Surgical Outcomes, Choice of Procedure or Something Else

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Disclosures

Research/Educational Grants: Novo Nordisk, Ethicon, Medtronic

Consulting/SAB: Morphic Medical, GT ,Metabolic Solutions, Keyron

Speaking Honoraria: Medtronic, Ethicon, Novo Nordisk, Lilly

Others: President, Metabolic Health Institute (nonprofit)

REVIEW

ANNALS OF SURGERY
Vol. 236, No. 5, 554–559

Potential of Surgery for Curing Type 2 Diabetes Mellitus

Francesco Rubino, MD,* and Michel Gagner, MD, FACS, FRCSC†

*From the *IRCAD-Eu
Sinai Medical Center,*

FEATURE

Effect of Duodenal–Jejunal Exclusion in a Non-obese Animal Model of Type 2 Diabetes

A New Perspective for an Old Disease

Francesco Rubino, MD, and Jacques Marescaux, MD, FRCS

Background: The Roux-en-Y gastric bypass and the biliopar
diversion effectively induce weight loss and long-term cor
type 2 diabetes in morbidly obese individuals. It is unknown v
the control of diabetes is a secondary outcome from the treat

Is Type 2 Diabetes an Operable Intestinal Disease?

A provocative yet reasonable hypothesis

FRANCESCO RUBINO, MD

TYPE 2 DIABETES: IS IT AN INTESTINAL DISEASE? — The rapid resolution of diabetes after Roux-

Potential of Surgery for Curing Type 2 Diabetes Mellitus

Francesco Rubino, MD,* and Michel Gagner, MD, FACS, FRCSC†

*From the *IRCAD-European Institute of Telesurgery, Strasbourg, France, and the †Division of Laparoscopic Surgery, Mount Sinai Medical Center, New York, New York*

Newsweek

“A surgical Cure of Diabetes?”

…“Rubino's idea boils down to one impolite word used to refer to the excrement of cows”….“BS”

Leslie Stahl:
Can Surgery Cure Diabetes? Yes/No

FR: …I can’t answer the question as a yes or no

LS: You only have yes and no for an answer

FR: …I should say no then….

Is Surgery a Cure of Type 2 Diabetes?

October 2009

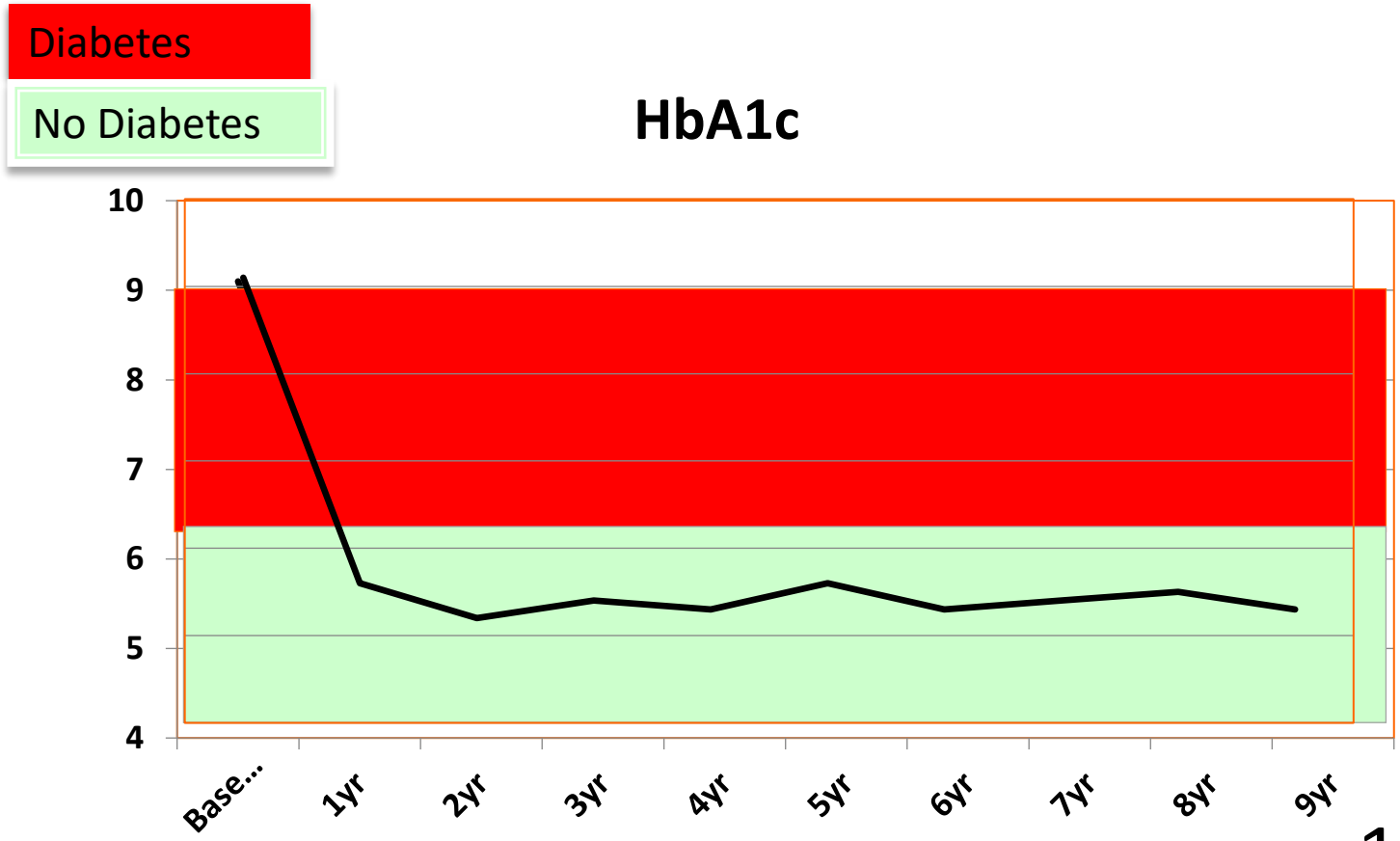
> RYGB

October 2021

Normal Glycemia
Meds: Multivitamins

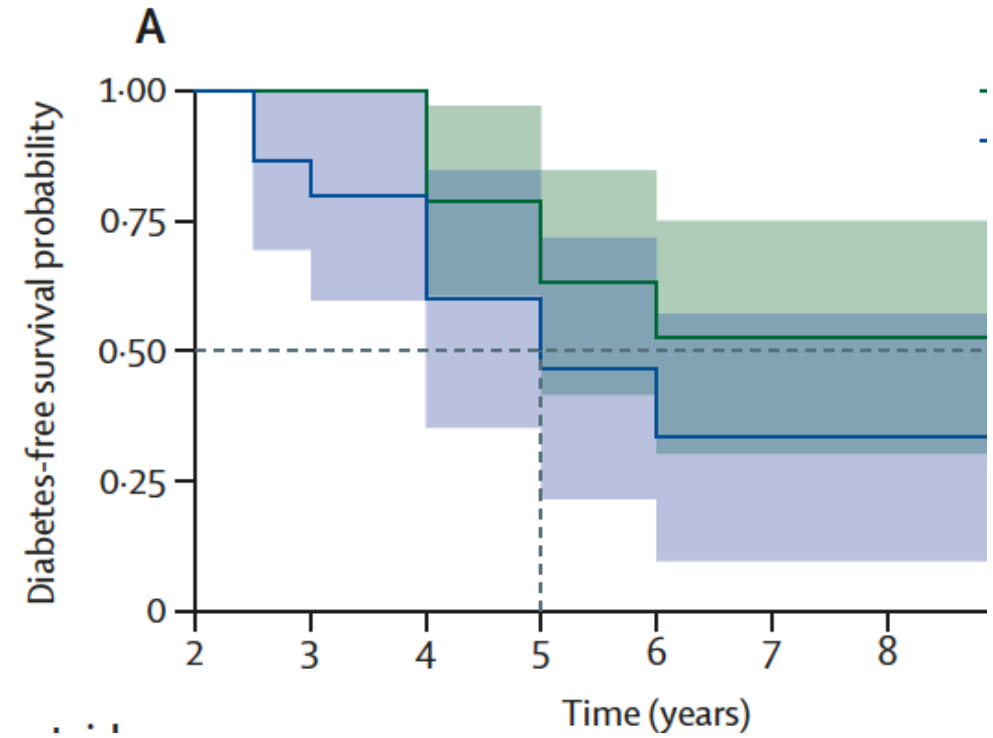
42yo F- Type 2-Diabetes
> 8-year disease duration

Preop Medications: Insulin + Liraglutide + Metformin
Preop HbA1c 9.1



...14yr

10-year Remission of Diabetes



PP analysis,

- Surgery (Total) : **37.5%**
- MT: 0

BPD (50%; CI: 30.0; 70.1),

RYGB (25%; CI: 11.2; 46.9)

(P=0.19, Fisher exact test between surgical procedures)

Weight Loss and Diabetes

Weight changes did not predict diabetes remission or relapse among surgical patients.

Weight regain at 10-year:

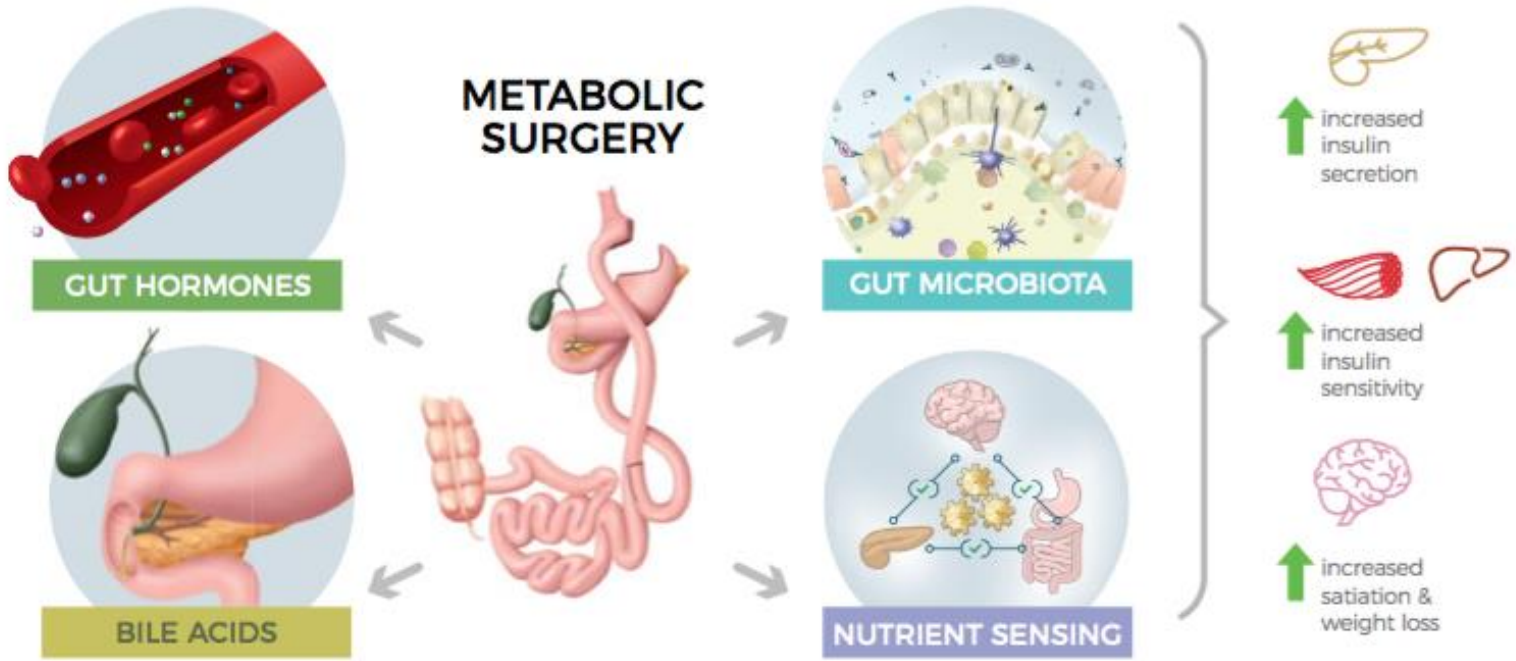
- Pts with Remission: 7.05±6.89%
- Pts with Relapse: 8.21+6.15%

