Long-term Effects of Bariatric Surgery

Lee M. Kaplan, MD, PhD
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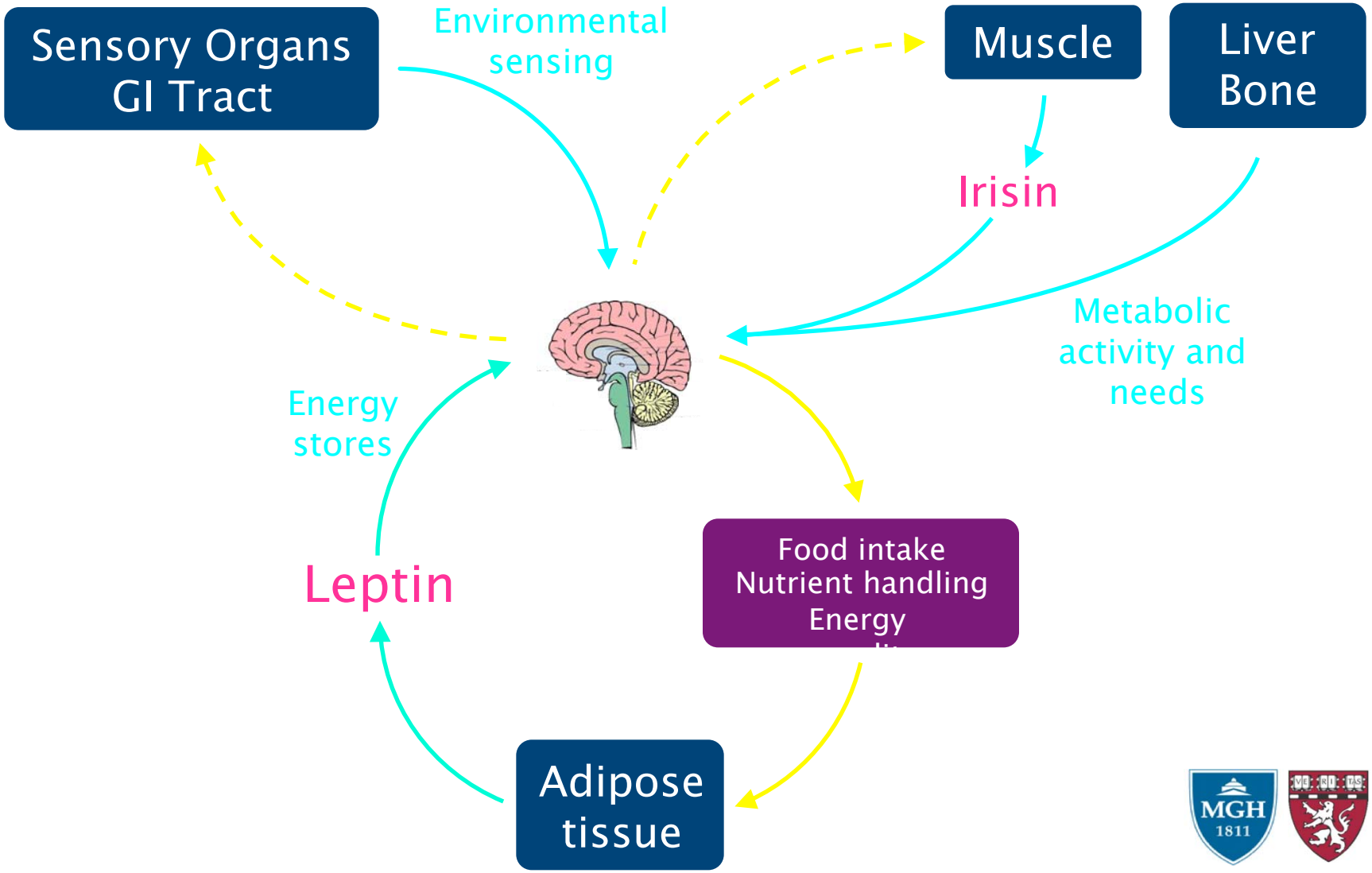
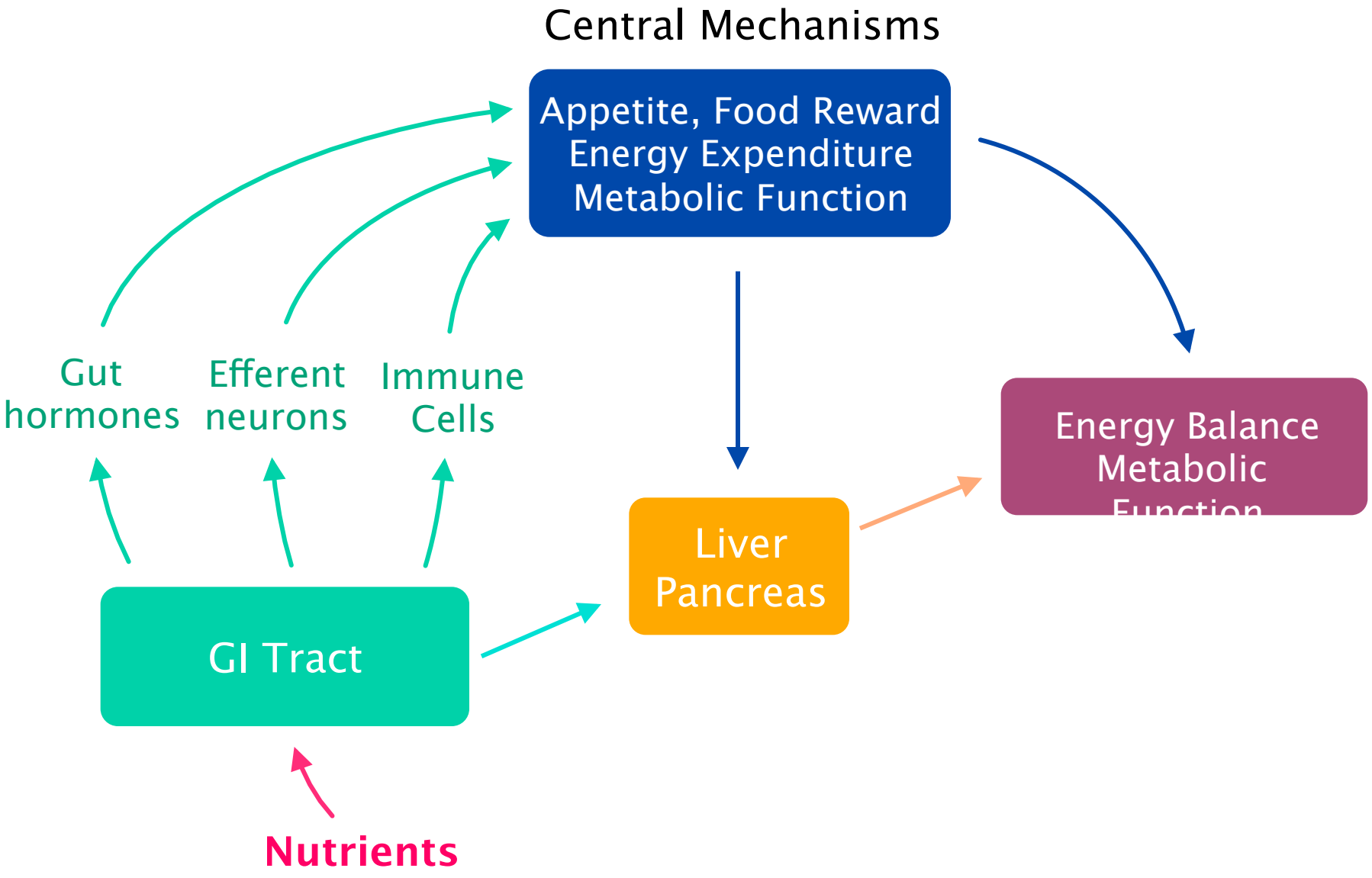
Harvard Medical School
Boston, Massachusetts

Feedback Regulation of Energy Metabolism



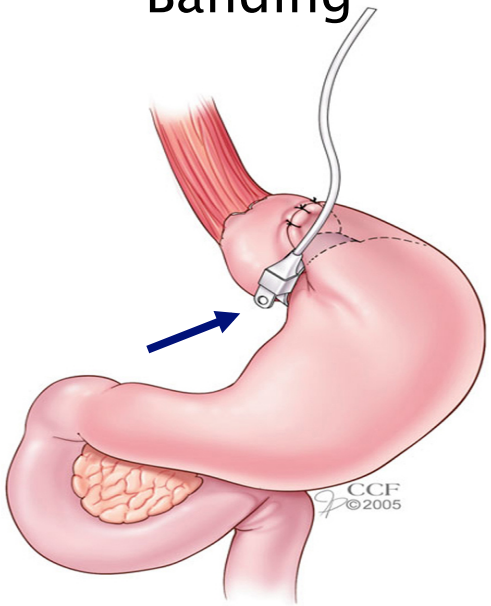
GI Regulation of Metabolic Function



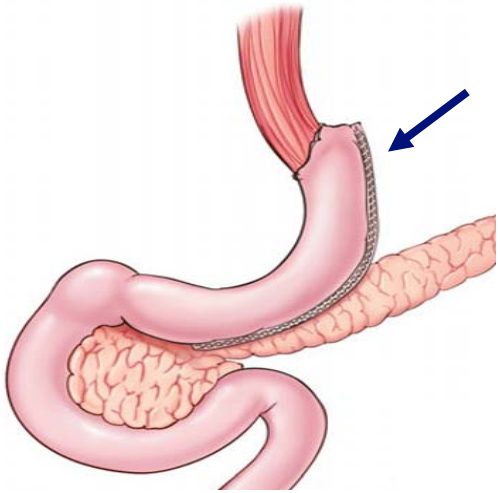
Weight Loss Surgery

Gastric

Adjustable Gastric Banding



Vertical Sleeve Gastrectomy



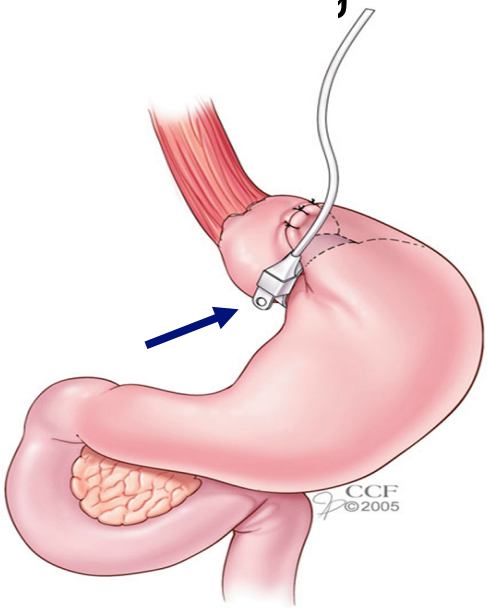
Combination

Roux-en-Y Gastric Bypass

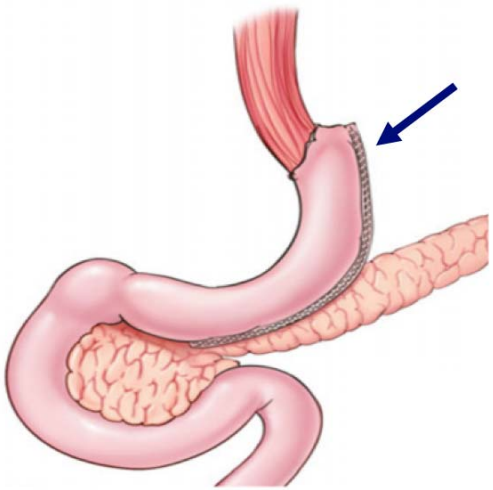
Metabolic Surgery

Weight-independent Metabolic Benefits

Adjustable Gastric Banding

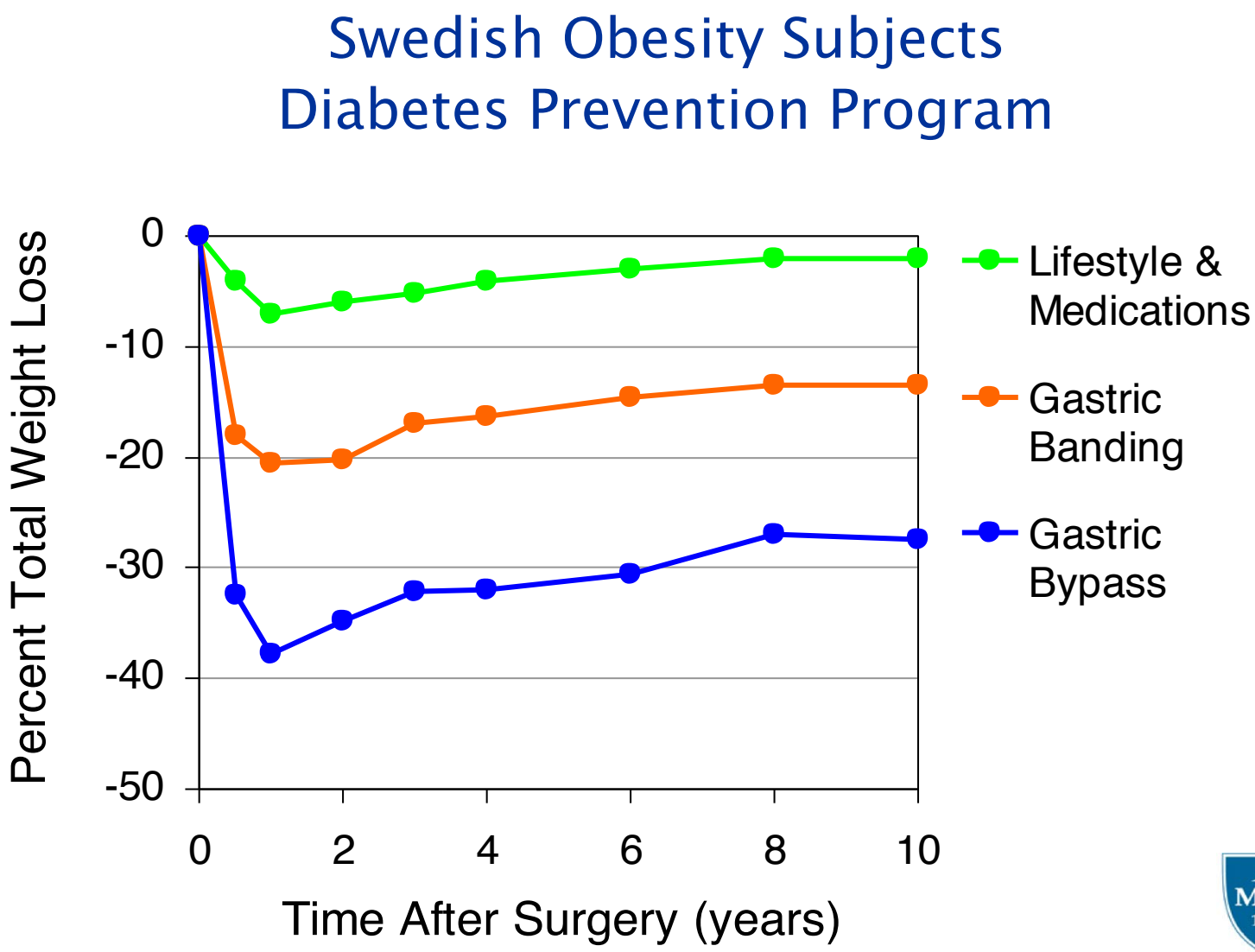


Vertical Sleeve Gastrectomy



Roux-en-Y Gastric Bypass

Effectiveness of Obesity Treatments



Why is bariatric surgery so effective?

Mechanisms of Bariatric Surgery

Classical model:
Mechanical

Restricted food intake

Malabsorption

Current model:
Physiological

Altered GI signals to brain

- Endocrine
- Neuronal

Altered GI signals to other tissues (pancreas, liver)

RYGB Induces System-wide Physiological Changes

Cholesterol

- LDL
- HDL

Taste

- Sweet preference
- Fat preference

Energy Balance

- Hunger
- Energy expenditure

Hormones

- GLP-1
- PYY
- Ghrelin
- Leptin

GI factors

- Δ Bile acids
- Δ Gut microbiota

Glucose Homeostasis

- Beta cell function
- Insulin sensitivity

The effects of bariatric surgery are fundamentally and broadly different from the effects of other types of weight loss

RYGB is the Opposite of Restrictive Dieting

	Diet	RYGB
Energy expenditure	↓	
Appetite	↑	
Hunger	↑	
Satiety	↓	
Reward-based eating	↑	
Stress response	↑	
Gut peptides		
Ghrelin	↑	
GLP-1, PYY, CCK, amylin	↓	

