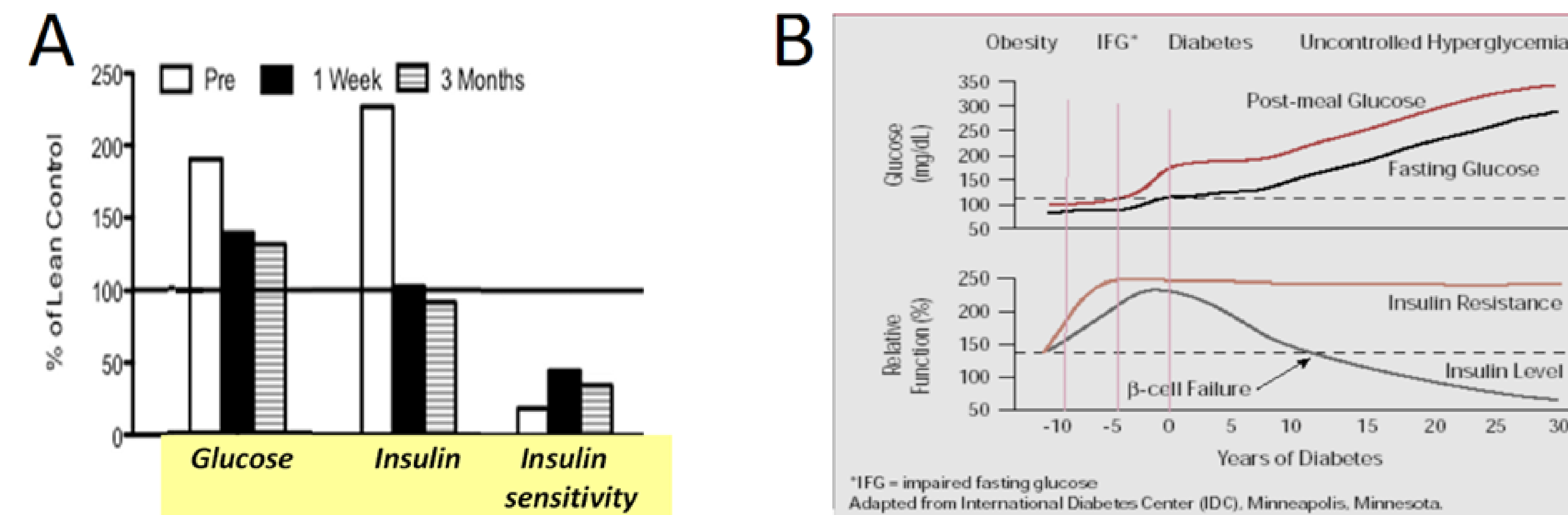
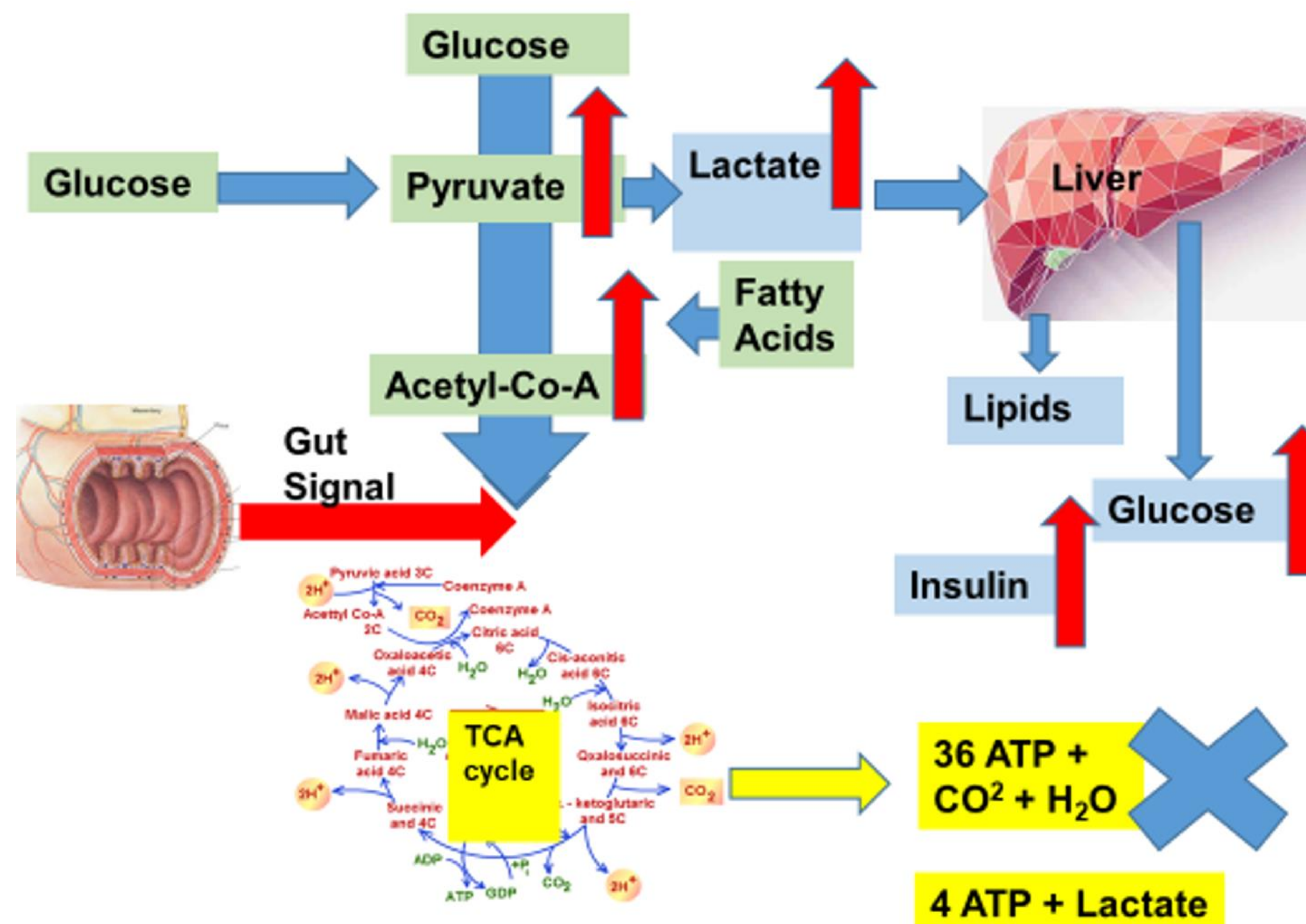