(P= NS)

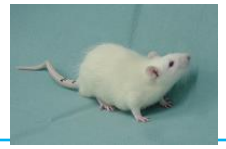
Supporting weight-independent mechanisms of GI bypass procedures

How does surgery improve diabetes

Metabolic Surgery changes various mechanisms of GI physiology involved in metabolic regulation [3, 4]



"Given its role in metabolic regulation, the GI tract constitutes a clinically and biologically meaningful target for the management of T2D." DSS-II [2]



Weight independent effects of GI Surgery in rodents

A LONG ROAD

Observations that diabetes can be improved or even resolved by surgical operations have been reported for almost a century.

1955 Weight-loss (bariatric) sugery introduced.

Jejuno-ileal bypass

1978 Ahmad et al; Diabetes Care

1981 Ackerman NB. Surg Gynecol Obstet.

2004 Experimental evidence in rats links gastroin-testinal surgery and glucose metabolism[6].

2007 First DSS.

2015 Second Diabetes Surgery Summit.

1920 1930 1940 1950 1960 1970 1980 1990 2000 2010 2020

1925-50 Several reports document diabetes resolution after stomach surgery.

World's heaviest family in 1929.

2016 Guidelines for the surgical treatment of diabetes published in Diabetes Care[1].

1970-95 Several reports consistently document remission of diabetes after bariatric surgery

2006-07 Studies in humans start to explore the use of surgery as an intentional treatment of diabetes[10].

2008-15 Publication of several randomized clinical trials demonstrates effects of surgical treatment of diabetes.

Gastric Bypass

1979 Printen et al; Ann Surg

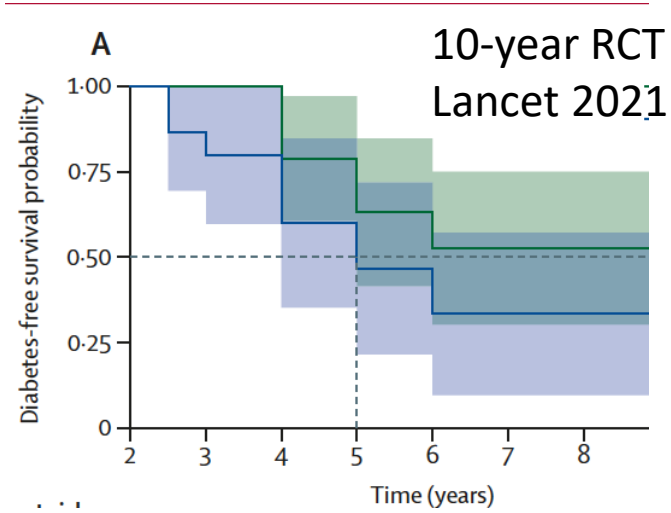
1987 Pories et al; Ann Surg.

1995 Pories et al; Ann Surg.: "Who would have thought…"

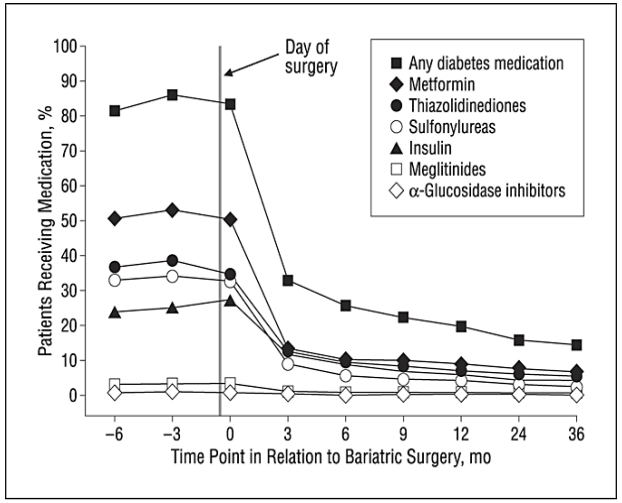
F. Rubino *Nature* 533, 459–461 (2016).

Outcomes of Surgical Treatment in pts with T2D

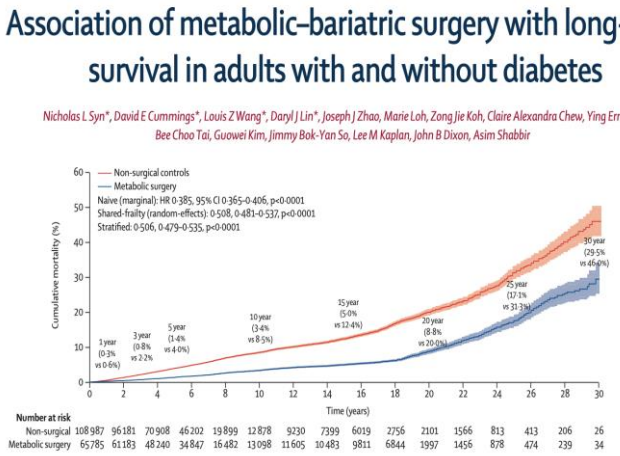
Durable Remission (>10Yr) ”Cure” of T2D



Use of diabetes medication (> 60% reduction within 3 months)

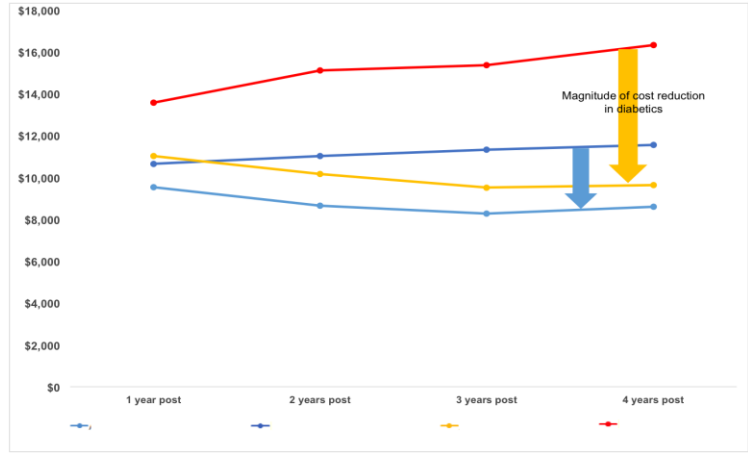


Greater Reduction All Cause-Mortality (60% vs 30% reduction T2D vs no T2D)

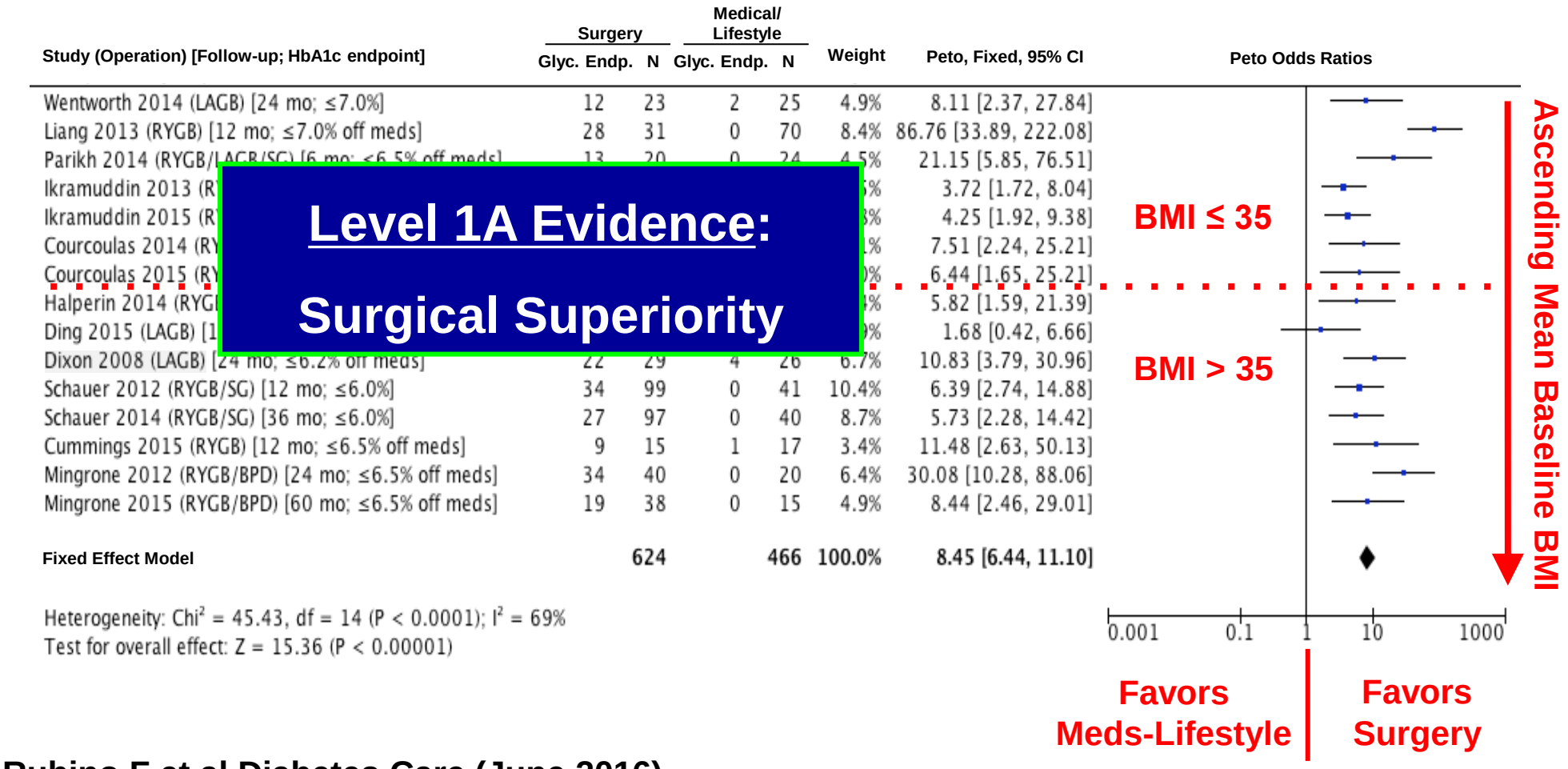

Association of metabolic–bariatric surgery with long-term survival in adults with and without diabetes