RYGB is the Opposite of Restrictive Dieting

	Diet	RYGB
Energy expenditure		
Appetite		
Hunger		
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Reward-based eating		
Stress response		
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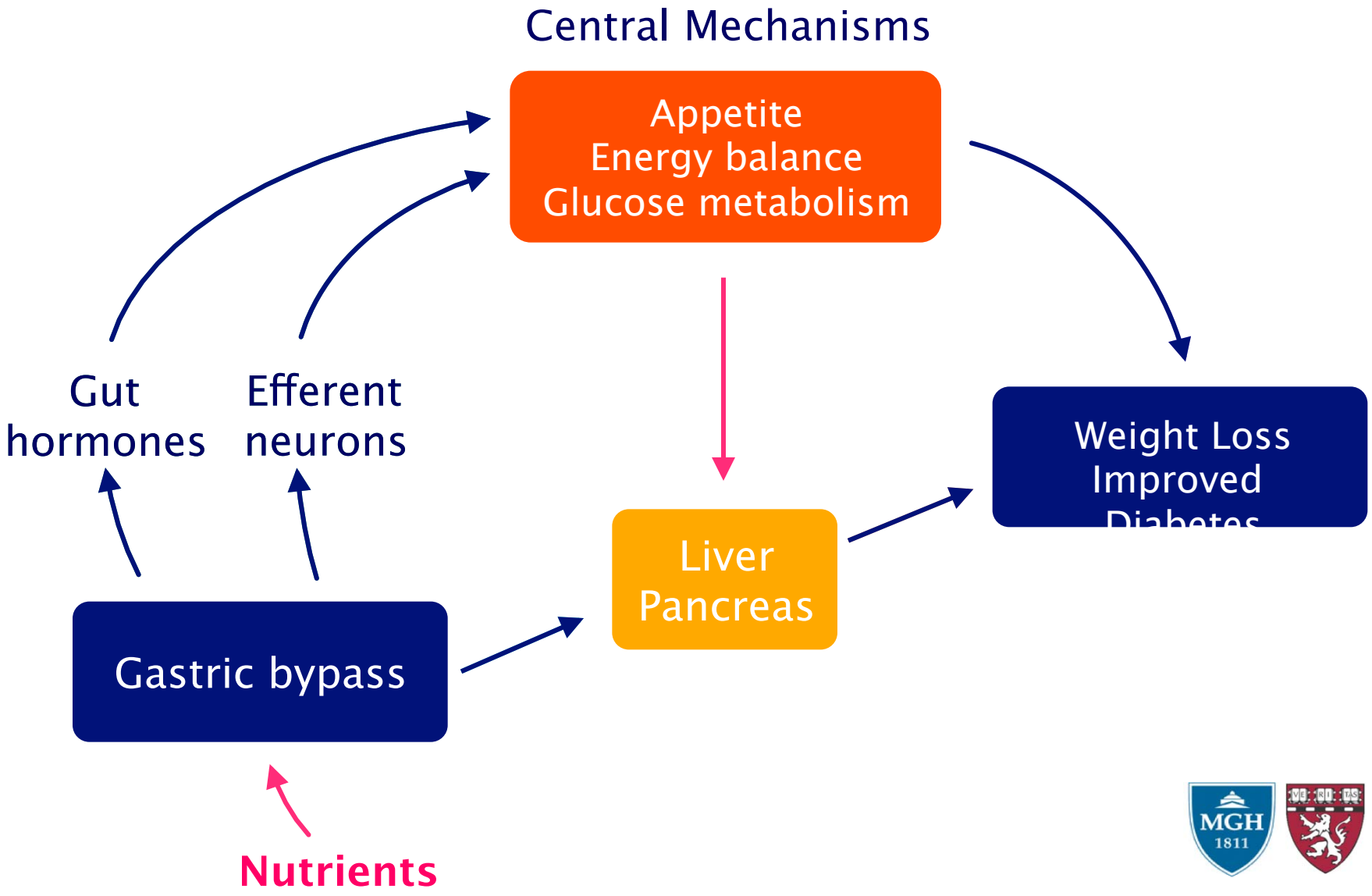
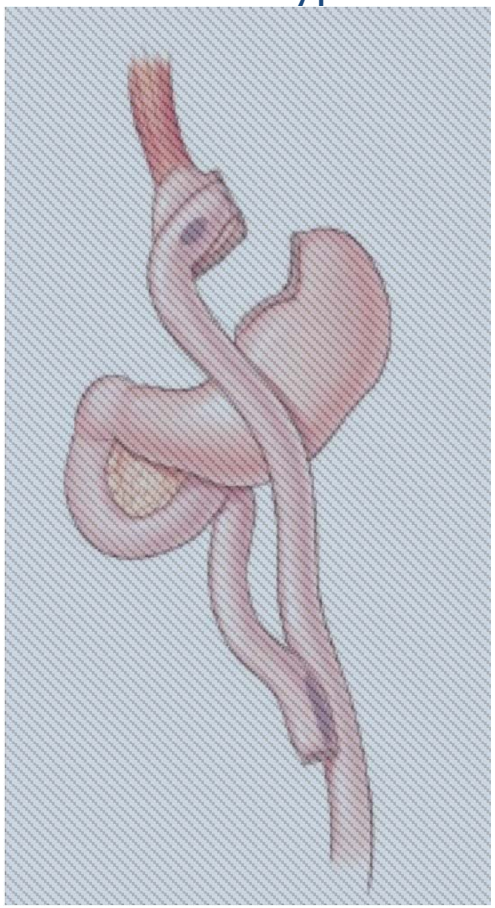
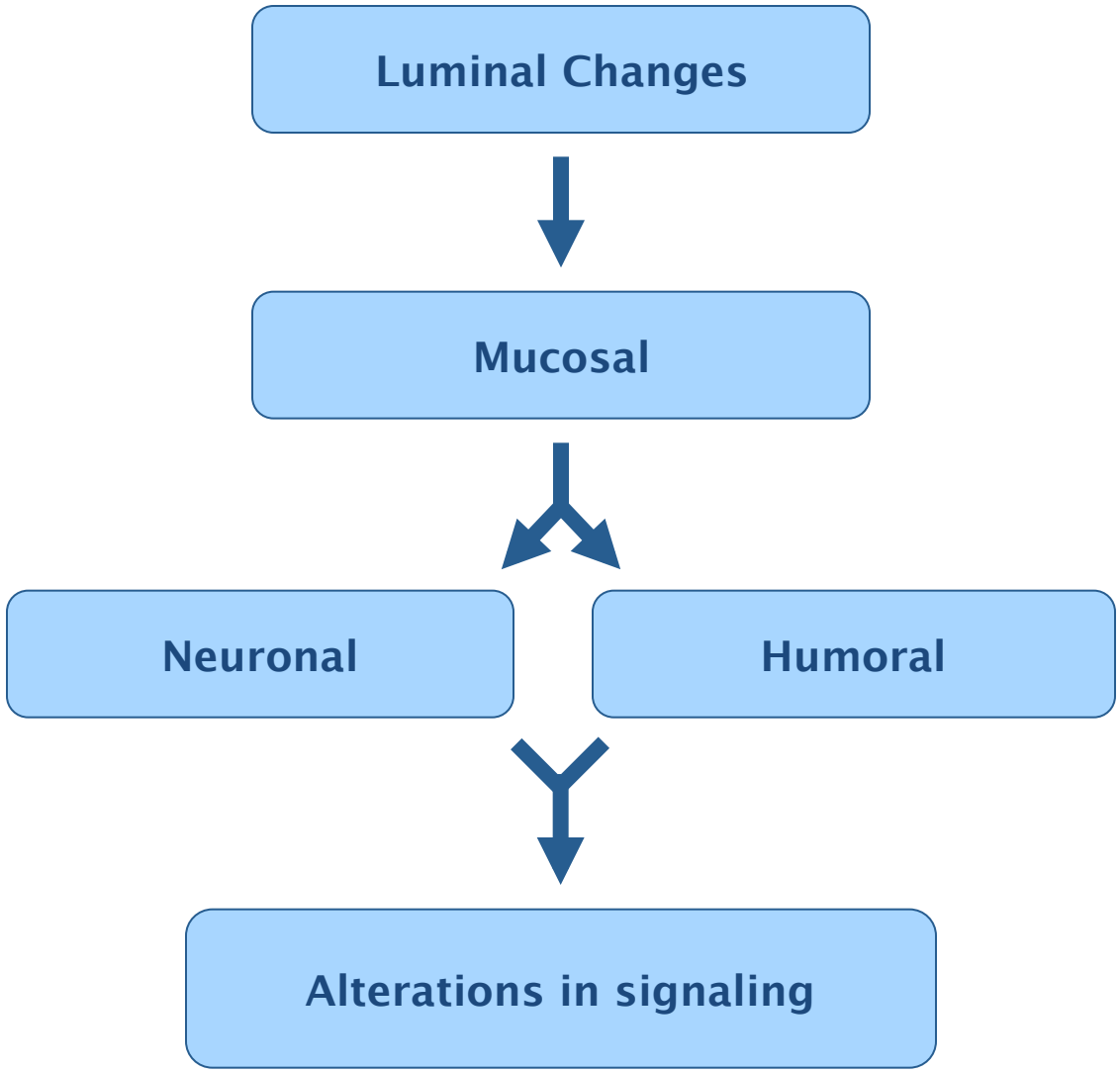
GI Regulation of Metabolic Function



Bariatric Surgery Illuminates GI Regulation of Metabolic Function

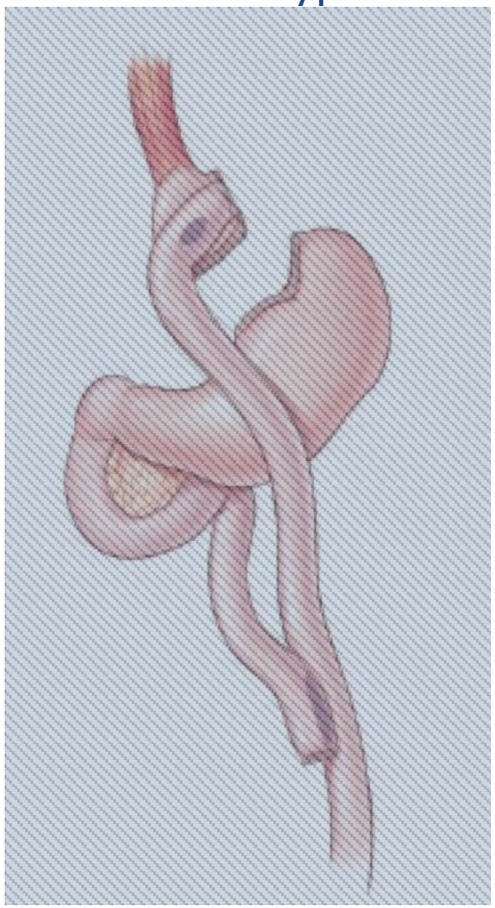
Roux-en-Y
Gastric Bypass





What Are the Luminal Contributors?