Fig. 1. Changes in glucose insulin, and insulin sensitivity index (ISI) after Roux-en-Y (RYGB). (A) Glucose, insulin, and ISI for diabetic patients before surgery (Pre) and after RYGB (1 week and 3 months) expressed as a percent of lean control subjects. (B) (top graph) Description of the progression of Diabetes over time (before and after diabetes) using post-meal and fasting glucose levels. The graph on the bottom uses the percent function of beta cells compared to Insulin resistance.

Typically, IR is not alleviated for another 3 to 6 months, while at the same time the patient's glucose level stays at normal healthy limits (Pories et al, 2021). Ince the glucose levels are brought under control, yet the IR is still present in these post diabetic patients, this suggests a different cause of Type 2 Diabetes.



## DISCUSSION

- A new hypothesis has come to light. Deleterious signaling originating from the gastric fundus causes a malfunction in the metabolic pathway, damaging the mitochondria, which operates as the "generators" of cells.
- It appears the failing generators of cells cause widespread damage to most cell types in the body. Beta cells are not exempt.
- If this is true as the research suggests, damage to the beta cells in the pancreas results in the inability to control blood glucose levels as the pancreas cannot secrete enough insulin.
- A more extensive literature review needs to be conducted to further investigate the validity of the accepted causes of type 2 diabetes mellitus.

## REFERENCES

- Beale EG. Insulin signaling and insulin resistance. *J Investig Med*. 2013
- Bikman BT, Zheng D, Pories WJ, Chapman W, Pender JR, Bowden RC, Reed MA, Cortright RN, Tapscott EB, Houmard JA, Tanner CJ, Lee J, Dohm GL. Mechanism for improved insulin sensitivity after gastric bypass surgery. *J Clin Endocrinol Metab*. 2008
- Chen Y, Huang L, Qi X, Chen C. Insulin Receptor Trafficking: Consequences for Insulin Sensitivity and Diabetes. *Int J Mol Sci*. 2019
- Dar M, Pories WJ. Bariatric surgery: what is the effect on type 2 diabetes? *Curr Opin Investig Drugs*. 2009
- Shanik MH, Xu Y, Skrha J, Dankner R, Zick Y, Roth J. Insulin resistance and hyperinsulinemia: is hyperinsulinemia the cart or the horse? *Diabetes Care*. 2008
- Yaribeygi H, Farrokhi FR, Butler AE, Sahebkar A. Insulin resistance: Review of the underlying molecular mechanisms. *J Cell Physiol*. 2019
- Zou K, Houmard JA, Lynis Dohm G, Spaniolas K, Pories WJ. Comment on: Early effect of Roux-en-Y gastric bypass on insulin sensitivity and signaling. *Surg Obes Relat Dis*. 2016
- Image: <http://www.totalbodyhs.net/2012/01/22/diabetes-3/>
- Purnell JQ, Selzer F, Smith MD, Berk PD, Courcoulas AP, Inabnet WB, King WC, Pender J, Pomp A, Raum WJ, Schrope B, Steffen KJ, Wolfe BM, Patterson EJ; LABS Research Group. Metabolic syndrome prevalence and associations in a bariatric surgery cohort from the Longitudinal Assessment of Bariatric Surgery-2 study. *Metab Syndr Relat Disord*. 2014
- Marceau P, Biron S, Marceau S, Hould FS, Lebel S, Lescelleur O, Biertho L, Simard S, Kral JG. Long-Term Metabolic Outcomes 5 to 20 Years After Biliopancreatic Diversion. *Obes Surg*. 2015
- Pories WJ, Jones TE, Houmard JA, DeMaria E, Dohm GL. Ockham's razor and the metabolic syndrome. *Surg Obes Relat Dis*. 2021

## ACKNOWLEDGEMENTS

- I want to thank Dr. Pories, Mrs. Bullard, and Blake Savage for their help on this project. You all played a role in shaping my views on research and I look forward to working with the Surgical team on other research projects.
- I also want to thank my teammates Virginia and Josh. Thank you for being great team players and it was a pleasure working with both of you.