Nicholas L Syn*, David E Cummings*, Louis Z Wang*, Daryl J Lin*, Joseph J Zhao, Marie Loh, Zong Jie Koh, Claire Alexandra Chew, Ying Ern Loo, Bee Choo Tai, Guowei Kim, Jimmy Bok-Yan So, Lee M Kaplan, John B Dixon, Asim Shabbir

Greater Cost-effectiveness (greater magnitude of cost-reduction)



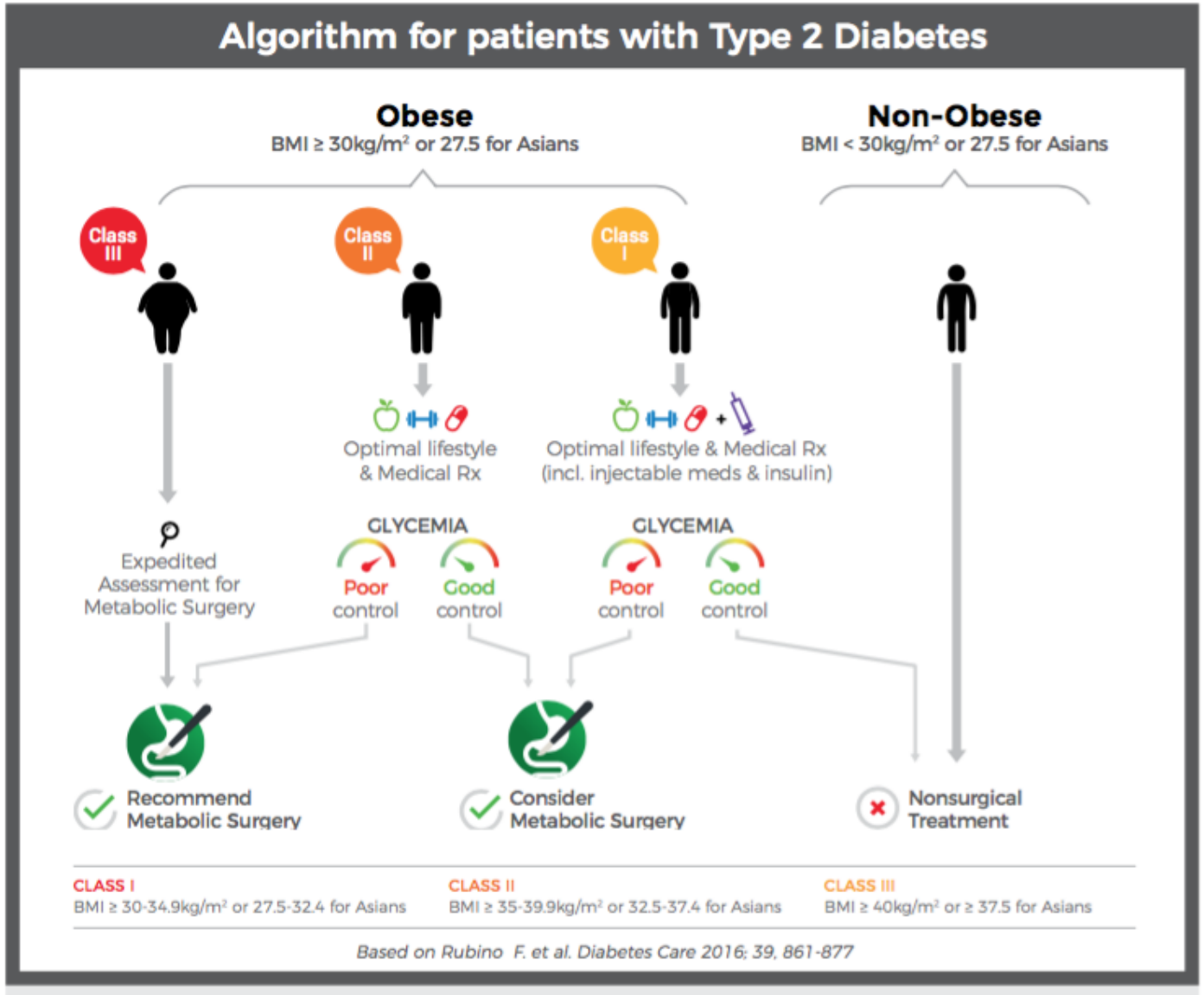
RCTs of Surgery *vs*. Meds/Lifestyle Care for T2DM



Rubino F et al Diabetes Care (June 2016)

Indications for Surgical Treatment

"There is now sufficient clinical and mechanistic evidence to support inclusion of metabolic surgery among antidiabetes interventions for people with T2D and obesity." DSS-II[2]



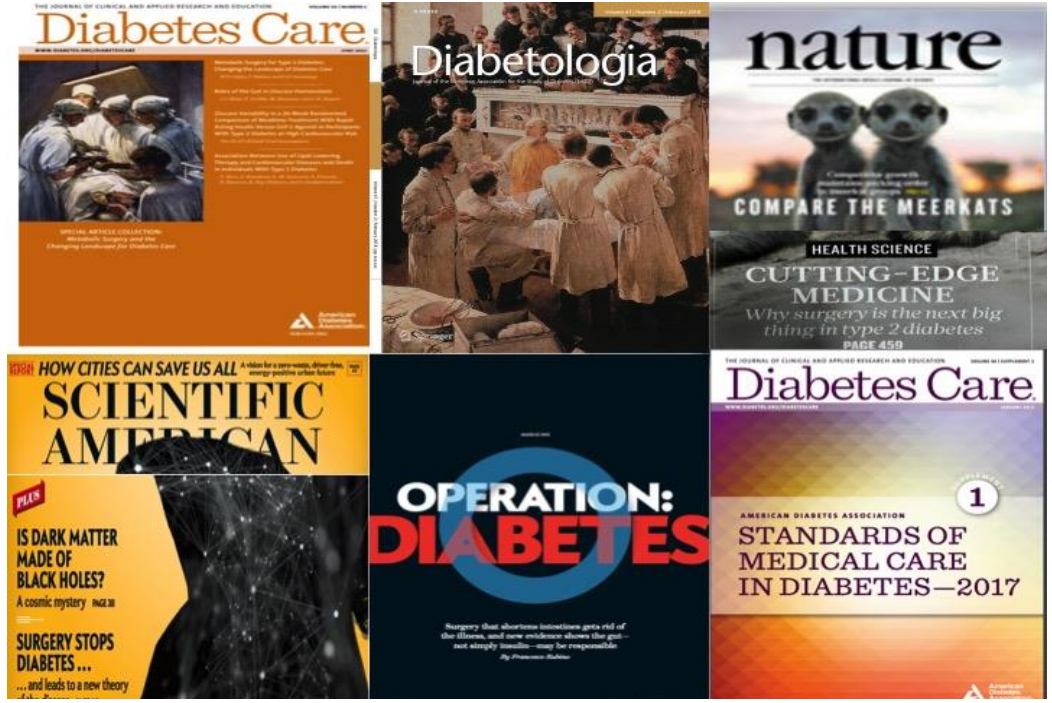
THE LANCET

Volume 397 · Number 10271 · Pages 253-346 · January 23-29, 2021 www.thelancet.com

"Metabolic surgery is more effective than conventional medical therapy in the long-term control of type 2 diabetes."

See Articles page 293

£5.00 Registered as a newspaper · ISSN 0140-6736
Founded 1823 · Published weekly



"Why surgery is the next big thing for Type 2 Diabetes"

Nature (cover page) 26 May 26, 2016 — nature

"Surgery should be an option for diabetics"

time.com/4345470/gastric-bypass-surgery-diabetes/ — TIME

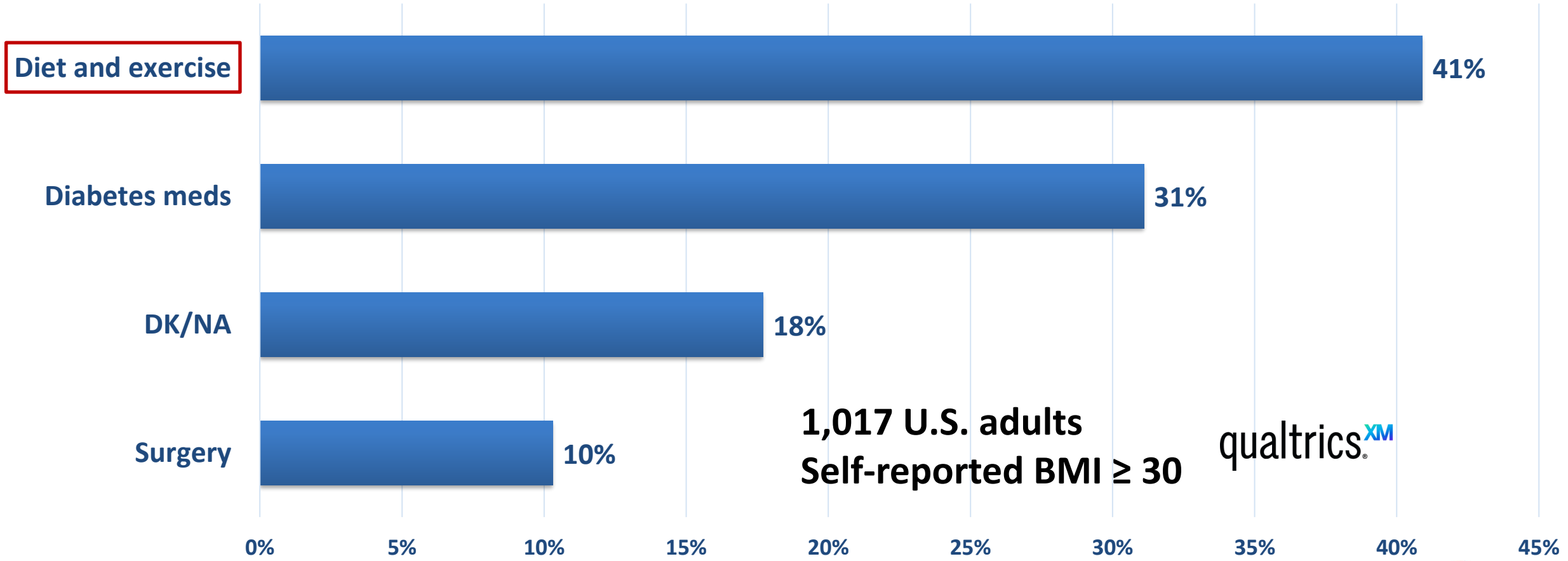
"One of the most significant changes in treating diabetes since the discovery of insulin in 1921"

New Scientist, 28 May, 2016 — NewScientist

"Metabolic Surgery for Type 2 Diabetes: Changing the Landscape of Diabetes Care"

Diabetes Care 2016 Jun; 39 (6): 857-860 — Diabetes Care

"What is most effective treatment today for type 2 diabetes?"