Roux-en-Y
Gastric Bypass



Luminal

Nutrients
- Lipids
- Carbohydrates
- Proteins / amino acids

Pancreatic enzymes

Bile acids

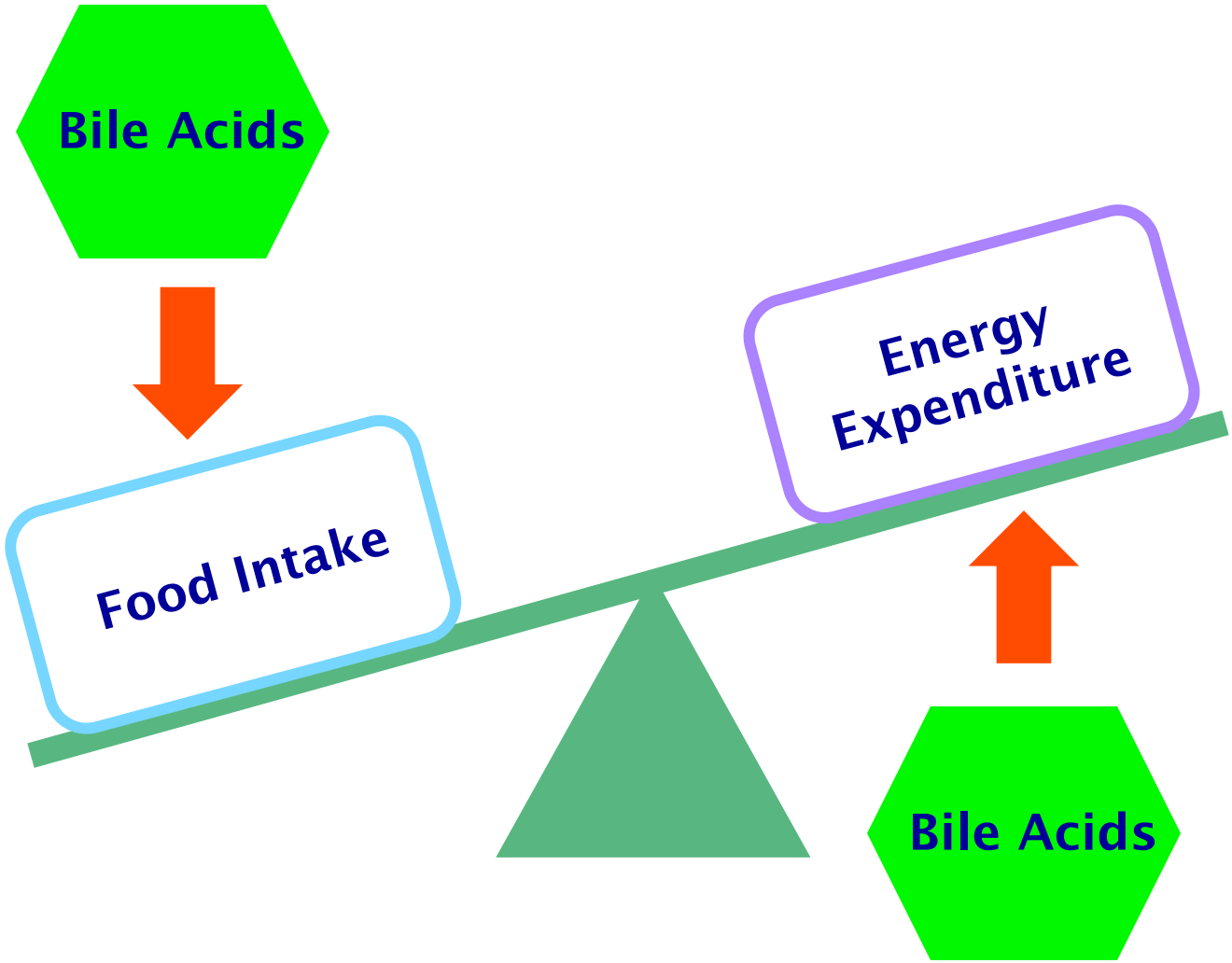
Microbiota

Neuronal | **Humoral**

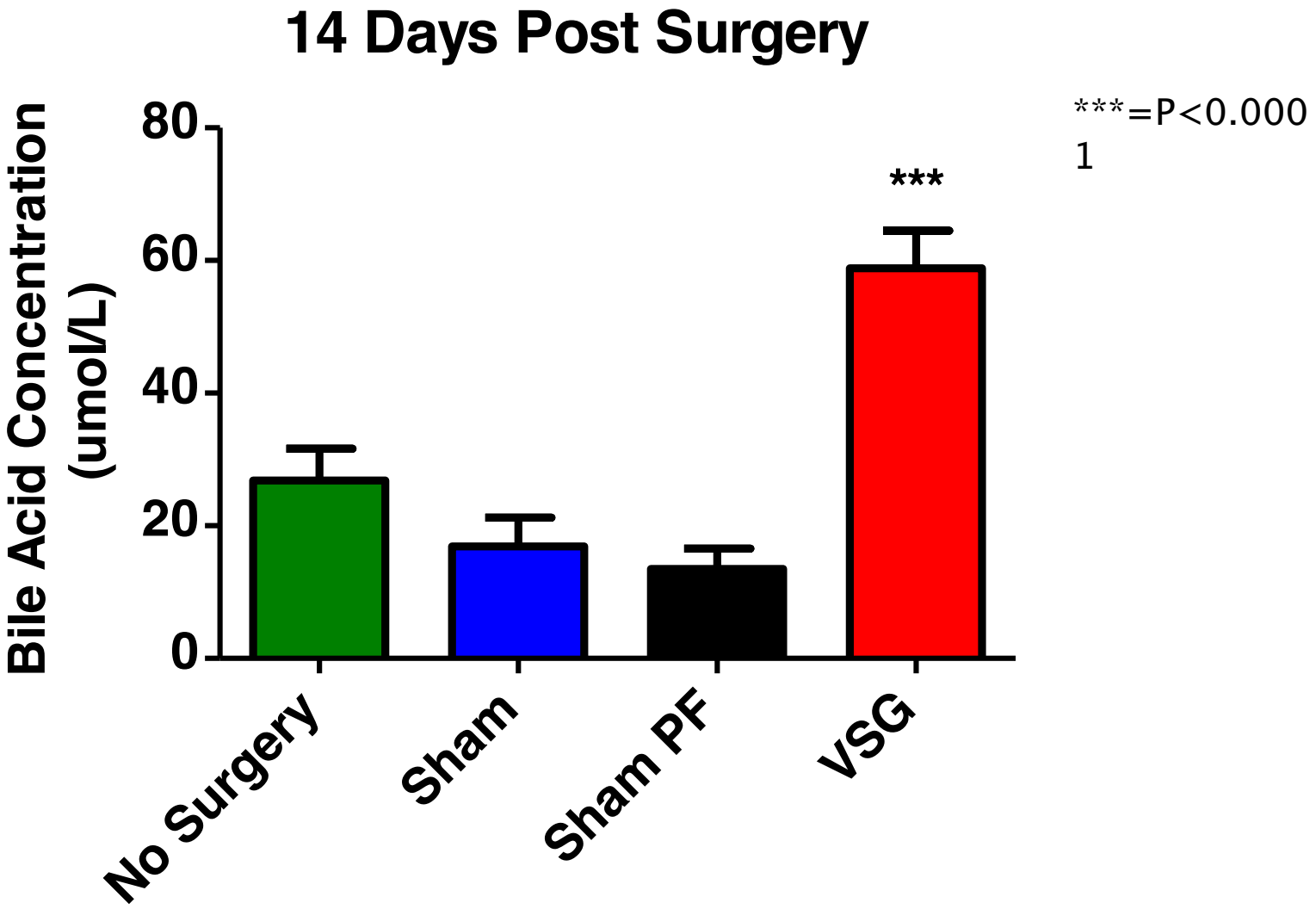
Alterations in signaling

Bile Acids

Bile Acids Regulate Energy Balance

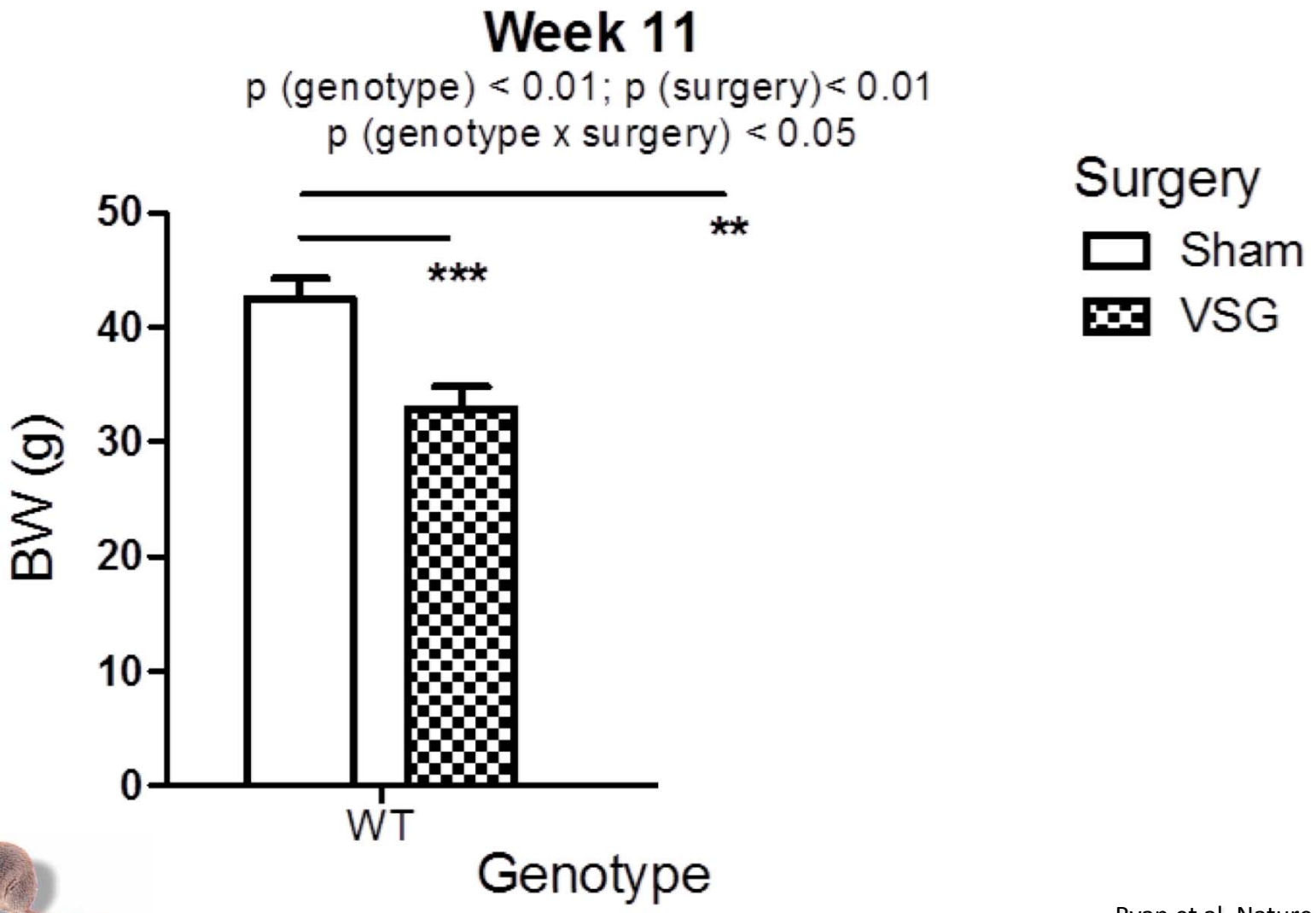


Elevated Fasting Serum Bile Acid Levels after VSG



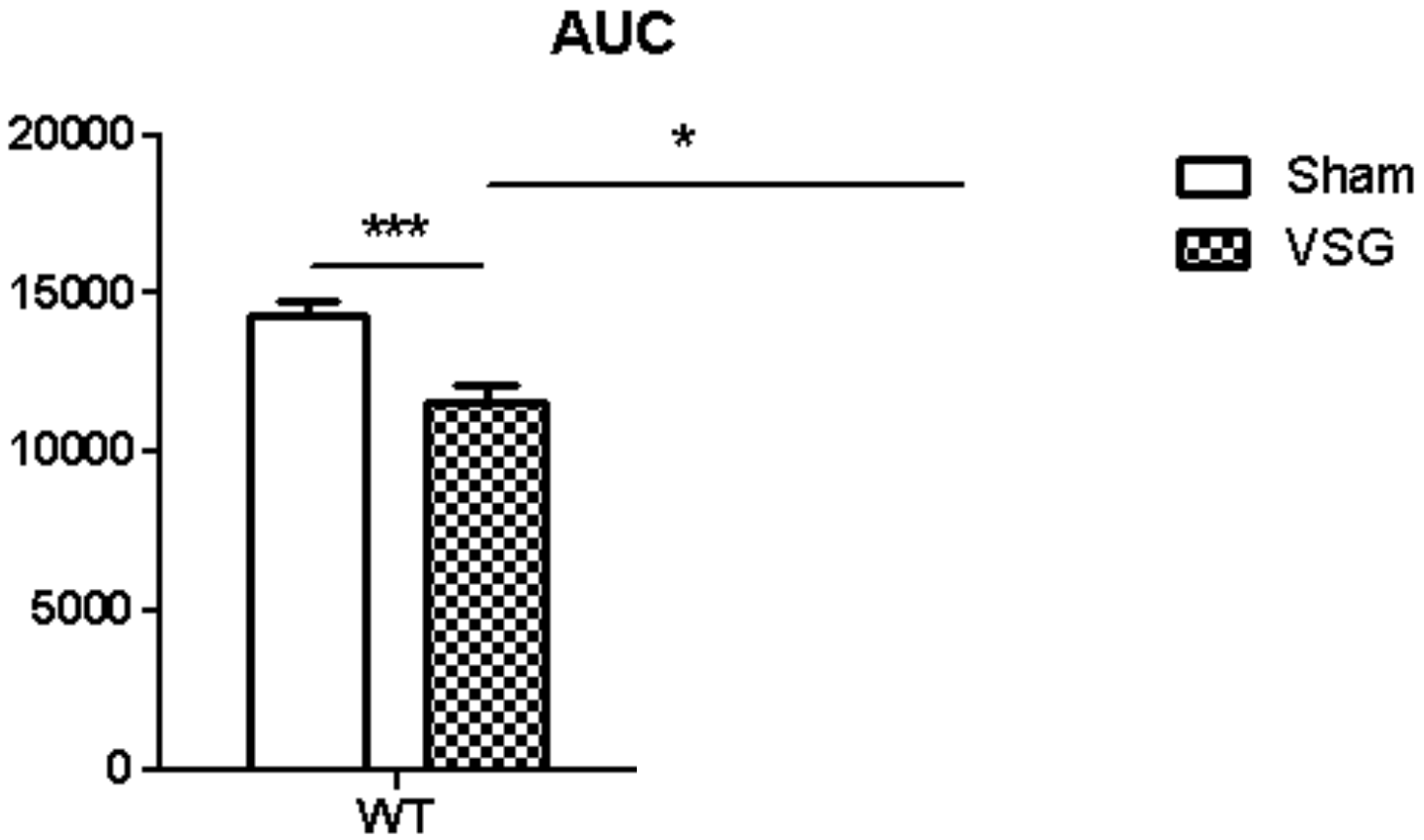
Ryan et al. Nature 2014;8:183-8.

Bile Acid Receptor FXR Required for VSG Action



Ryan et al. Nature 2014;8:183-8.

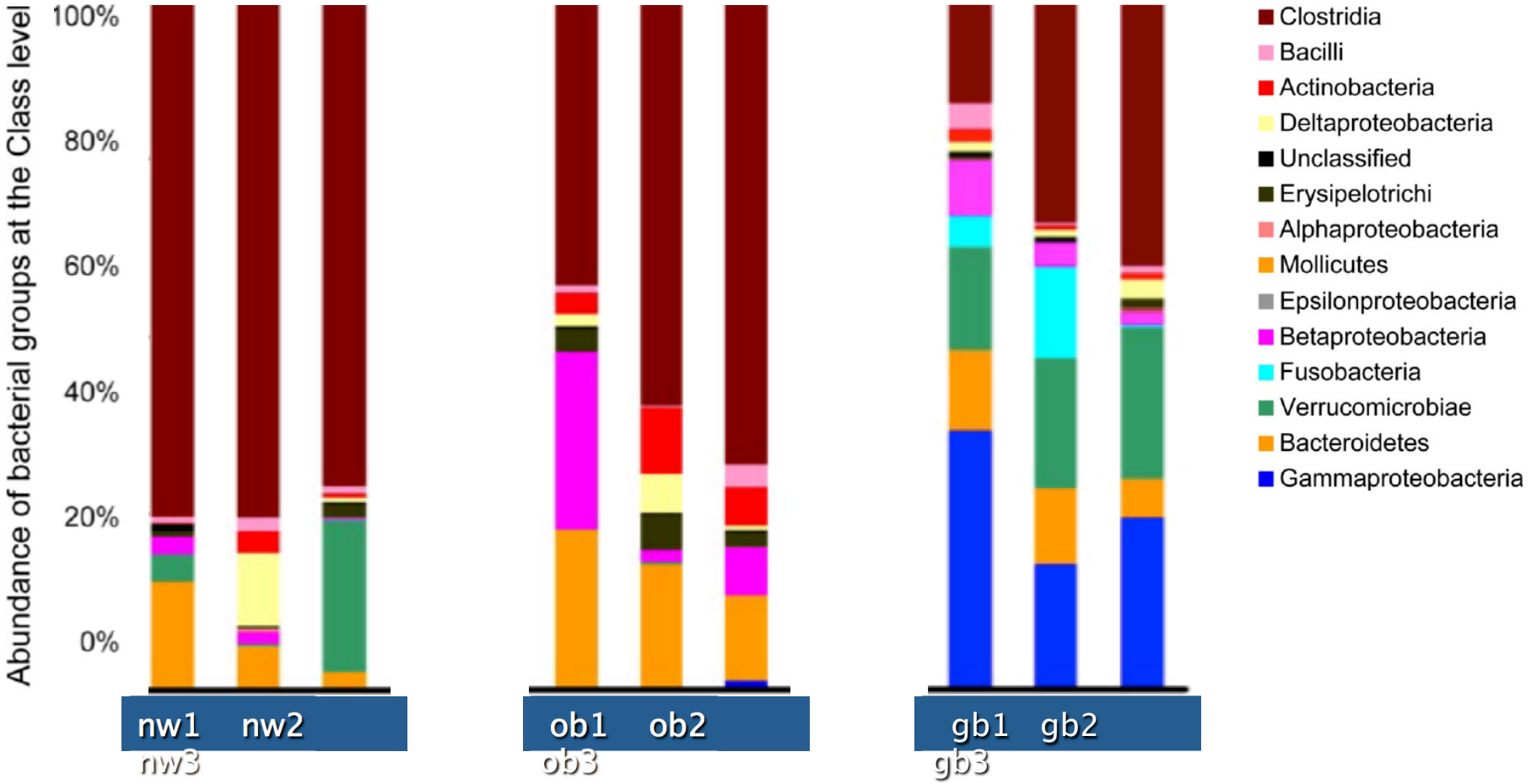
Bile Acids Contribute to Antidiabetic Effects of VSG



Ryan et al. Nature 2014;8:183-8.

Intestinal Microbiota

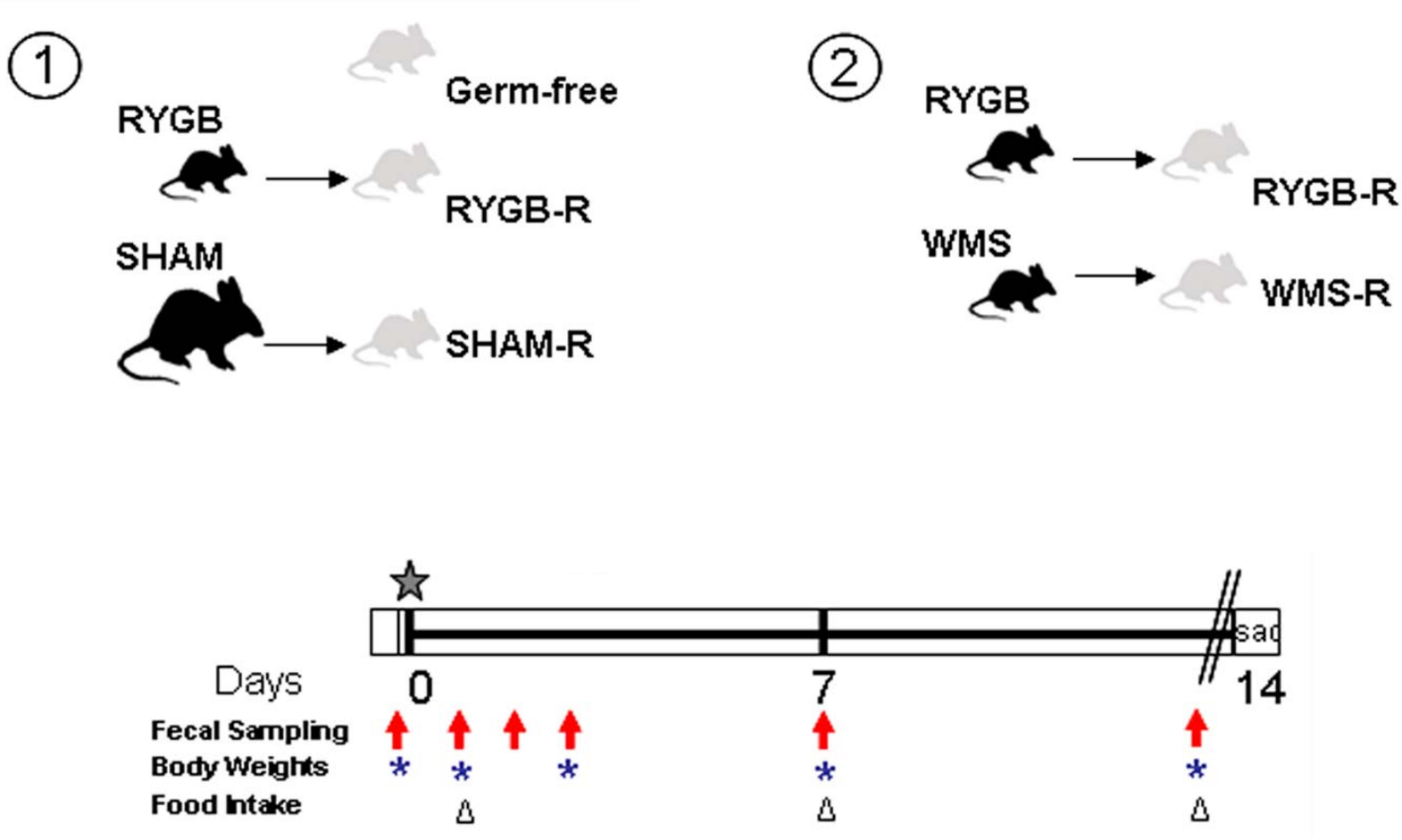
Gut bacterial profile differs among lean, obese, and post gastric bypass human patients



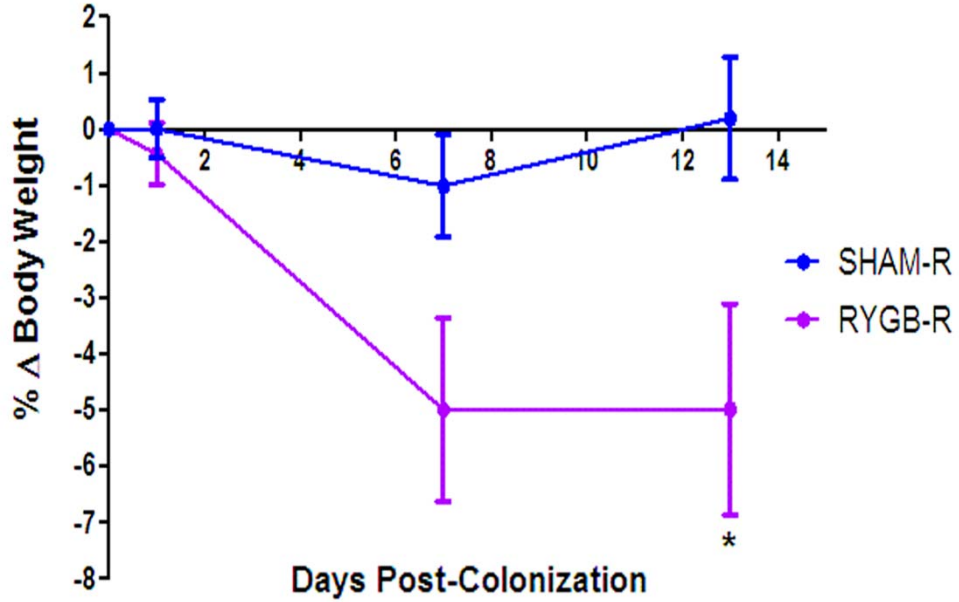
Zhang et al. PNAS 2009;106:2365-70.

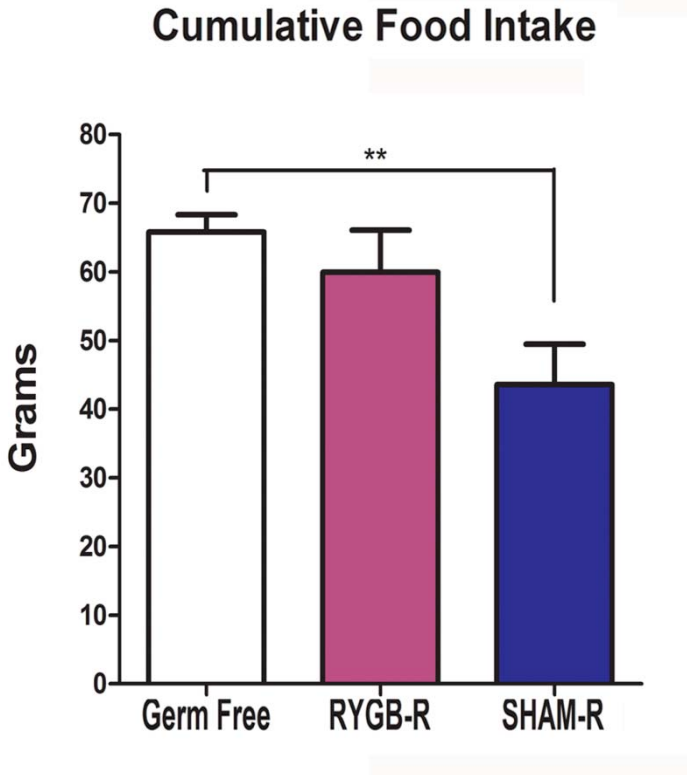
Do these changes contribute to the outcomes after RYGB?

Experimental Design



Microbiota Can Transmit Beneficial Effect of RYGB





Liou et al. Science Transl Med. 2013;5:178r41.