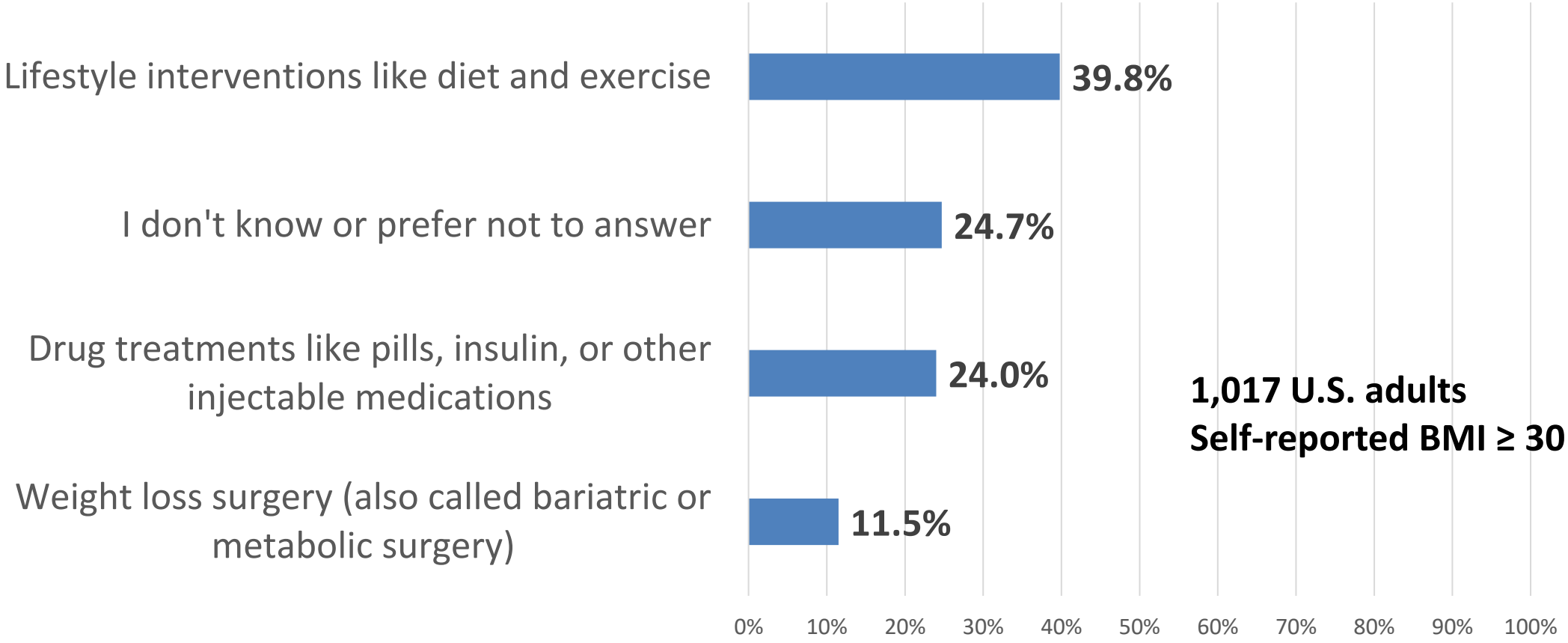
1,017 U.S. adults
Self-reported BMI ≥ 30

qualtrics XM

Metabolic Health Institute

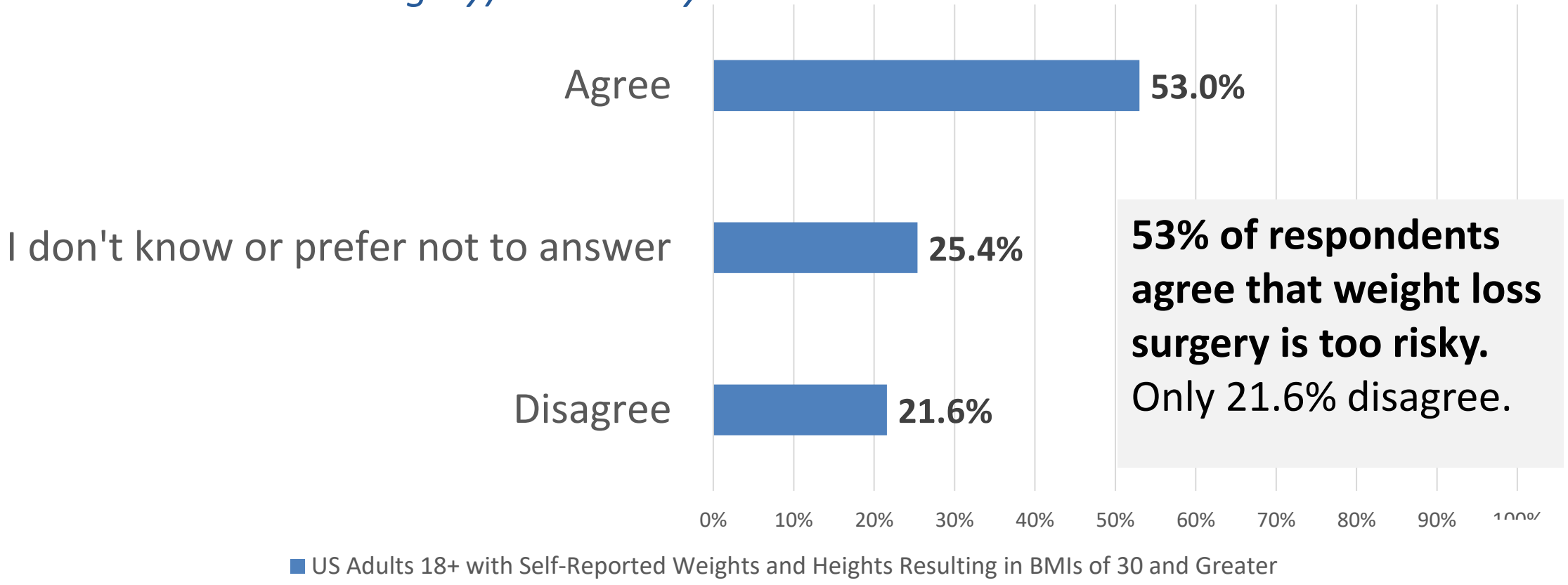
Most People Prefer Lifestyle Interventions or Medications as a Treatment of Type 2 Diabetes

Which one of the following interventions would be best for someone like you as a treatment for Type 2 diabetes? (Select one.)



Bariatric/Metabolic Surgery Continues to be Seen as “Too Risky”

Do you agree or disagree with the following statement? "Weight loss surgery (also known as bariatric or metabolic surgery) is too risky.”



53% of respondents agree that weight loss surgery is too risky.
Only 21.6% disagree.

SAFETY PROFILE AND HEALTHCARE USAGE OF BARIATRIC-METABOLIC SURGERY COMPARED TO COMMONLY PERFORMED ELECTIVE PROCEDURES

G. Chamseddine, R. McIntyre, S. Panagiotopoulos, A. Assiri, J. Crane, F Rubino

Safety of Bariatric Surgery Compares Favorably with Other Elective Surgery

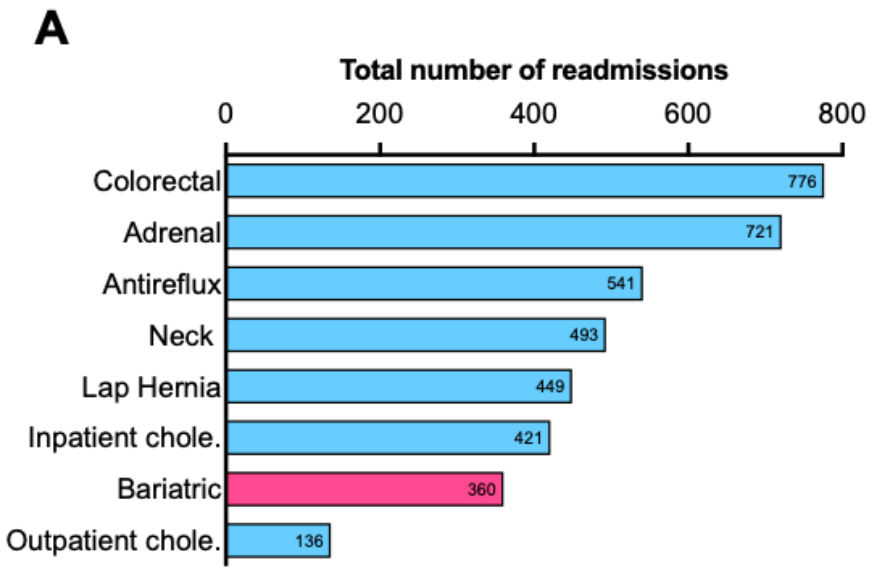
30-Day Post-Operative Safety Outcomes (Data from NHS Digital)