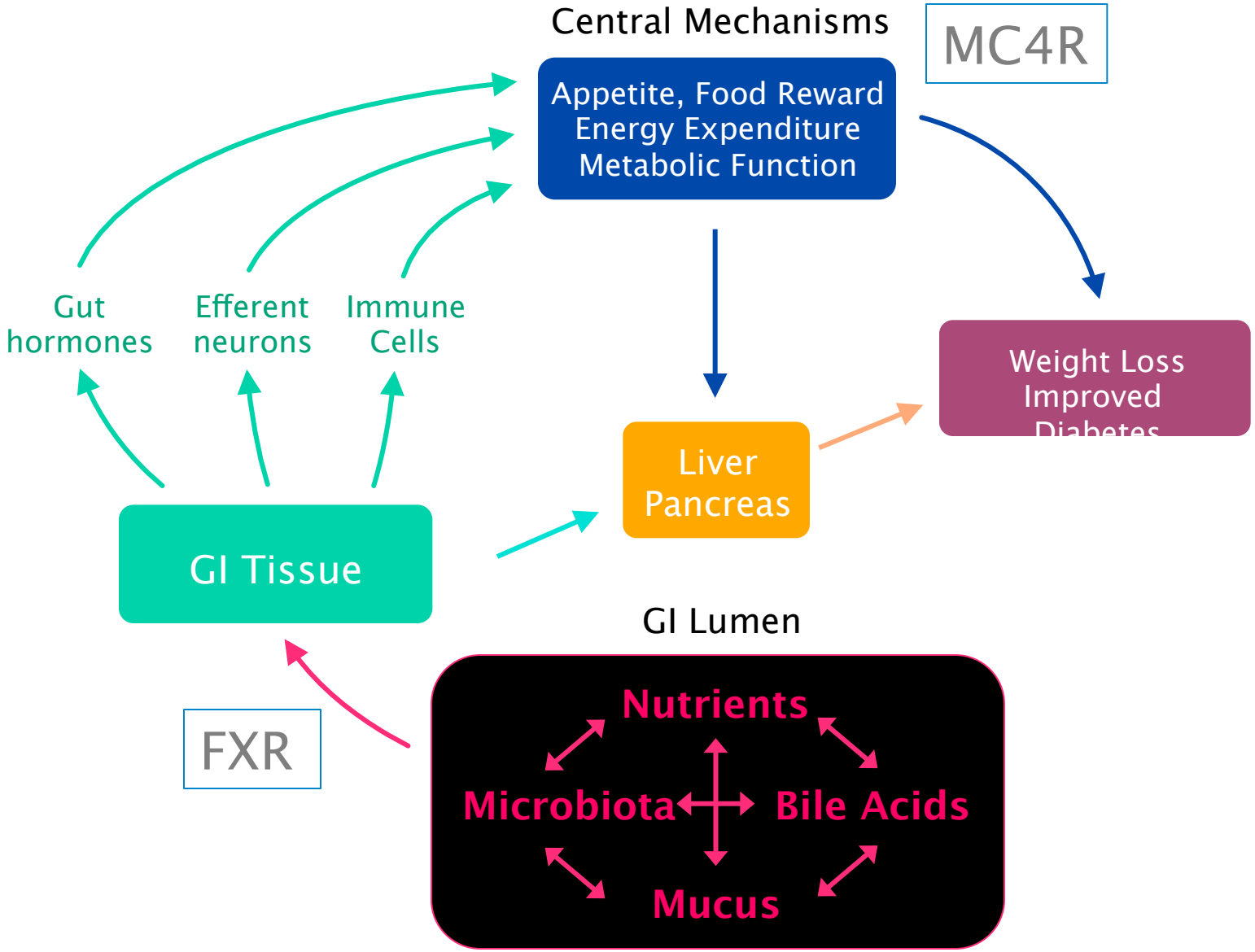
Summary – The Physiology of Bariatric Surgery

- RYGB and VSG induce weight loss by changing the physiological regulation of energy balance and lowering the fat mass set point.
  - Decreased appetite
  - Increased energy expenditure for RYGB and BPD/DS
  - Weight loss-dependent AND independent improvement in diabetes
- RYGB and VSG act at multiple levels, beginning in the gut lumen.
  - Luminal changes regulate GI mucosal activity
  - Resulting GI-derived neural, endocrine and immune cell-mediated signals influence CNS and peripheral metabolic regulation
- RYGB and VSG influence bile acid biology.
  - Elevated circulating levels with faster postprandial rise

Summary – Bariatric Surgery and the Gut Microbiota

- RYGB and VSG rapidly and durably alter gut microbial ecology, primarily in the distal gut.
- RYGB alterations of the microbiota are independent of weight loss and independent of dietary changes.
- Microbiota altered by RYGB contribute to several metabolic outcomes of this operation, including body weight, adiposity, lipids and insulin.
- Alterations in the gut microbiota after RYGB appear to influence energy balance primarily by increasing energy expenditure.

GI Regulation of Metabolic Function



Cardiometabolic Health Congress

The Long-term Effect of Bariatric Surgery

Lee M. Kaplan, MD, PhD

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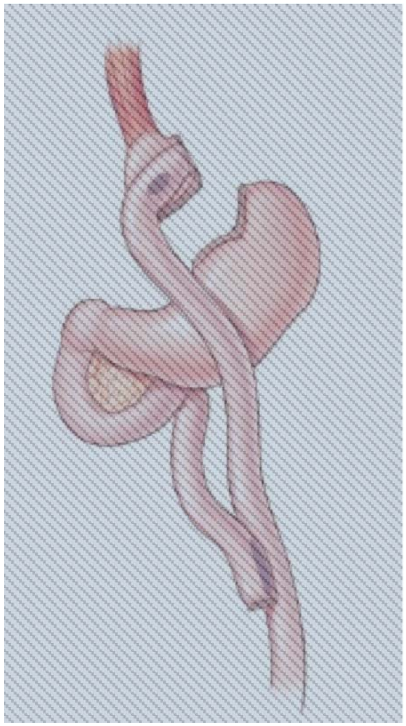
Harvard Medical School

LMKaplan@partners.org



October 25, 2014

Long-term Effects of Metabolic Surgery

Prof. Francesco Rubino, M.D.
Chair, Bariatric and Metabolic Surgery
King's College London

DISCLOSURE SLIDE

- NGM Biopharmaceuticals (SAB Member)
- Fractyl Laboratories (Advisor/Consultant)

Randomized Clinical Trials

(2007-2014)

Bariatric surgery versus non-surgical treatment for obesity: a systematic review and meta-analysis of randomised controlled trials

BMJ Oct 22, 2013

Viktoria L Gloy *junior researcher*[1], Matthias Briel *assistant professor*[1 2], Deepak L Bhatt *professor*[3], Sangeeta R Kashyap *associate professor of medicine*[4], Philip R Schauer *medical director, professor of surgery*[5], Geltrude Mingrone *professor*[6], Heiner C Bucher *director*[1], Alain J Nordmann *associate professor*[1]

Study
Mingrone 2012[16]
Schauer 2012[19]
Reis 2010[20]
Ikramuddin 2013[19]
Liang 2013[24]
O'Brien 2006[23]
O'Brien 2010[21]
Dixon 2008[25]
Dixon 2012[22]
Mingrone 2002[17]
Heindorff 1997[26]

- 11 studies, 796 patients, BMI 27-53
- Surgery superior to med Rx
  - Wt. loss, HbA1c, T2DM remission, TG, HDL, remission of metabolic syndrome, QOL, medication reduction
- No difference in BP or LDL
- No CV events or death after surgery
- Anemia (15%), Reoperation (8%)

2 Recent RCT's
JAMA Surgery June 4, 2014

Surgical vs Medical Treatments for Type 2 Diabetes Mellitus: A Randomized Clinical Trial

Anita P. Courcoulas, MD, MPH; Bret H. Goodpaster, PhD; Jessie K Eagleton, MPH; Steven H. Belle, PhD, MScHyg; Melissa A. Kalarchian, PhD; Wei Lang, PhD; Frederico G. S. Toledo, MD; John M. Jakicic, PhD

Roux-en-Y Gastric Bypass Surgery or Lifestyle With Intensive Medical Management in Patients With Type 2 Diabetes Feasibility and 1-Year Results of a Randomized Clinical Trial

Florencia Halperin, MD; Su-Ann Ding, MD; Donald C. Simonson, MD, MPH, ScD; Jennifer Panosian, BA; Ann Goebel-Fabbri, PhD; Marlene Wewalka, MD; Osama Hamdy, MD, PhD; Martin Abrahamson, MD; Kerri Clancy, RN; Kathleen Foster, RN; David Lautz, MD; Ashley Vernon, MD; Allison B. Goldfine, MD

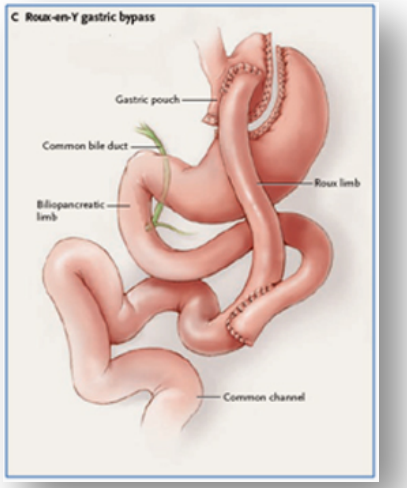
Both Show Superiority of Surgery vs. Intensive Medical R

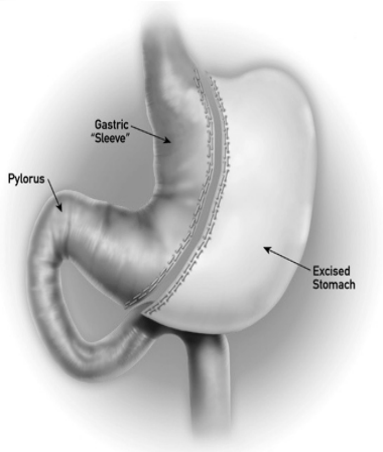
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Bariatric Surgery versus Intensive Medical Therapy for Diabetes — 3-Year Outcomes

Philip R. Schauer, M.D., Deepak L. Bhatt, M.D., M.P.H., John P. Kirwan, Ph.D., Kathy Wolski, M.P.H., Stacy A. Brethauer, M.D., Sankar D. Navaneethan, M.D., M.P.H., Ali Aminian, M.D., Claire E. Pothier, M.P.H., Esther S.H. Kim, M.D., M.P.H., Steven E. Nissen, M.D., and Sangeeta R. Kashyap, M.D., for the STAMPEDE Investigators*





(n.48) (n.48)

Surgery

Medical Therapy (n.48)

Primary and Secondary Endpoints at 36 Months

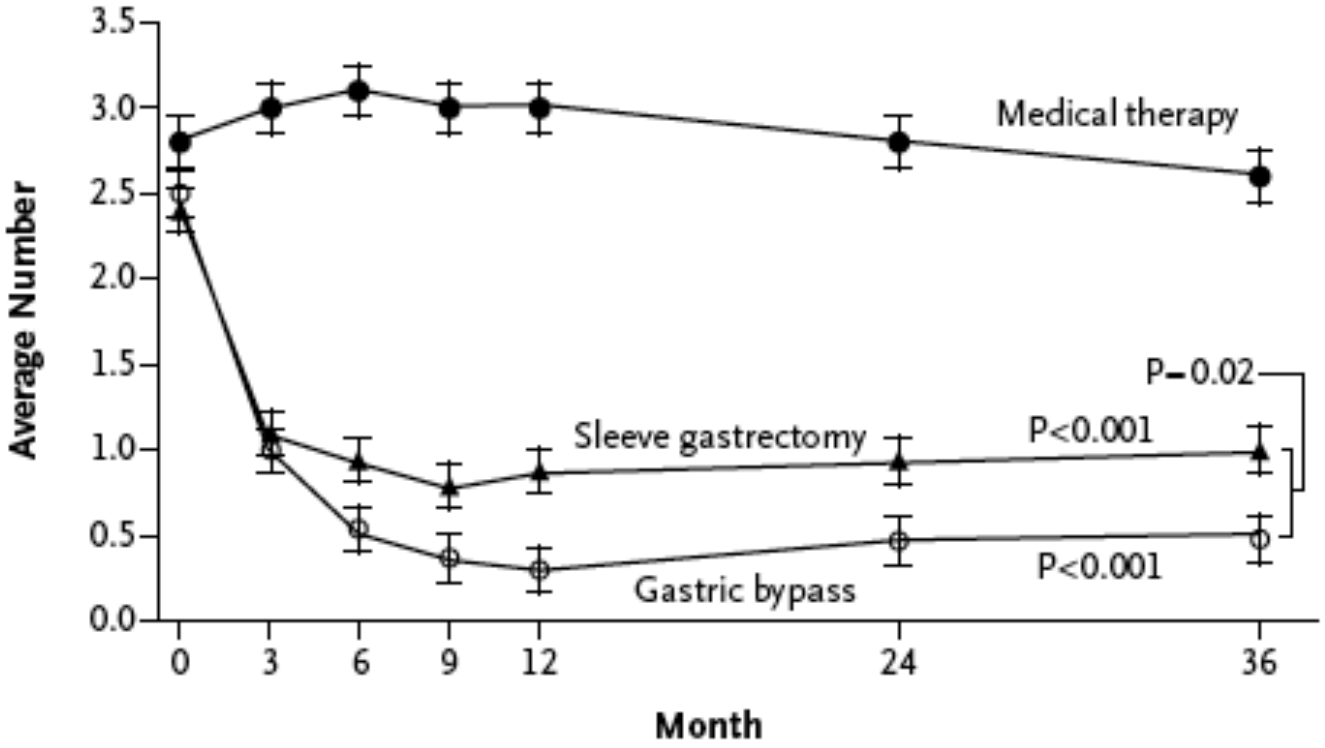
Parameter	Medical Therapy (n=40)	Bypass (n=48)	Sleeve (n=49)	P Value[1]	P Value[2]
HbA1c ≤ 6%	**5%**	**37.5%**	**24.5%**	**<0.001**	**0.012**
HbA1c ≤ 6% (without DM meds)	0%	35.4%	20.4%	<0.001	0.002
HbA1c ≤ 7%	40%	64.6%	65.3%	0.02	0.02
Change in FPG (mg/dL)	-6	-85.5	-46	0.001	0.006
Relapse of glycemic control	80%	23.8%	50%	0.03	0.34
% change in HDL	+4.6	+34.7	+35.0	<0.001	<0.001
% change in TG	-21.5	-45.9	-31.5	0.01	0.01

[1] Gastric Bypass vs Medical Therapy; [2] Sleeve vs Medical Therapy

Schauer et al. NEJM 2014

Change in Diabetes Medications

C Diabetes Medications

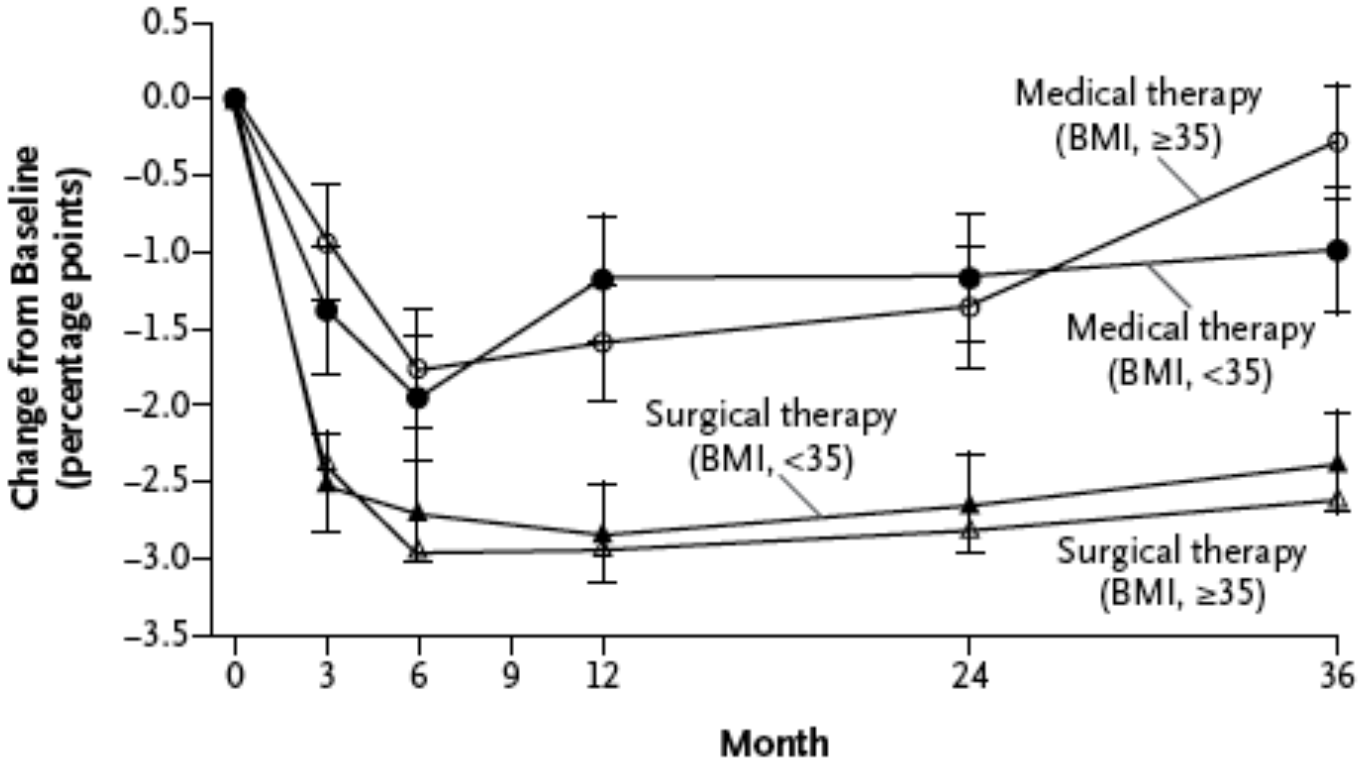


Value at Visit					
Medical therapy	2.8	3.1	3.0	2.8	2.6
Sleeve gastrectomy	2.4	0.94	0.88	0.94	1.0
Gastric bypass	2.5	0.54	0.3	0.47	0.48