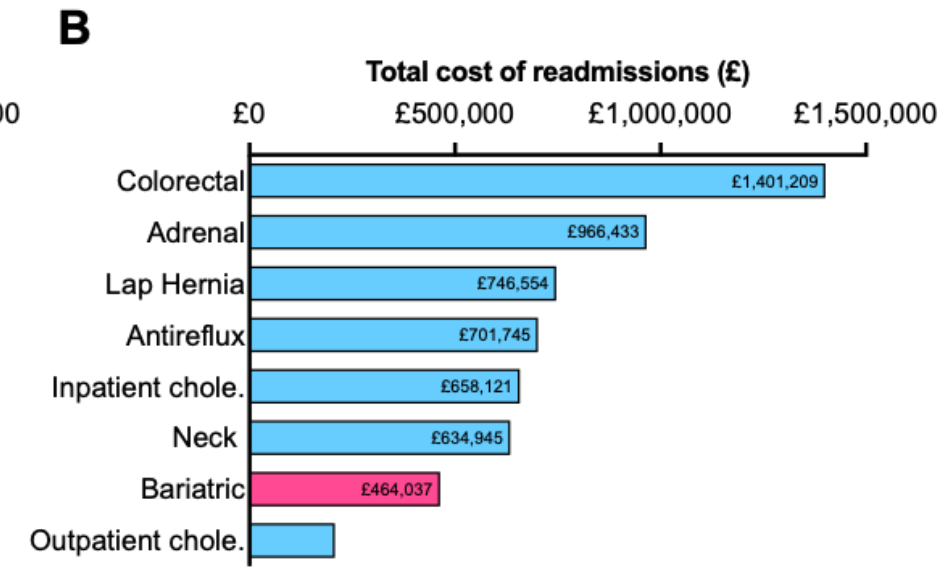
		Bariatric	Adrenal	GEJ	Colorectal	Inpatient Cholecystectomy	Lap Hernia	Neck	Outpatient Cholecystectomy
Morbidity	Major morbidity (%)	0	1	8 **	6 *	2	1	1	1
	Reoperation rate (%)	0	0	3	4	1	1	1	1
Readmission rate	All causes (%)	7	26 *	13	21 *	10	7	8	8
	Procedure-related (%)	4	14 *	7	15 *	7	3	2	5
Readmissions Length of stay	All causes (days)	0.3 ± 0.4	1.1 ± 1.0	1.9 ± 1.0 **	2.6 ± 1.9**	1.9 ± 1.1 **	1.8 ± 2.5	5.1 ± 2.3 **	1.1 ± 1.1
	Procedure-related (days)	1.0 ± 1.2	1.0 ± 0.9	2.4 ± 1.5	3.6 ± 2.6	2.4 ± 1.2	1.0 ± 0.8	3.7 ± 3.8	1.7 ± 1.8
Total cost for all re-dmsisions	All causes (£)	10,067	64,651	25,624	51,186	16,599	16,212	40,618	12,954
	Procedure-related (£)	9,405	39,345	15,980	41,027	14,142	10,532	2,180	6,681
Cost per re-admission	All causes (£)	719 ± 734	1,658 ± 351**	1,602 ± 657**	1,765 ± 523**	1,037 ± 256**	1,474 ± 664*	2,389 ± 664**	1,295 ± 504*
	Procedure-related (£)	2,351 ± 2,236	1,874 ± 570	1,776 ± 968	2,051 ± 703	1,088 ± 312	1,505 ± 593	1,090 ± 6,772	1,114 ± 706

Mean Data are represented as means ± 95% confidence intervals. **denotes different from bariatric surgery, $P < 0.01$; *denotes different from bariatric surgery, $P < 0.05$.

Submitted, under peer-review

Overall Readmissions Over 5-Year





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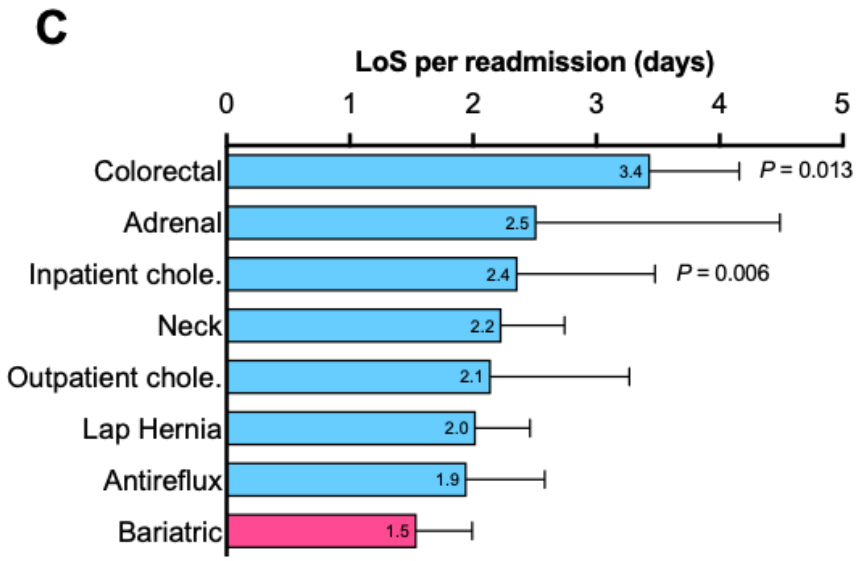
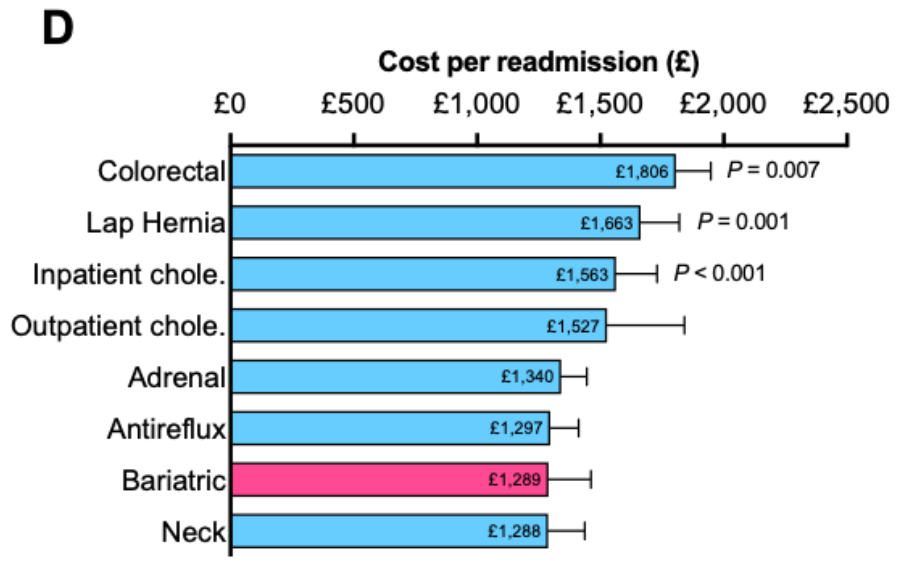
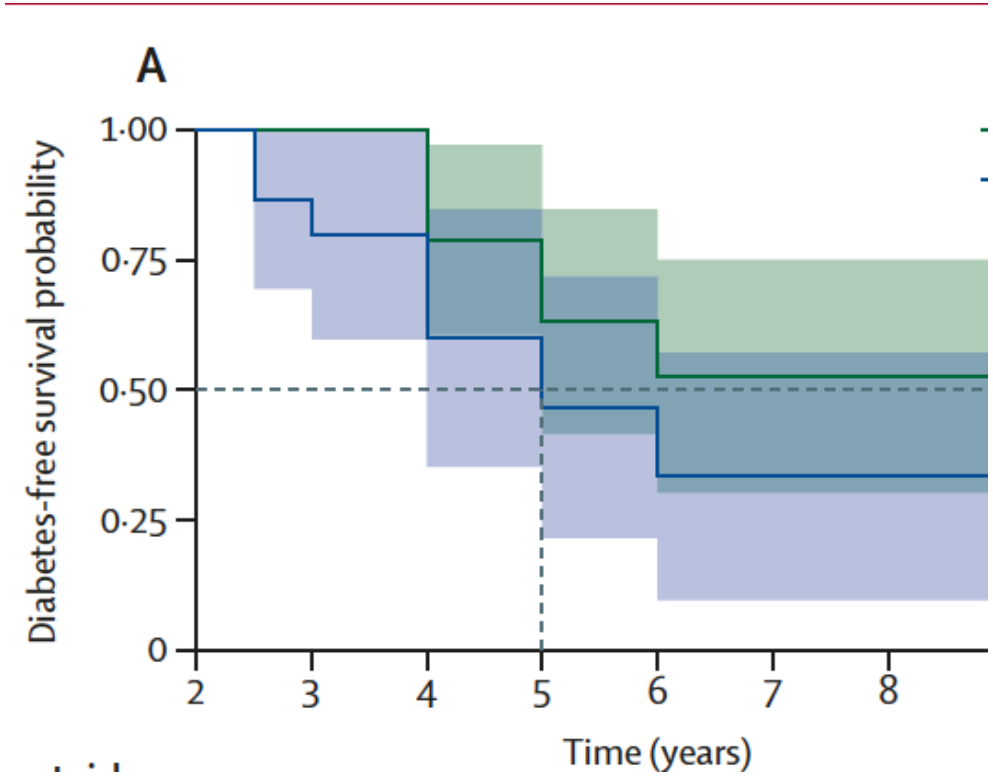




Choosing the Procedure for T2D

10-year Remission of Diabetes



PP analysis,

- Surgery (Total) : **37.5%**
- MT: 0

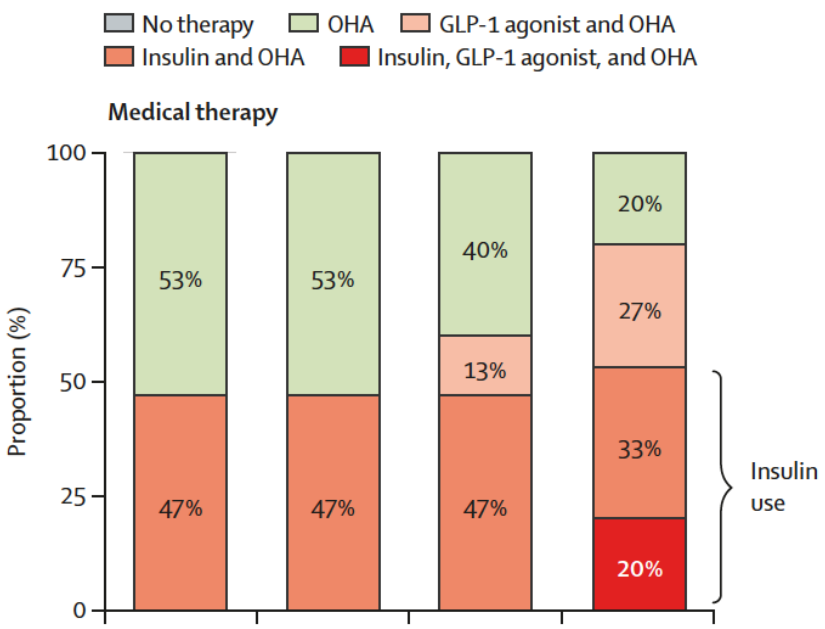
BPD (50%; CI: 30.0; 70.1),

RYGB (25%; CI: 11.2; 46.9)

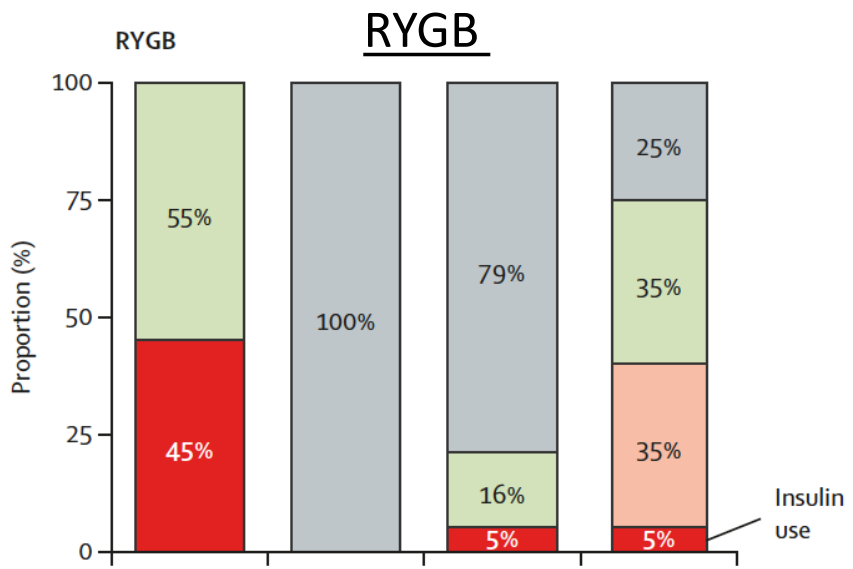
(P=0.19, Fisher exact test between surgical procedures)