Schauer et al. NEJM 2014

Stampede Trial
BMI < 35 vs. BMI ≥ 35

B Glycated Hemoglobin According to Body-Mass Index



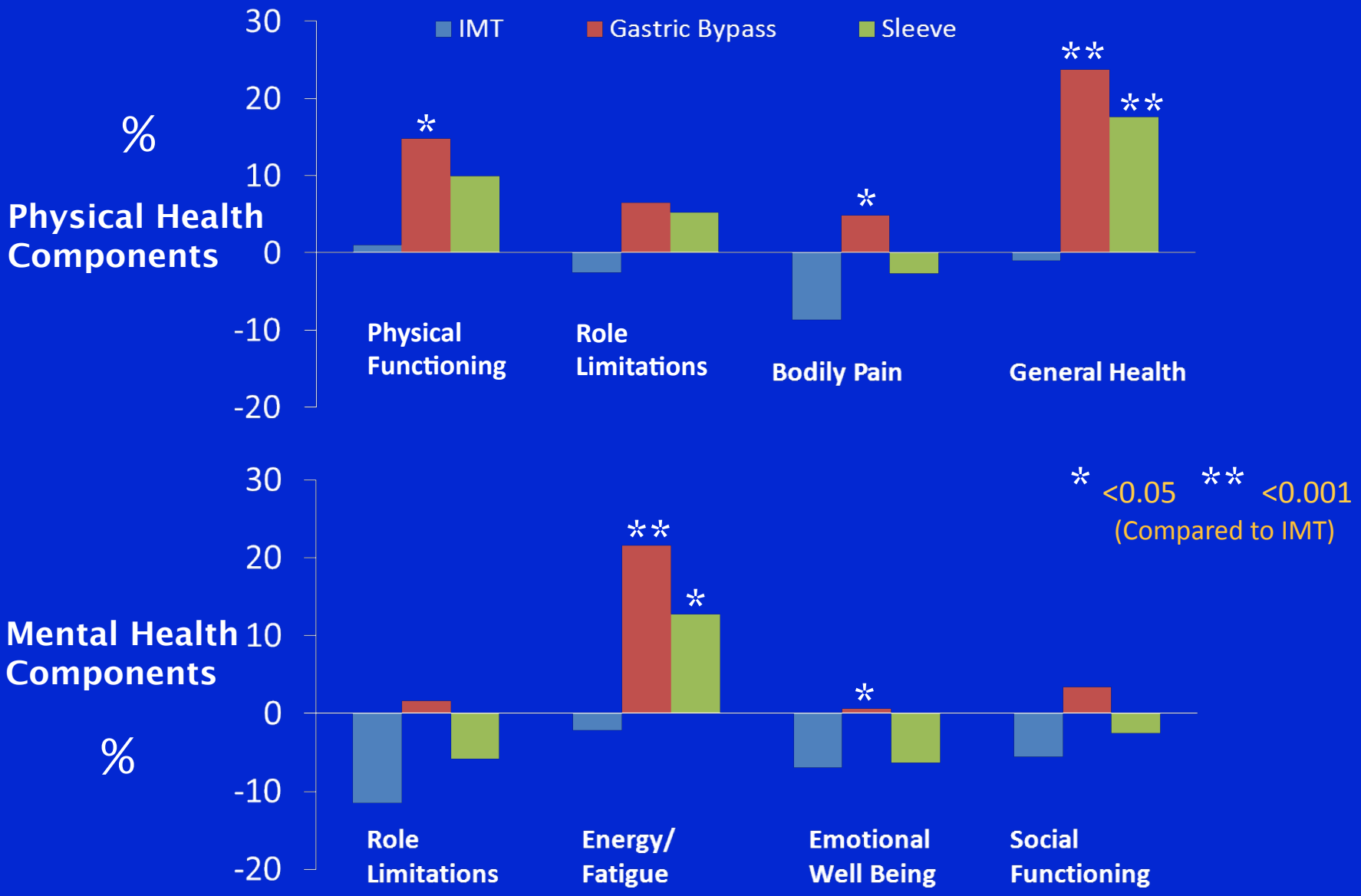
Value at Visit					
Medical <35 BMI	9.1 (8.9)	7.2 (6.8)	7.9 (6.9)	8.0 (7.4)	8.1 (7.8)
Medical ≥35 BMI	8.8 (8.5)	7.1 (6.8)	7.2 (6.7)	7.4 (6.9)	8.5 (7.3)
Surgical <35 BMI	9.4 (9.1)	6.7 (6.9)	6.6 (6.6)	6.8 (6.8)	7.1 (6.7)
Surgical ≥35 BMI	9.3 (9.2)	6.4 (6.2)	6.4 (6.1)	6.6 (6.4)	6.7 (6.4)

Cardiovascular Medications at Baseline and Month 36

CV medications – number (%)	Medical Therapy (n=40)	Bypass (n=48)	Sleeve (n=49)
Baseline			
None	0 (0)	3 (6.3)	2 (4.1)
1 – 2	19 (47.5)	17 (35.4)	28 (57.1)
≥ 3	21 (52.5)	28 (58.3)	19 (38.8)
Month 36			
None	1 (2.5)	33 (68.8) *	21 (42.9) *
1 – 2	18 (45)	14 (29.2)	25 (51)
≥ 3	21 (52.5)	1 (2.1)	3 (6.1)

* P value <0.05 with Medical Therapy group as

Surgical pts had improved physical function, overall general health, energy and emotional well being; had less body pain. No significant improvement in the medical-therapy group.



Adverse Events through 36 Months

- No Deaths
- Reoperations: 4 (sleave leak, gallstones, bleeding, abd pa

Table 3. Complications at 3 Years.*

Complication	Medical Therapy (N=43)	Gastric Bypass (N=50)	Sleeve Gastrectomy (N=49)
Gastrointestinal			
Bowel obstruction	1 (2)	1 (2)	1 (2)
Stricture	0	1 (2)	1 (2)
Ulcer	1 (2)	4 (8)	0
Leak	0	0	1 (2)
Intraabdominal bleeding	0	2 (4)	0
Dumping syndrome	0	4 (8)	1 (2)
Gallstone diseases	0	1 (2)	1 (2)

Courtesy of Dr Schauer

RCT Surgery vs MT for T2DM

- Published
  - Dixon et al; JAMA 2008
  - Mingrone et al NEJM 2012
  - Schauer et al NEJM 2012
  - Ikramuddin et al JAMA 2013
  - Schauer et al NEJM 2014
  - O'Brien et al; Lancet Diab End 2014
  - Joslin Trial
  - Pittsburg Trial

- Upcoming/in press
  - COSMID Trial (India)

Ø **Surgery more effective than M**

Ø **Gradient BPD > RYGB > Sleeve**

Ø **Efficacy for BMI above and below 35kg/m2**

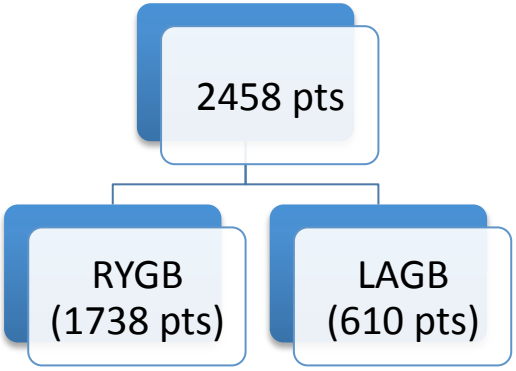
Long-term clinical outcomes of metabolic surgery

Original Investigation

Weight Change and Health Outcomes at 3 Years After Bariatric Surgery Among Individuals With Severe Obesity

Anita P. Courcoulas, MD, MPH; Nicholas J. Christian, PhD; Steven H. Belle, PhD, MScHyg; Paul D. Berk, MD; David R. Flum, MD, MPH; Luis Garcia, MD; Mary Horlick, MD; Melissa A. Kalarchian, PhD; Wendy C. King, PhD; James E. Mitchell, MD; Emma J. Patterson, MD; John R. Pender, MD; Alfons Pomp, MD; Walter J. Pories, MD; Richard C. Thirlby, MD; Susan Z. Yanovski, MD; Bruce M. Wolfe, MD
for the Longitudinal Assessment of Bariatric Surgery (LABS) Consortium

JAMA Dec 2013



3-year results	RYGB	LAGB
Weight Loss	31.5%	15.9%
Diabetes Remission (HbA1c<6.5%)	67.5%	28.6%
Resolution of Dyslipidemia	61.9%	27.1%
Resolution of Hypertension	38.2%	17.4%

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JAMA Dec 2013

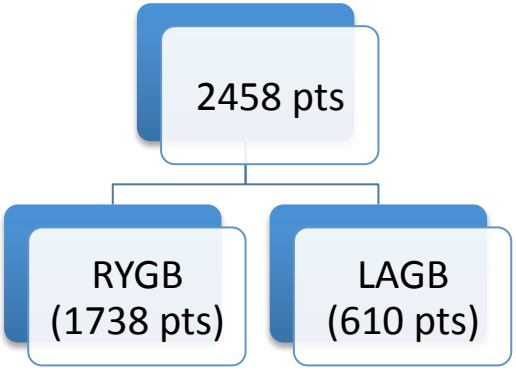
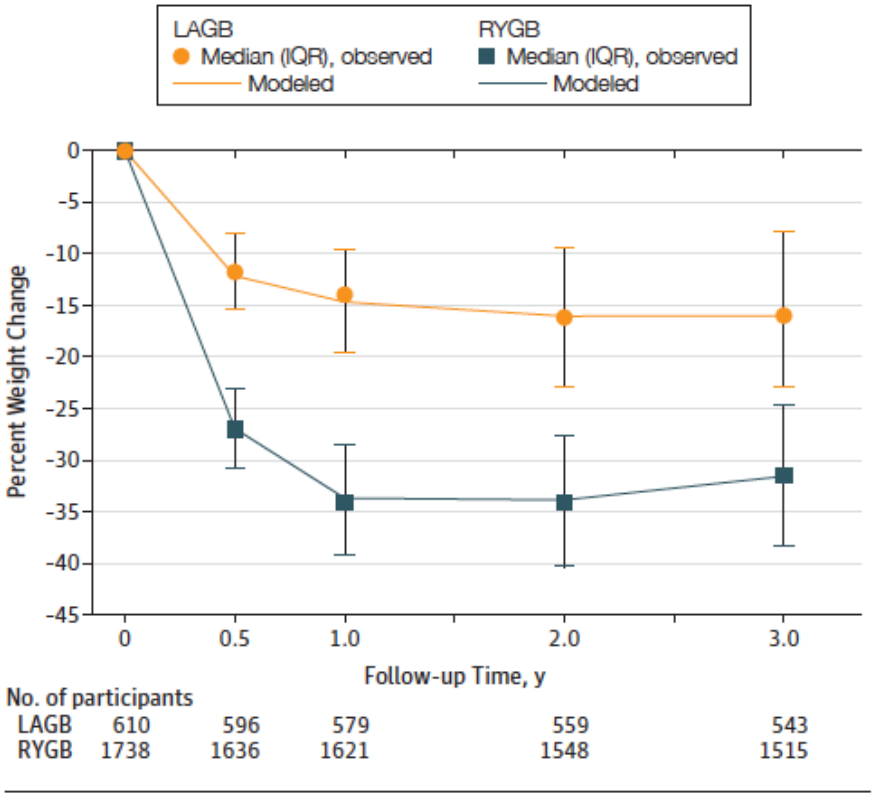


Figure 2. Observed and Modeled Percent Weight Change by Time Point



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JAMA Dec 2013

RYGB

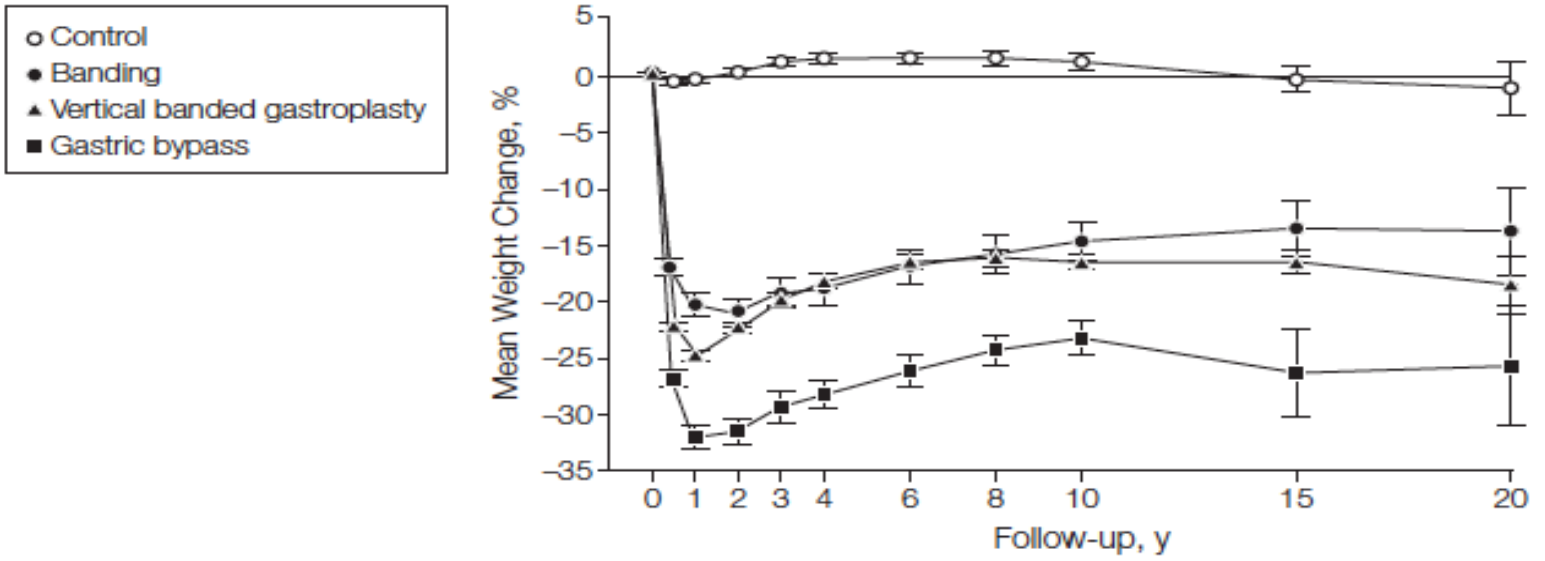
	No. of Participants	Rate[a] (95% CI)
Roux-en-Y Gastric Bypass (n = 1738)		
Deaths	16[b]	0.9 (0.5-1.5)
Within 30 days of surgery	3	0.2 (0.04-0.5)
Sepsis	1	
Cardiovascular disease	1	
Pulmonary embolism	1	
More than 30 days after surgery	13	0.8 (0.4-1.3)
Bowel obstruction	1	
Sepsis	1	
Respiratory failure	1	
Cardiovascular disease	3	
Suicide/substance abuse	2	
Cancer	1	
Indeterminate after adjudication	4	
Subsequent bariatric surgery procedures	4	0.3 (0.1-0.9)
Revision	2	
Reversal	2	

LAGB

Laparoscopic Adjustable Gastric Band (n = 610)		
Deaths	5	0.8 (0.3-1.9)
Within 30 days of surgery	0	0 (0-0.6)
More than 30 days after surgery	5	0.8 (0.3-1.9)
Organ failure	2	
Respiratory failure	1	
Cancer	1	
Indeterminate after adjudication	1	
Subsequent bariatric surgery procedures	77	17.5 (13.8-21.9)
Band replacement	7	
Port revision	19	
Other revision	10	
Band removal	21	
Revision to another bariatric procedure	20	

20-Year follow up in the SOS Study: Long-term Weight Loss

Figure 1. Mean Weight Change Percentages From Baseline for Controls and the 3 Surgery Groups Over 20 Years in the Swedish Obese Subjects Study

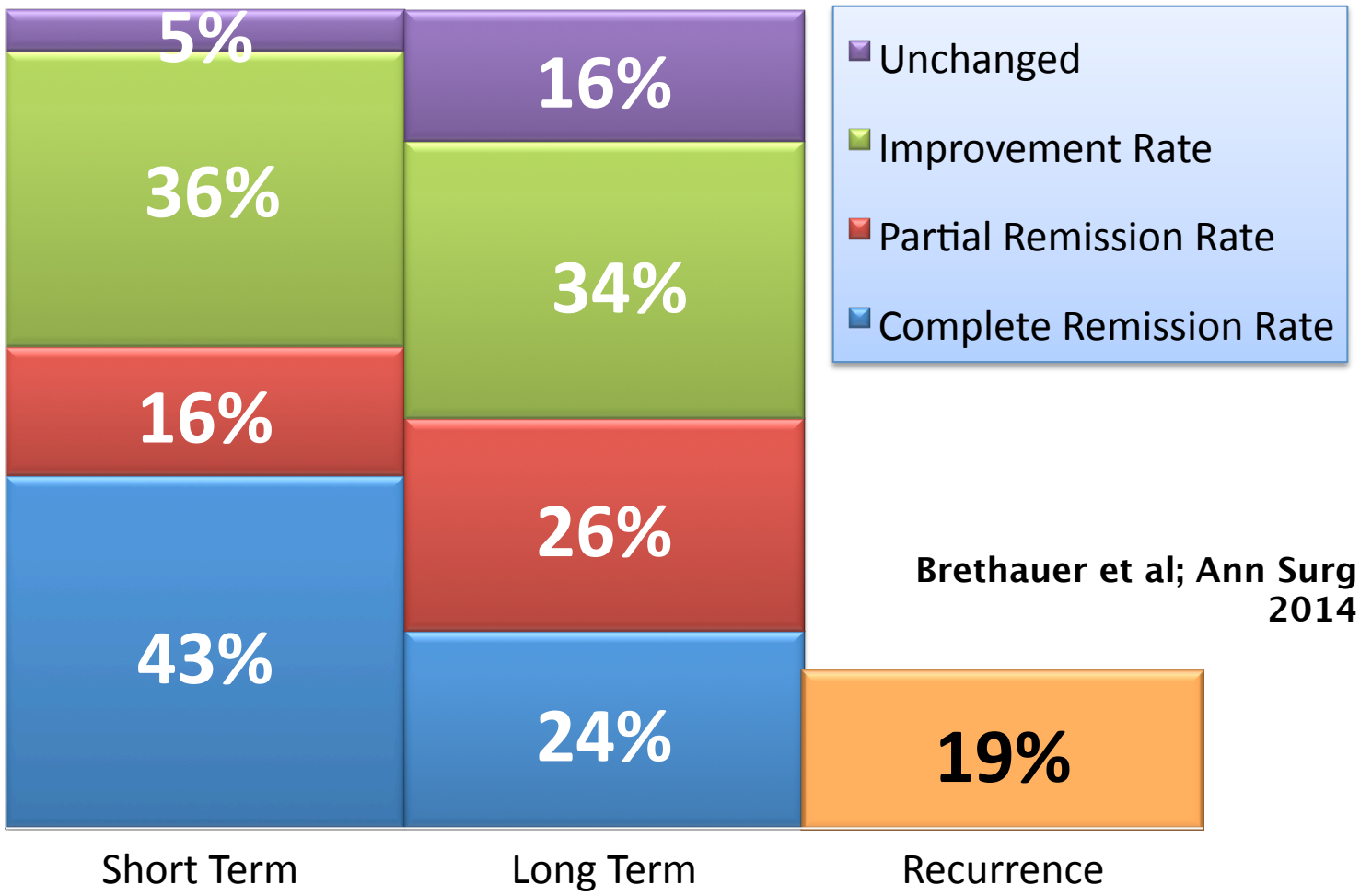


No. of patients						
Control	2037	1490	1242	1267	556	176
Banding	376	333	284	284	150	50
Vertical banded gastroplasty	1369	1086	987	1007	489	82
Gastric bypass	265	209	184	180	37	13

Data shown for controls obtaining usual care and for surgery patients obtaining banding, vertical banded gastroplasty, or gastric bypass at baseline. Percentage weight changes from the baseline examination and onward are based on data available on July 1, 2011. Error bars represent 95% CIs.