Medications Usage (Diabetes)

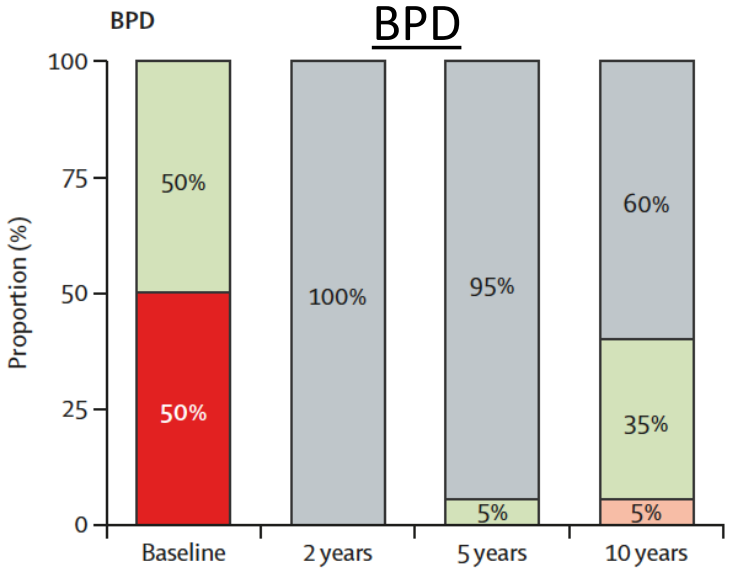
MT Group



RYGB



BPD

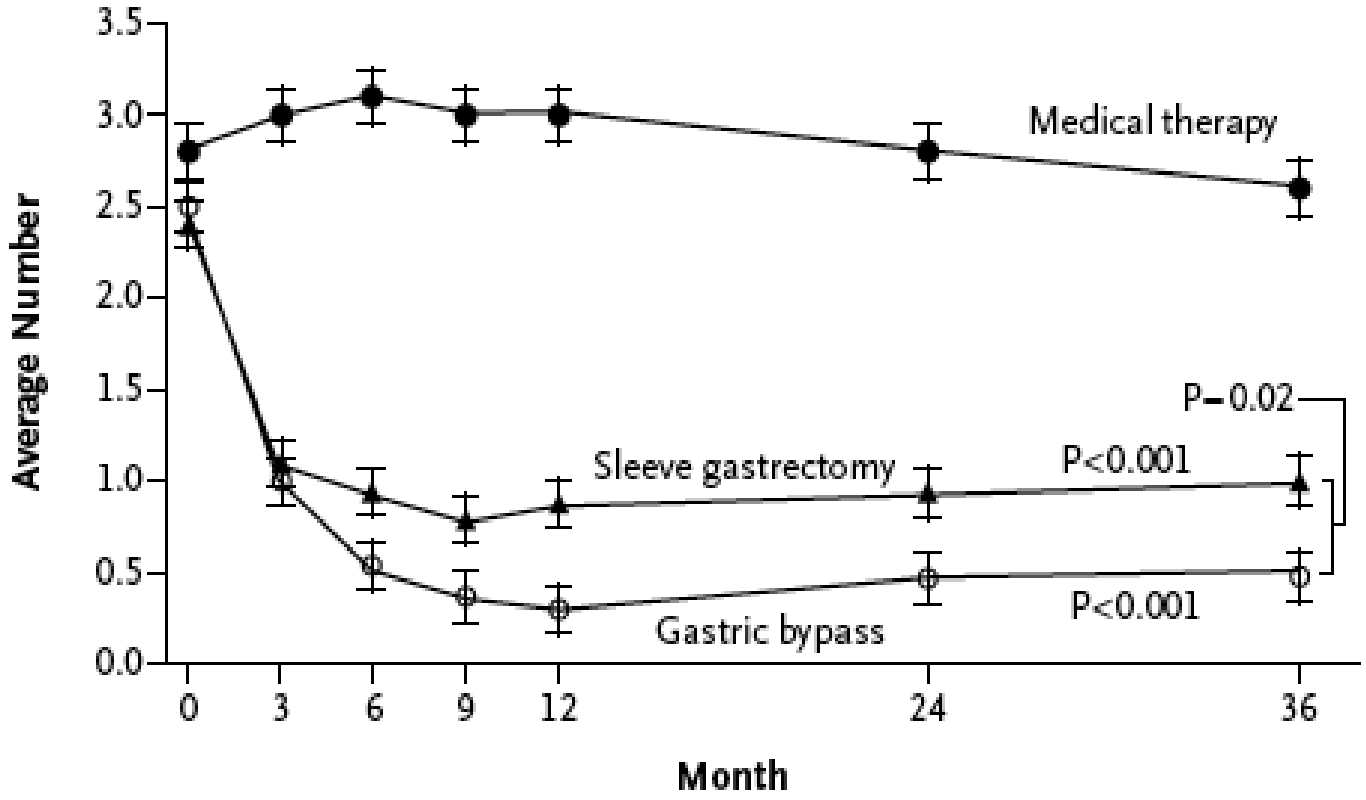


Early and Late Surgical Complications

	BPD group				RYGB group				Medical therapy group			
	0–2 years	2–5 years	5–10 years	10-year total	0–2 years	2–5 years	5–10 years	10-year total	0–2 years	2–5 years	5–10 years	10-year total
Major 30-day postoperative complications												
Deep vein thrombosis or pulmonary embolism	1	0	0	1	1	0	0	1	0	0	0	0
Atrial fibrillation episode	1	0	0	1	0	0	0	0	0	0	0	0
Late surgical complications												
Intestinal occlusion	0	0	0	0	1	0	0	1	0	0	0	0
Incisional hernia	1	0	0	1	0	0	0	0	0	0	0	0
Recurrent or chronic diarrhoea	12	10	8	30	0	0	0	0	0	0	0	0
Nutritional or metabolic complications												
Iron-deficiency anaemia	0	5	3	8	0	3	2	5	0	0	0	0
Hypoalbuminaemia, plasma albumin <3·5 mg/dL	0	3	2	5	0	0	0	0	0	0	0	0
Osteopenia*	0	3	3	6	0	1	1	2	0	1	2	0
Osteoporosis†	0	1	2	3	0	0	0	0	0	0	0	0
Transient nyctalopia	0	1	2	3	0	0	0	0	0	0	0	0
Renal calculus	0	2	1	3	0	0	0	0	0	0	0	0
Symptomatic hypoglycaemia‡	0	0	0	0	0	2§	0	2	0	0	0	0

Stampede Trial
SG vs RYGB @ 36 months

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

[redacted]

RYGB results in greater reduction of CV medications compared to sleeve gastrectomy

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)

Stampede Trial; NEJM, March 2014

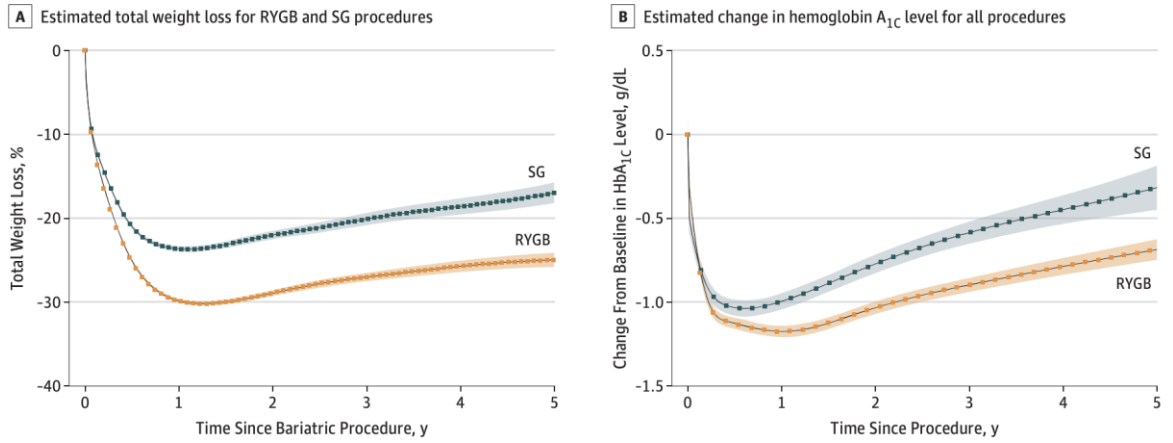
JAMA Surgery | Original Investigation

Comparing the 5-Year Diabetes Outcomes of Sleeve Gastrectomy and Gastric Bypass
The National Patient-Centered Clinical Research Network (PCORNet) Bariatric Study

Kathleen M. McTigue, MD; Robert Wellman, MS; Elizabeth Nauman, MPH, PhD; Jane Anau, BS; R. Yates Coley, PhD; Alberto Odor, MD; Julie Tice, MS; Karen J. Coleman, PhD; Anita Courcoulas, MD; Roy E. Pardee, JD; Sengwee Toh, ScD; Cheri D. Janning, MS; Neely Williams, MDiv; Andrea Cook, PhD; Jessica L. Sturtevant, MS; Casie Horgan, MPH; David Arterburn, MD; for the PCORnet Bariatric Study Collaborative

cohort study in 34 US health system sites
9710 Adult patients with T2DM who had bariatric surgery between January 1, 2005, and September 30, 2015,

Figure 1. Adjusted Total Weight Loss and Change in Hemoglobin A_{1c} Level by Procedure Over 5 Years of Follow-up



Shaded areas represent 95% pointwise CIs for procedure-specific changes in hemoglobin A_{1c} levels. RYGB indicates Roux-en-Y gastric bypass; SG, sleeve gastrectomy.

Roux-en-Y gastric associated with

- 10% higher T2DM remission rates
- better glycaemic control
- fewer T2DM relapse events

RCT Surgery vs MT for T2DM

- **Surgery more effective than MT**
- **Gradient BPD > RYGB > Sleeve**
- **Efficacy for BMI above and below 35kg/m2**

Rubino F et al Diabetes Care (June 2016)

Examples of operated cases

46 yo male; T2D - BMI: 47Kg/m^{2P}

Poorly Controlled T2D on insulin

Interstitial Lung Disease (ILD) requiring Lung transplant – but patient ineligible due to excess weight & diabetes

- **Breathless on minimal exertion**
- **Resting Spo2 on air is 91%, 70% on mild exertion**
- **Requires Continuous oxygen on activity at 10L/min**
- **Estimated complication rates of ILD surgery (26% for lung and 11% non-lung surgery)**

- **Laparoscopic Sleeve Gastrectomy**
  - Operative time: 65 min
  - Extubated at end of Procedure. 24-hour HDU Level 2 bed
  - Total Length of Stay: 4 days
  - No postoperative complications

2.5 years Postoperatively

Weight: 84 Kg, BMI: 27.1 Kg/m^2

Weight loss: 62Kg, (42% TWL)

Diabetes in remission

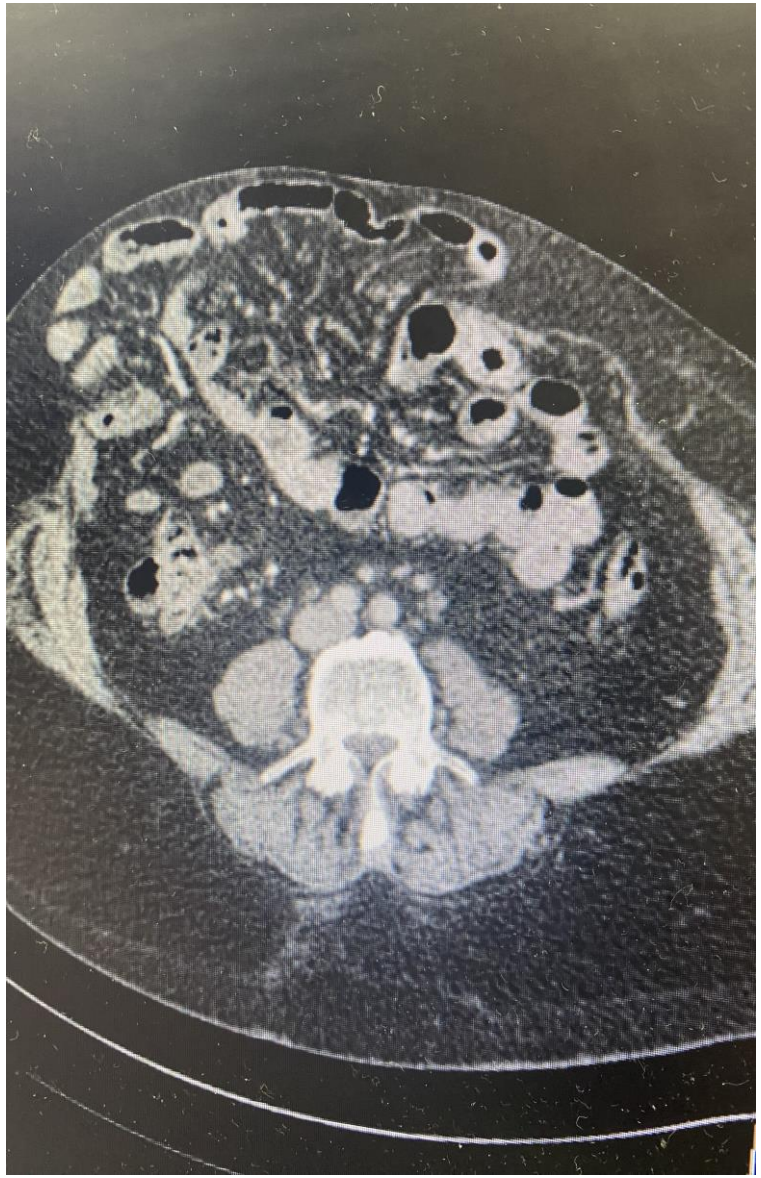
OFF CPAP,

No oxygen at rest

No longer indication to lung transplant

LAPAROSCOPIC SLEEVE POST LIVER TRANSPLANT

- T2D on insulin
- Liver Transplant
- NASH on graft
- Massive ventral hernia
- Hypertension
- Dyslipidemia



Metabolic Surgery Changes the Landscape of Diabetes Care

Metabolic Surgery for Type 2 Diabetes: Changing the Landscape of Diabetes Care

William T. Cefalu,[1] Francesco
David E. Cummings[3]

Diabetes Care 2016;39:857–860 | DOI: 10.2337/dc16-0686

The accelerating pandemic of diabetes is recognized as one of the greatest global public health threats of our time (1). When one reviews the latest estimates for diabetes prevalence and projections worldwide, it is easy to appreciate the magni-

UIG/GETTY

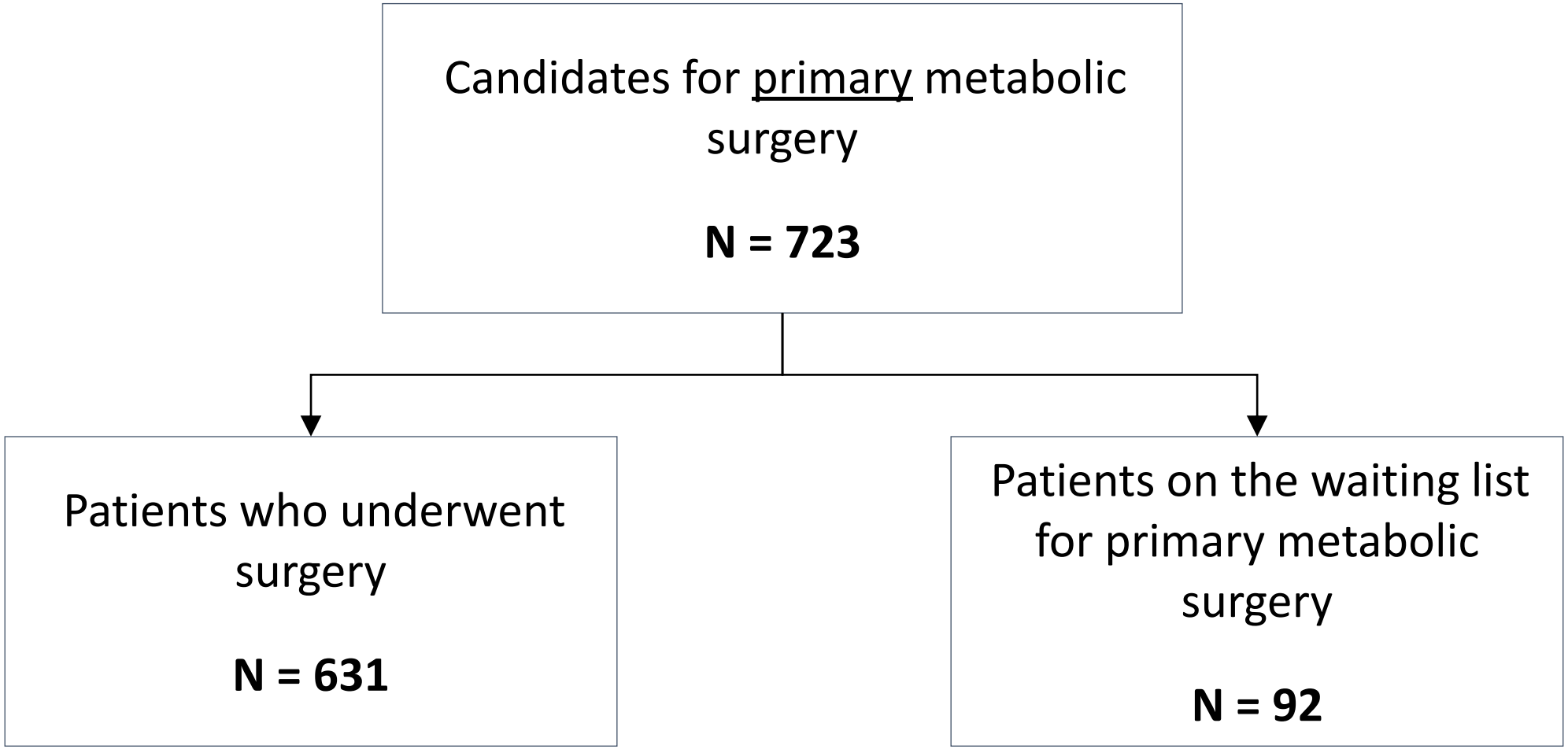
Surgery can be an effective treatment for type 2 diabetes.

Time to think differently about diabetes

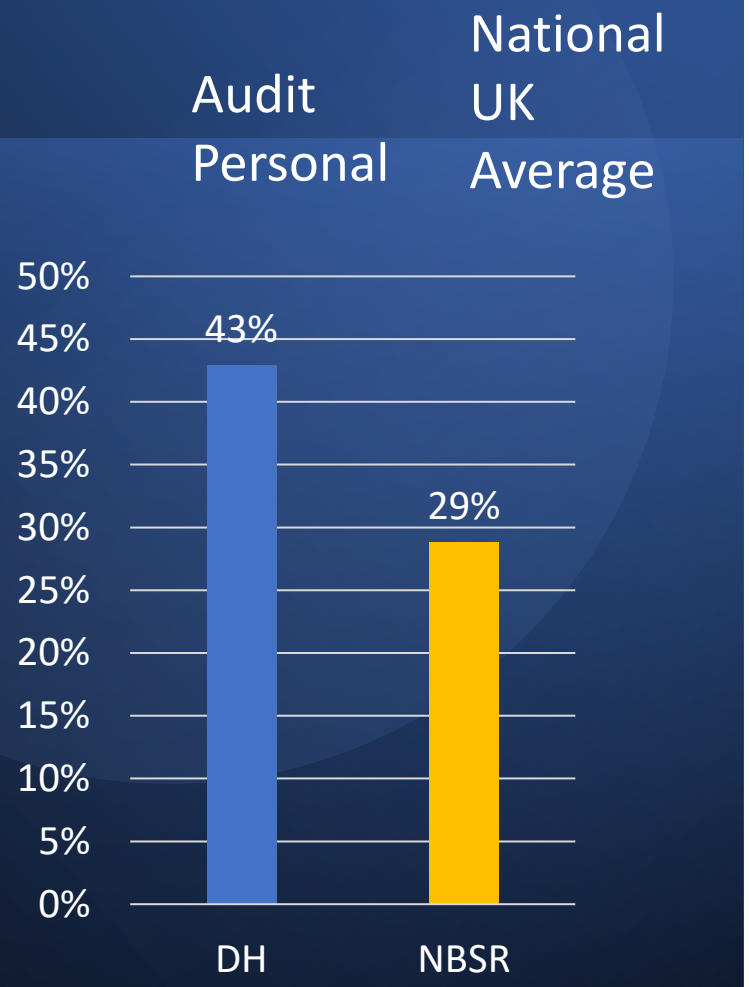
New guidelines for the surgical treatment of type 2 diabetes bolster hopes of finding a cure, writes **Francesco Rubino**, but long-standing preconceptions must be put aside.

How Does Diabetes Change the Landscape of Surgery?