Remission and Recurrence

Whole Cohort (n=217)



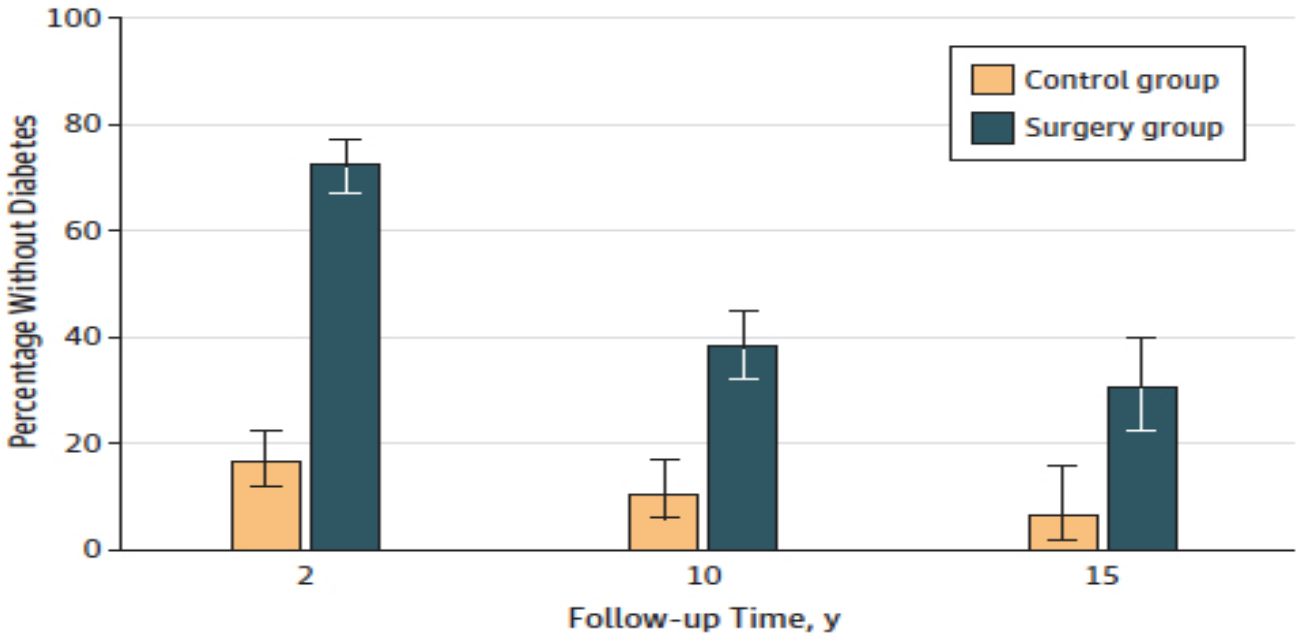
Brethauer et al; Ann Surg 2014

19% of patients developed recurrence of diabetes; 75% still had A1c <7%

Long-Term Durability of Surgical Control of Diabetes

SOS Study; Sjostrom et al; JAMA, June 2014

Figure 1. Prevalence of Diabetes Remission in the Bariatric Surgery and Control Groups



Total participants			
Control	207	135	62
Surgery	303	236	115
Odds ratio (95% CI)	13.3 (8.5-20.7)	5.3 (2.9-9.8)	6.3 (2.1-18.9)

Incidence of Remission in Adults With Type 2 Diabetes: The Diabetes & Aging Study

Andrew J. Karter,[1] Shantanu Nundy,[2,3] Melissa M. Parker,[1] Howard H. Moffet,[1] and Elbert S. Huang[4,5,6]

DOI: 10.2337/dc14-0874

Diabetes Care Publish Ahead of Print, published online September 17, 2014

122,781 patients UNDER MEDICAL MANAGEMENT ONLY

Time of Hx of DM – 6 years

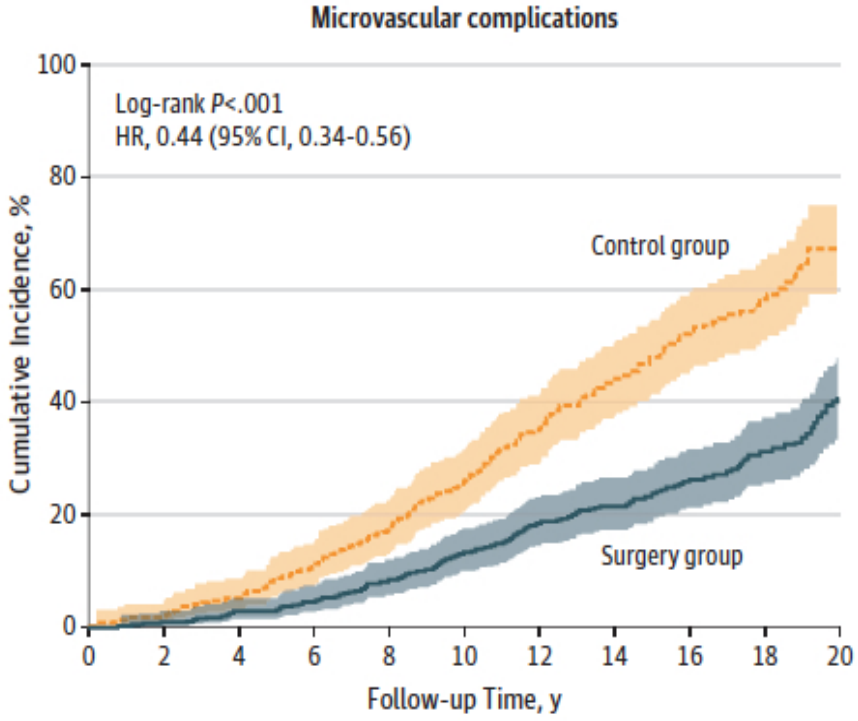
Partial remission – at least 1 year with A1c 5.7 to 6.4%
Complete – at least 1 y with A1c < 5.7%
Prolonged– Complete remission > 5 years

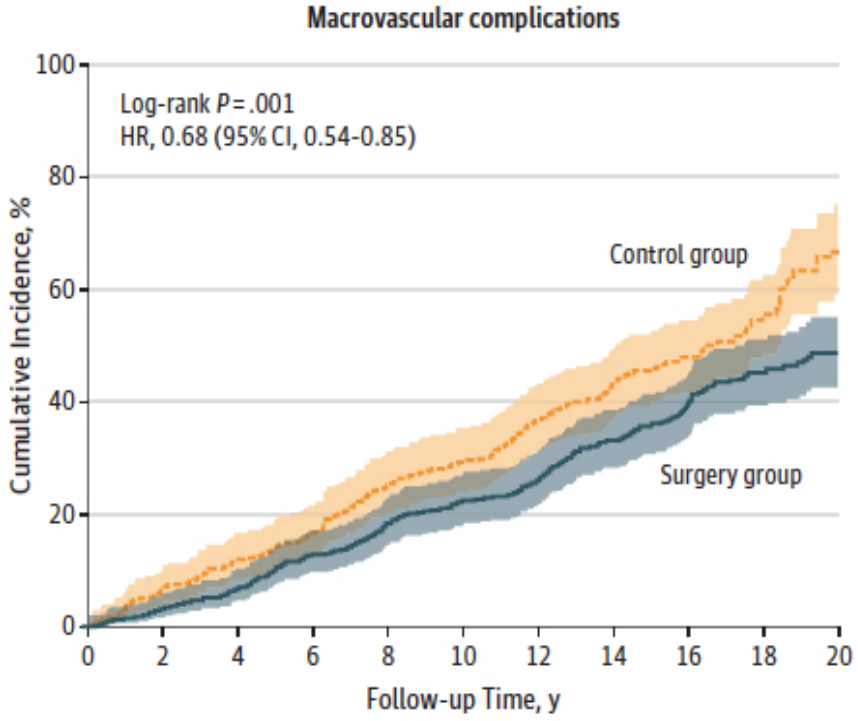
Partial	2.8%
Complete	0,24%
Prolonged	0,04%

Surgery Reduces Long-Term Microvascular and Macrovascular Diabetes Complications

SOS Study; Sjostrom et al; JAMA 2014

Figure 3. Cumulative Incidence of Microvascular and Macrovascular Diabetes Complications in the Surgery and Control Groups





No. at risk											
Control	260	251	239	222	201	177	146	104	68	46	19
Surgery	343	336	326	318	301	280	257	207	160	112	63

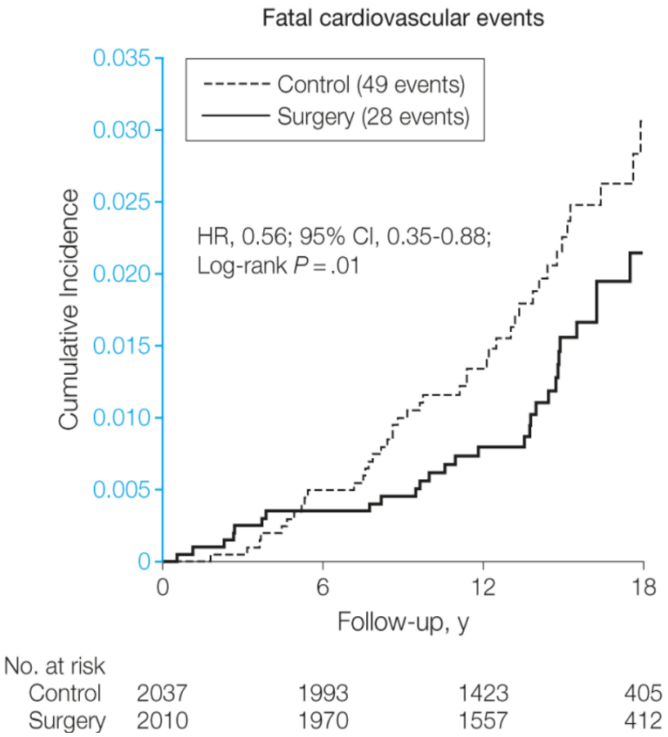
260	240	225	214	191	178	155	116	80	53	20
343	330	315	294	270	254	238	186	142	92	54

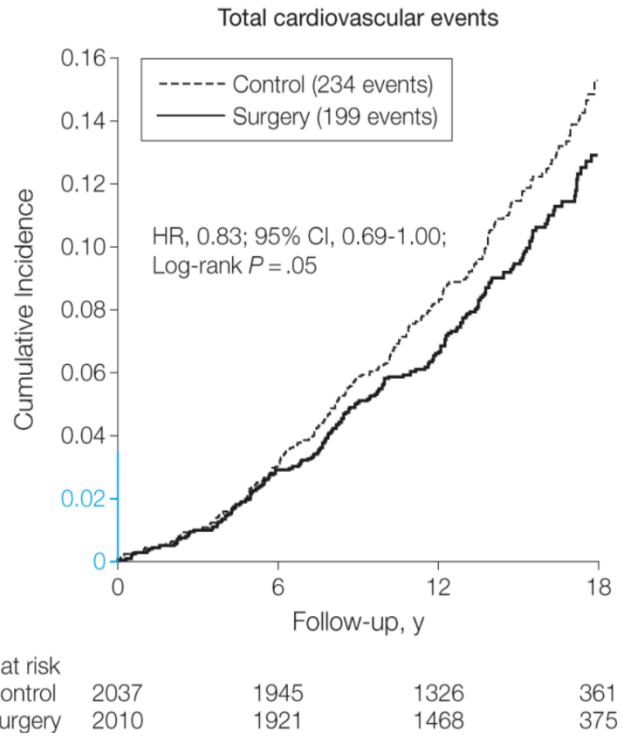
Bariatric Surgery and Long-term Cardiovascular Events

Lars Sjöström, MD, PhD Et al

JAMA 2012

Fatal and Total CV events





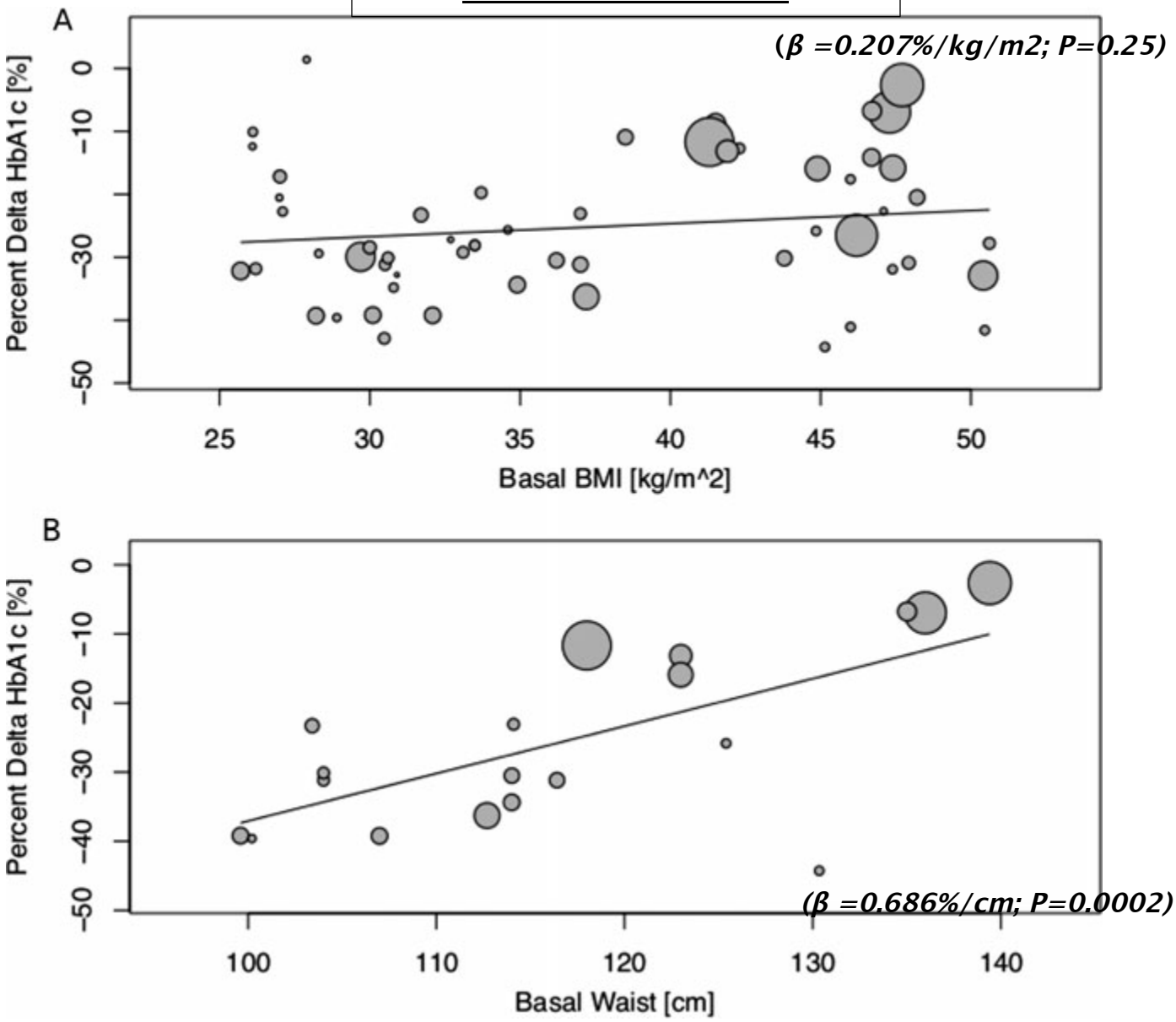
Bariatric Surgery Associated With Reduced Long-Term, All-Cause Mortality Compared With Non-Operated Controls

Study	Procedure	F/U	Mortality Reduction
MacDonald, 1997	RYGB	9 yr	88%
Flum, 2004	RYGB	4.4 yr	33%
Christou, 2004	RYGB	5 yr	89%
Sowemimo, 2007	RYGB	4.4 yr	63%
Dixon, 2007	LAGB	12 yr	72%
Adams, 2007	RYGB	8.4 yr	40%
Sjostrom, 2007	VBG/other	14 yr	31%
Perry, 2008	RYGB/LAGB	2 yr	48%

Predicting outcomes of metabolic surgery

Baseline BMI Does not predict glycemic improvements

1437 studies reviewed



Panunzi et al. Ann Surg 201

Patient Factors and Outcomes Associated with Remission of Hyperglycemia (N=191)

	Improved	Resolved	P
	33	158	
Age	48.2	47.8	0.724
Gender (% female)	70%	76%	0.615
Preop BMI	51	50	0.270
Postop BMI	37	33	0.002
%EWL	42	62	<0.001
Preop HA1C	8.8	8.1	0.033
Preop FPB	189	183	0.436
Duration of DM	10.7	4.1	<0.001
% insulin users	63%	23%	<0.001

Preoperative predicting factors:

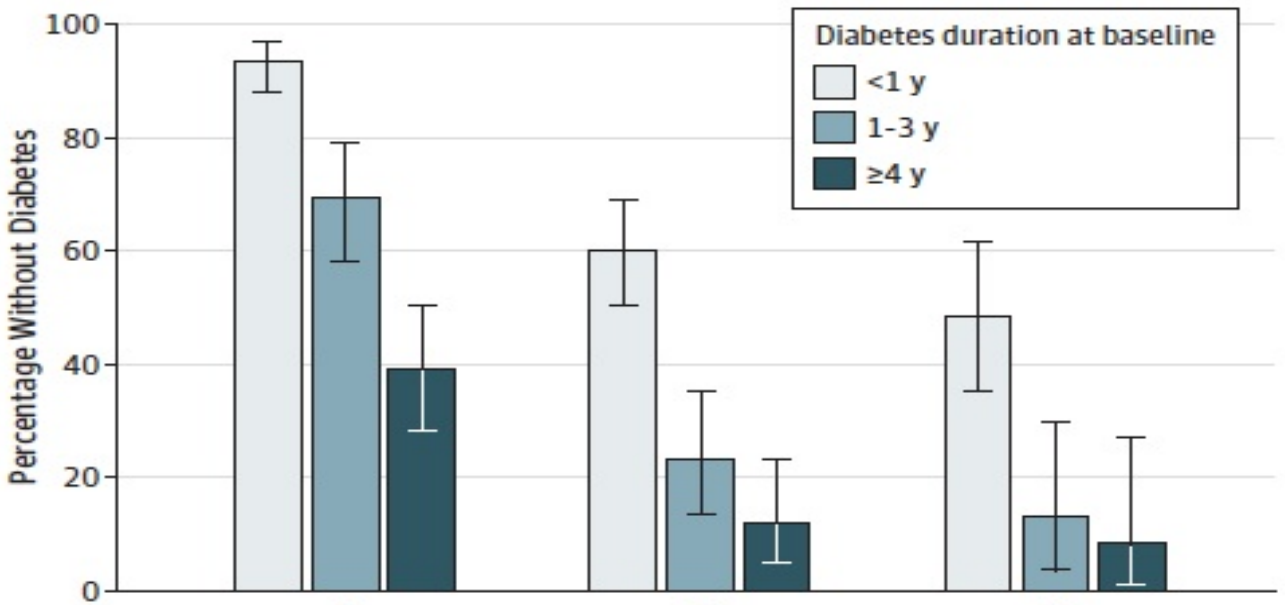
- **Duration of disease**
- Use of Insulin

Schauer et al; Ann Surg 2003

Longer duration of diabetes at baseline is associated with lower long-term disease remission-term

JAMA, June 2014

Figure 2. Diabetes Remission by Diabetes Duration in the Surgery Group



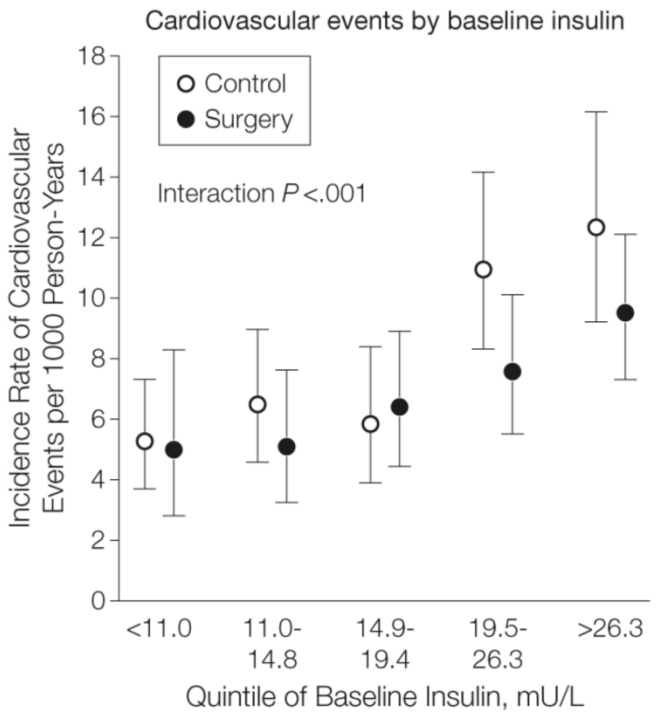
Total participants			
<1 y	139	113	60
1-3 y	82	65	31
≥4 y	82	58	24

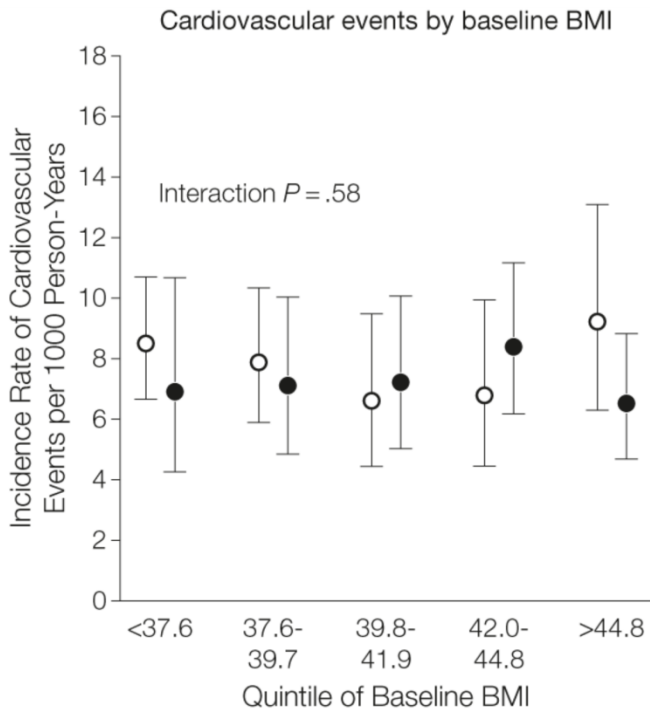
Bariatric Surgery and Long-term Cardiovascular Events

Lars Sjöström, MD, PhD Et al

JAMA 2012

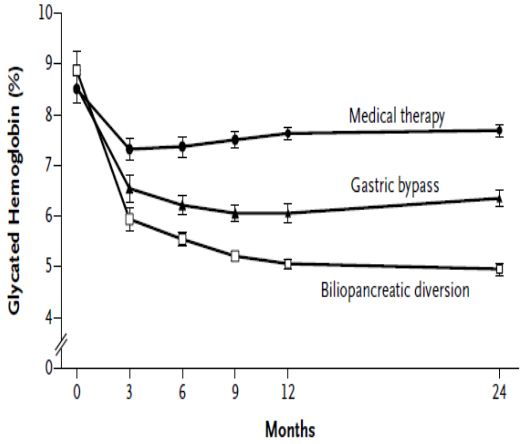
Reduction of CV Disease not predicted by Baseline BMI

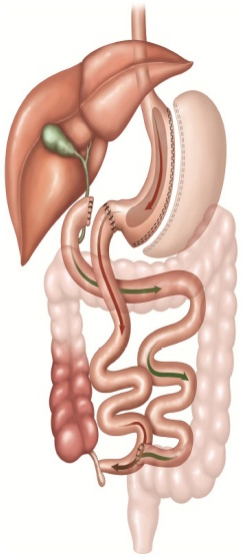




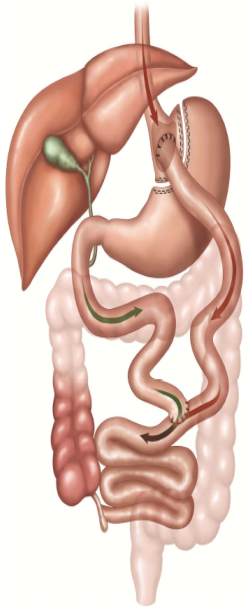
Comparing procedures

BPD vs RYGB





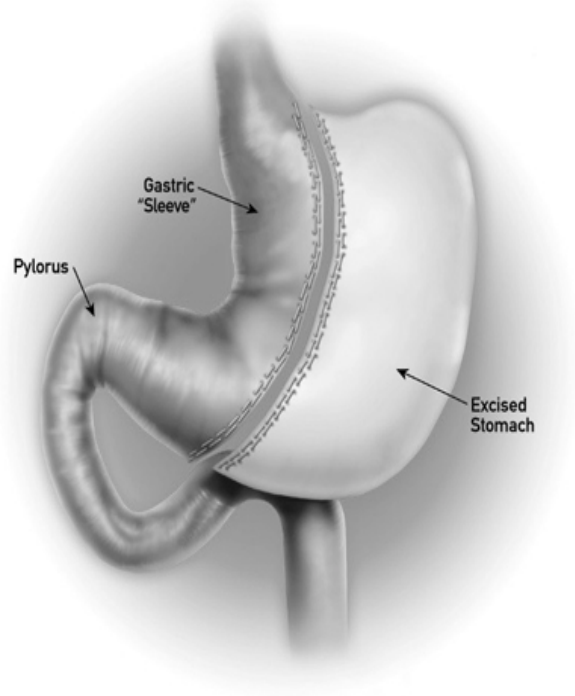
BPD

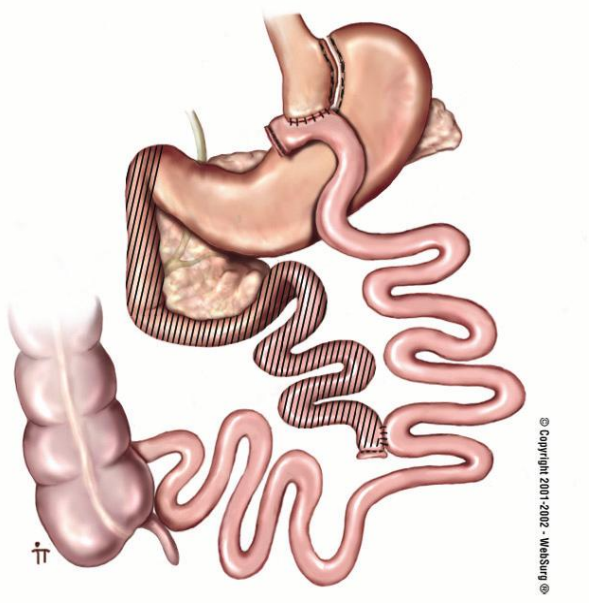


RYGB

	Late complications	
	BPD group	**RYGB group**
Incisional hernia (9 months)	**1 (5.3%)** **1 ♂**	**0**
Intestinal occlusion (6 months)	**0**	**1(5.3%)** **1 ♂**
Iron deficiency anemia	**2 (10.5%)*** **2 ♀**	**2 (10.5%)** **2 ♀**
Hypoalbuminemia <3.5 g/l	**2 (10.5%)*** **1 ♀ 1 ♂**	**0**
Osteopenia BMD T-score = –2	**1 (5.3%)** **1 ♀**	**0**
Osteoporosis BMD T-score =–2.7	**1(5.3%)*** **1 ♀**	**0**

Sleeve Gastrectomy vs RYGB





Metabolic Effects of Bariatric Surgery in Patients With Moderate Obesity and Type 2 Diabetes

Analysis of a randomized control trial comparing surgery with intensive medical treatment

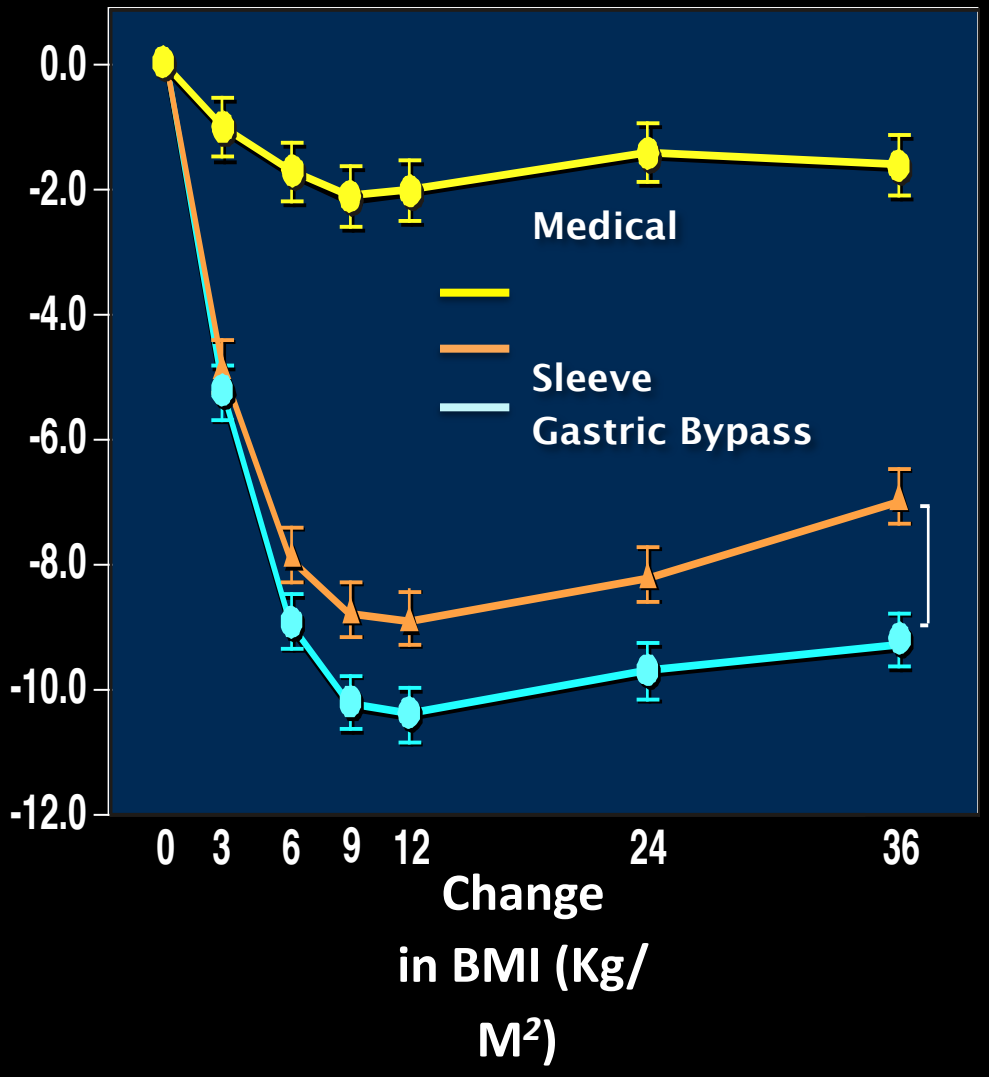
SANGEETA R. KASHYAP, MD[1]
DEEPAK L. BHATT, MD, MPH[2]
KATHY WOLSKI, MPH[3]
RICHARD M. WATANABE, PHD[4]
MUHAMMAD ABDUL-GHANI, MD, PHD[5]
BETH ABOOD, RN[1]
CLAIRE E. POTHIER, MPH[3]
STACY BRETHAUER, MD[6]
STEVEN NISSEN, MD[3]
MANJULA GUPTA, PHD[1]
JOHN P. KIRWAN, PHD[7]
PHILIP R. SCHAUER, MD[6]

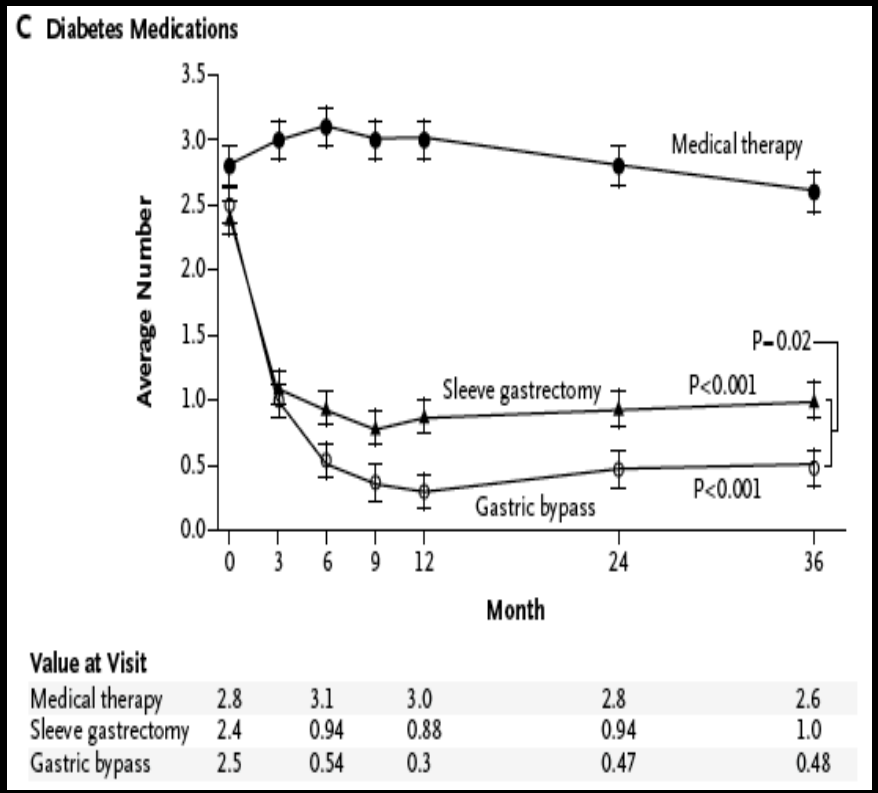
progressive hyperglycemia, subsequent microvascular complications, and macrovascular complications. Although lifestyle modifications and oral hypoglycemic agents improve glycemic control, the majority of patients do not achieve the optimal

STAMPEDE TRIAL: 24 months

Despite similar weight loss as sleeve gastrectomy, RYGB uniquely restores beta-cell function and reduces truncal fat"

Stampede Trial
SG vs RYGB @ 36 months





Value at Visit					
Medical therapy	2.8	3.1	3.0	2.8	2.6
Sleeve gastrectomy	2.4	0.94	0.88	0.94	1.0
Gastric bypass	2.5	0.54	0.3	0.47	0.48

Cardiovascular Medications at Baseline and Month 36

CV medications – number (%)	Medical Therapy (n=40)	Bypass (n=48)	Sleeve (n=49)
Baseline			
None	0 (0)	3 (6.3)	2 (4.1)
1 – 2	19 (47.5)	17 (35.4)	28 (57.1)
≥ 3	21 (52.5)	28 (58.3)	19 (38.8)
Month 36			
None	1 (2.5)	33 (68.8) *	21 (42.9) *
1 – 2	18 (45)	14 (29.2)	25 (51)
≥ 3	21 (52.5)	1 (2.1)	3 (6.1)

* P value <0.05 with Medical Therapy group as

QOL Changes

- Gastric Bypass: 5/8 domains improved
- Sleeve Gastrectomy: 2/8 domains improved
- Intensive Med Rx: 0/8 domains improved

Surgery for T2DM indicated in obese diabete (BMI>30 kg/m2)

Diabetes Surgery Summit
Rome, Italy
March 2007

POSITION STATEMENT

Standards of Medical Care in Diabetes—2009

AMERICAN DIABETES ASSOCIATION

American Diabetes Association

International Diabetes Federation

Position Statement 2011

NICE Draft Recommendations 2014

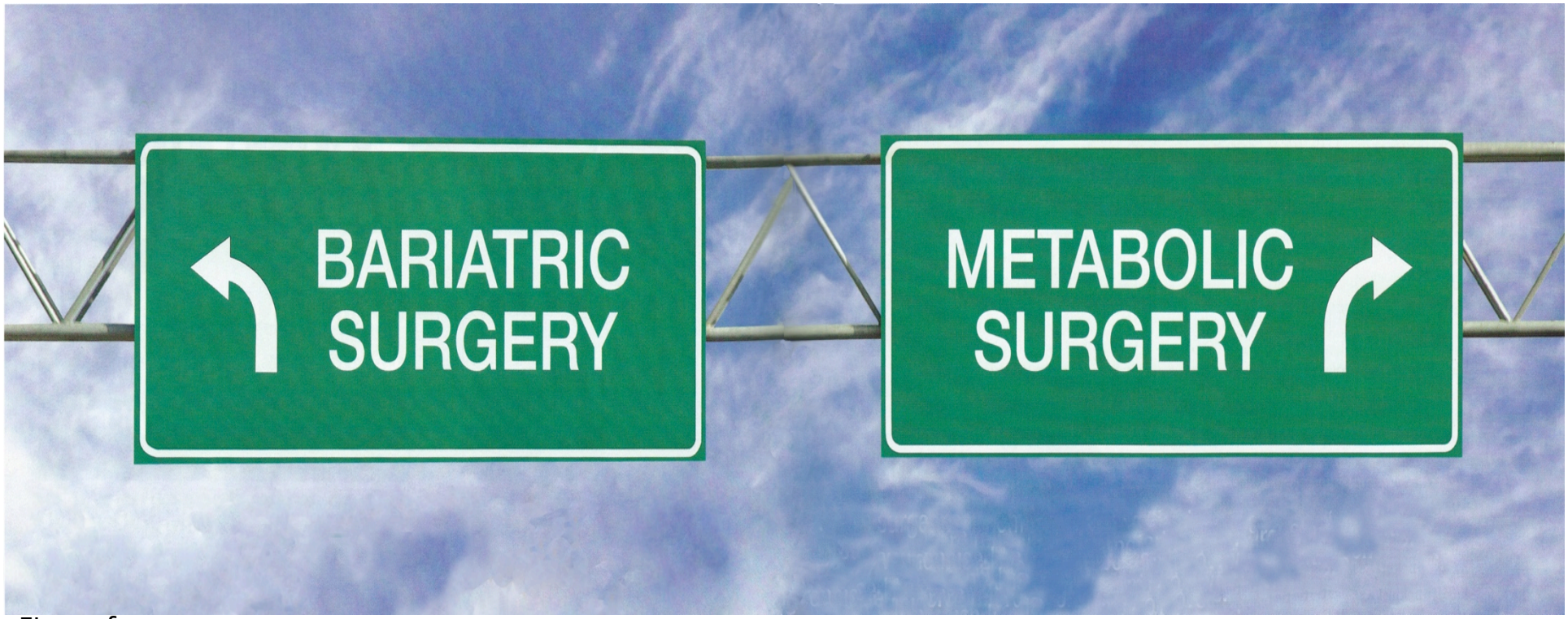


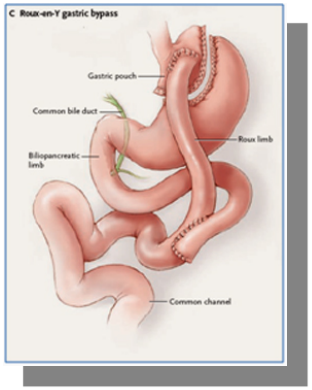
Figure from:
***Endocrine News*; Dec 2013**

Original Use/ Indication

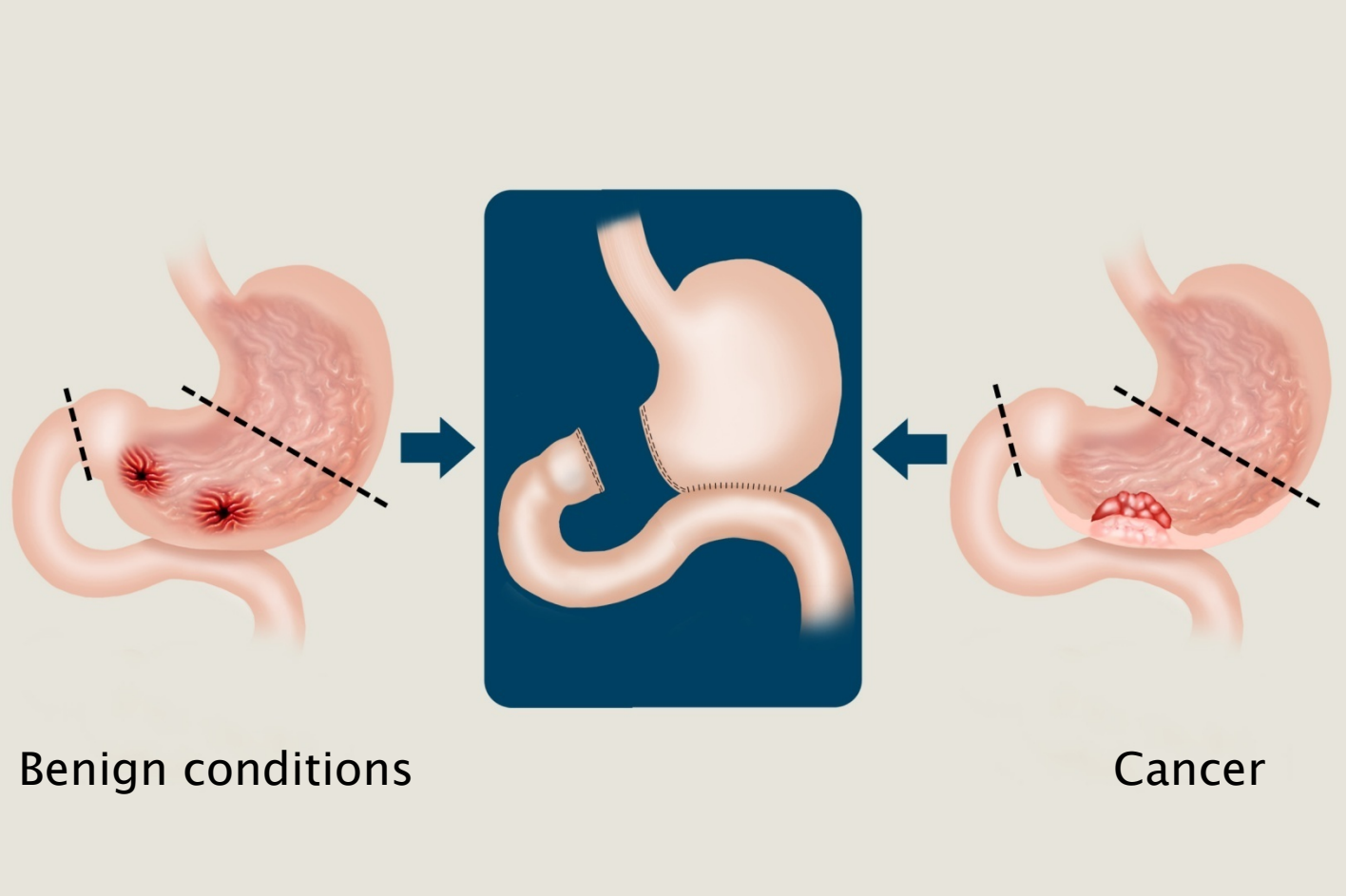
Clinical Observations Additional/Unexpected Benefits

New Understanding Mechanisms of Action

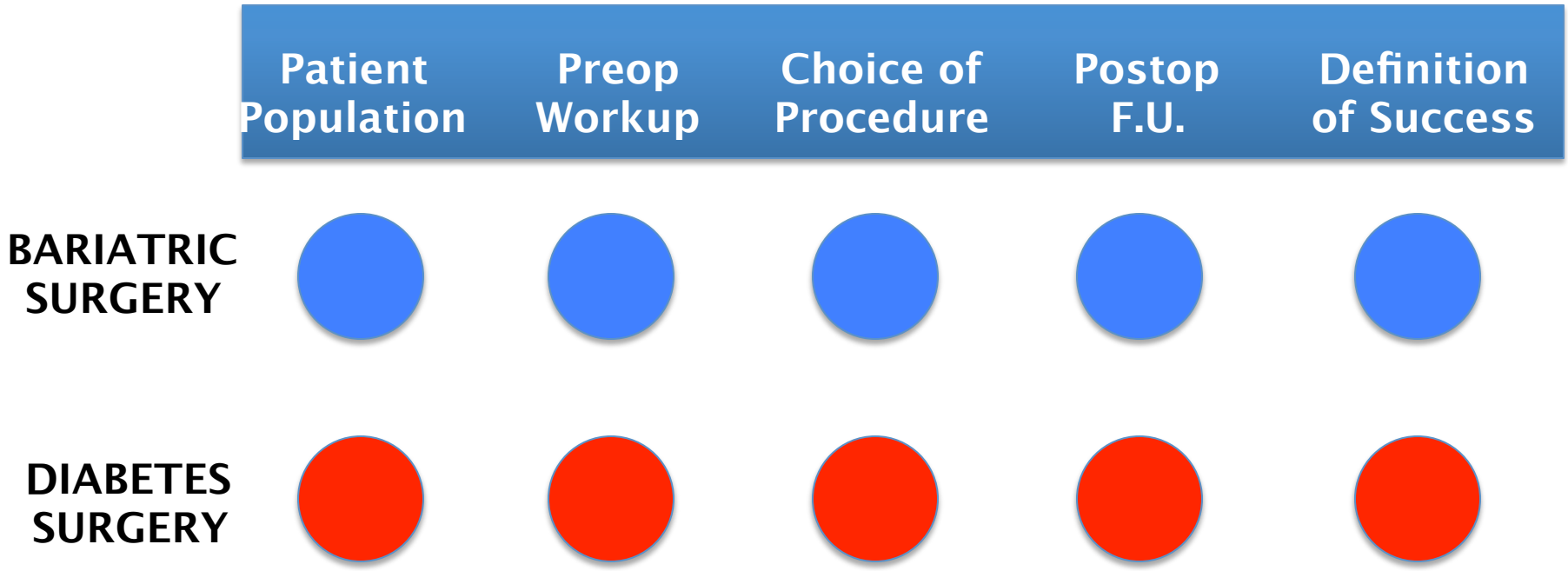
Treatment Approved for Other Indications



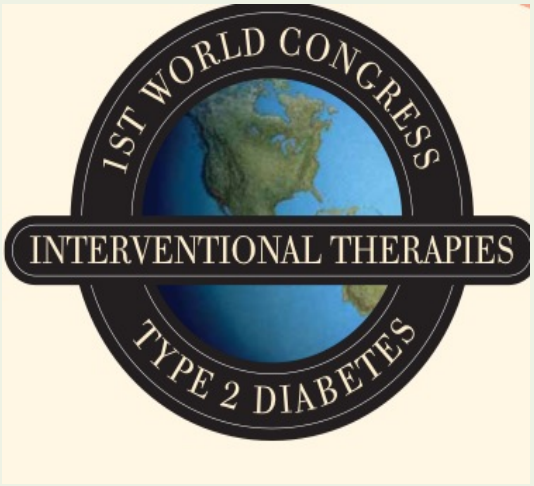
Surgical Disciplines are not defined by the type of procedure



BARIATRIC SURGERY vs DIABETES SURGERY



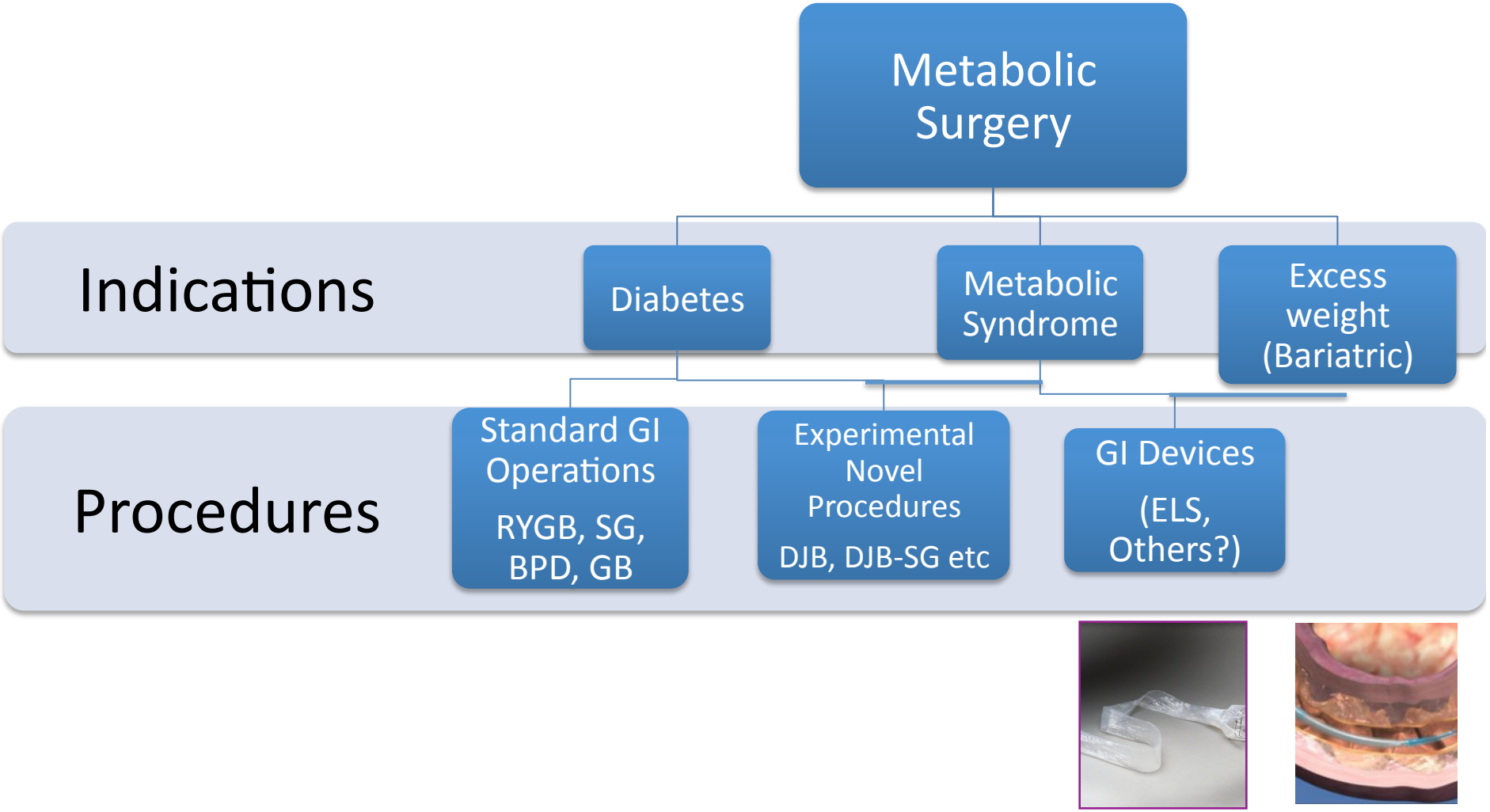
3rd World Congress on Interventional Therapies for Diabetes
&
2nd Diabetes Surgery Summit (DSS)



Joined Event

LONDON, UK
SEPTEMBER 2015

the most important event
in *Diabetes and Metabolic Surgery*
Witness history as we develop global guidelines that will shape the future of diabetes care!
More to come…


Metabolic Surgery
Indications
Diabetes
Metabolic Syndrome
Excess weight (Bariatric)
Procedures
Standard GI Operations
RYGB, SG, BPD, GB
Experimental Novel Procedures
DJB, DJB-SG etc
GI Devices
(ELS, Others?)

DIABETES AND OPERATION.

A NOTE ON THE EFFECT OF GASTRO-JEJUNOSTOMY UPON A CASE OF MILD DIABETES MELLITUS WITH A LOW RENAL THRESHOLD.

BY O. LEYTON, M.D. CAMB., F.R.C.P. LOND.,
PHYSICIAN TO THE LONDON HOSPITAL.

How can we account for the apparent improvement? The glycosuria was absent after operation in spite of a diet containing a fair amount of carbohydrate. In order to determine whether the operation

THE AMELIORATION OF DIABETES MELLITUS FOLLOWING SUBTOTAL GASTRECTOMY

MURRY N. FRIEDMAN, M.D., F.A.C.S., ANTONIO J. SANCETTA, M.D., and GEORGE J. MAGOVERN, M.D., Brooklyn, New York

1955

IN 1923, MURLIN noted the presence of a substance in extracts of the pancreas which could raise the blood sugar. Subsequently, this hyperglycemic factor was demonstrated

and duodenum. Therefore, when subtotal gastrectomy for duodenal ulcer resulted in marked amelioration of the diabetic state in 3 patients at the Brooklyn Veterans Hospi-

Potential of Surgery for Curing Type 2 Diabetes Mellitus

Rubino and Gagner, *Ann Surg* 2002

Hypothesis

- **Surgery to intentionally treat diabetes (diabetes surgery)**
- **Weight-independent mechanisms**
- **GI tract as a target for anti-diabetes drugs/interventions**
- **The GI Tract may harbor mechanisms of disease ("anti-incretin theory")**

…“Rubino's idea boils down to one impolite word used to refer to the excrement of steers” (= “bull….”)

Diabetes Volume 63, ■■■ 2014

Francesco Rubino and Stephanie A. Amiel

Is the Gut the "Sweet Spot" for the Treatment of Diabetes?

Diabetes 2014;63:1–4 | DOI: 10.2337/db14-0402

Oskar Minkowski possessed a rare combination of talents: He was an internist with the intuition of a scientist and the dexterity of a surgeon. One day in 1889, he and his

In particular, Roux-en-Y gastric bypass (RYGB) restores first-phase insulin response (10) and results in hypersecretion of C-peptide and insulin following nutrient in-

Diabetes, July 2014, in press