Audit Personal Practice @ King‘s



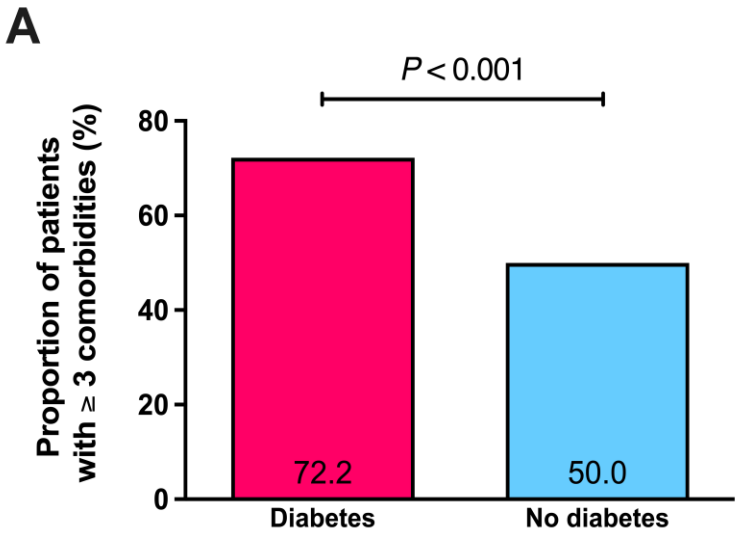
Prevalence of T2D in Surgical Practice



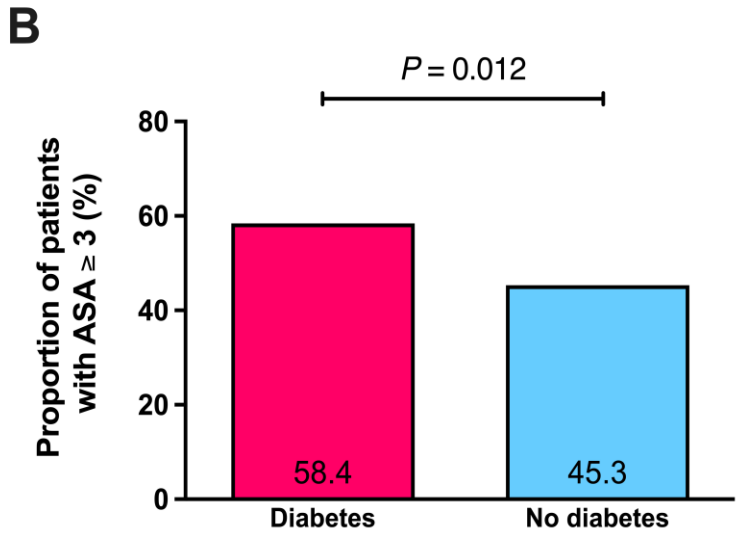
Surgical Candidates With vs Without T2D

Audit Personal Practice @King's

Pts with > 3 Co-morbidities



Pts with ASA score ≥ 3



Diabetes Status

Table 1. Summary of baseline characteristics in patients with diabetes vs no diabetes.

Clinical Characteristics	All patients *n* = 723	Diabetes *n* = 301 (41.6%)	No Diabetes *n* = 422 (58.4%)	*p* -value
Age (years)	47 ± 12	51 ± 11	45 ± 12	***p* < 0.001**
Gender, female (%)	518 (71.6%)	192 (63.8)	326 (77.3)	***p* < 0.001**
BMI (kg/m^2)	48 ± 8	47 ± 8	49 ± 8	***p* < 0.001**
CCI score	1.6 ± 1.6	2.5 ± 1.7	0.8 ± 1.1	***p* < 0.001**
Estimated 10-year survival (%)	93.0	85.0	96.5	**p < 0.001**
ASA score	2.6 ± 0.5	2.7 ± 0.5	2.5 ± 0.6	**p < 0.001**
Number of comorbidities	3.8 ± 2.3	4.9 ± 2.1	3.0 ± 2.1	***p* < 0.001**
Number of medications	1.7 ± 2.1	3.3 ± 2.1	0.6 ± 1.0	***p* < 0.001**
BMI ≥ 50 (%)	270 (37.3%)	102 (33.9)	167 (39.8)	*p* = 0.105
CVD (%)	117 (16.2%)	68 (22.6)	49 (11.6)	***p* < 0.001**

Continuous data are presented as mean ± SD and anlaysed by two-sided T-test. Categorical data are presented as count (%) and analysed by Pearson's Chi-Square test. CVD, Cardiovascular Disease; CCI, Charlson Comorbidity Index; ASA, American Society of Anaesthesiologists.

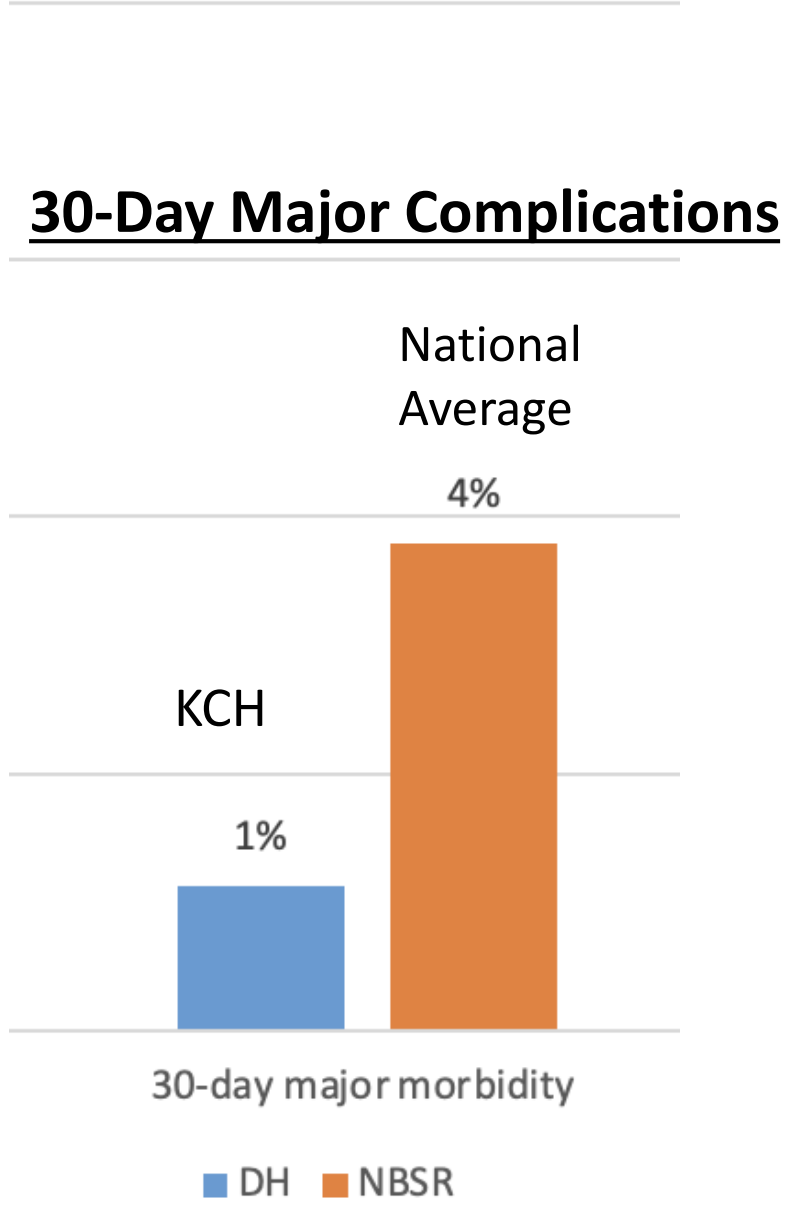
Audit Personal Practice (unpublished)

Metabolic Surgery at KCH

Diseases and Conditions in Pts Undergoing Bariatric/Metabolic Surgery at KCH

- **Type 2 Diabetes**
- Coronary Heart Disease
- Heart Failure
- NASH
- Chronic Kidney Disease
- Respiratory disease (OSA, Hypoventilation Syndrome)
- Patients awaiting other time-sensitive surgery (i.e. transplants, CABG, orthopedic surgery)
- Pre- or Post-Liver Transplant

30-Day Major Complications



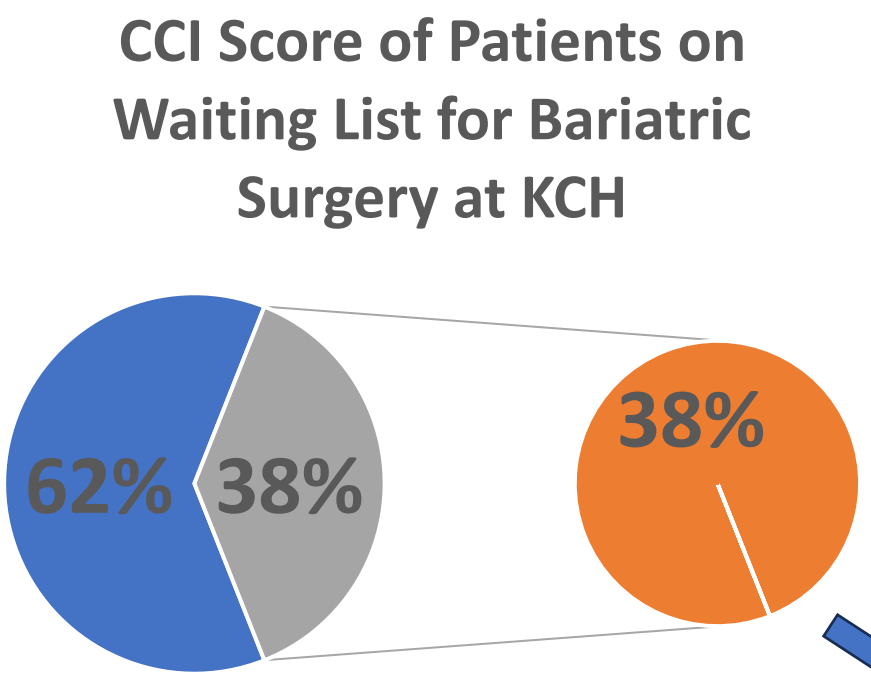
Anaesthetic Pre-Assessment Form

Anaesthetic History / Airway	Problems with previous anaesthetics	*Yes*
	Mallampati	*2*
Allergies / Meds / Surgical History	Allergies to medication / food / latex etc	*Yes*
Review of Systems	Stairs without stopping	*less than 1 flight*
	Hypertension	*Yes*
	Chest pain / Angina	*Yes*
	MI	*Yes*
	CHF / Cardiomyopathy	*Yes*
	OSA / Symptoms	*Yes*
	Renal Impairment	*Yes*
	Diabetes	*Yes*
	Anaemia	*Yes*
	Anticoagulation	*Yes*
	Cerebrovascular disease	*Yes*
	Joint replacement or orthopaedic metalware	*Yes*
	Anxiety / depression / mental illness	*Yes*
	Any other relevant medical conditions	*Yes*

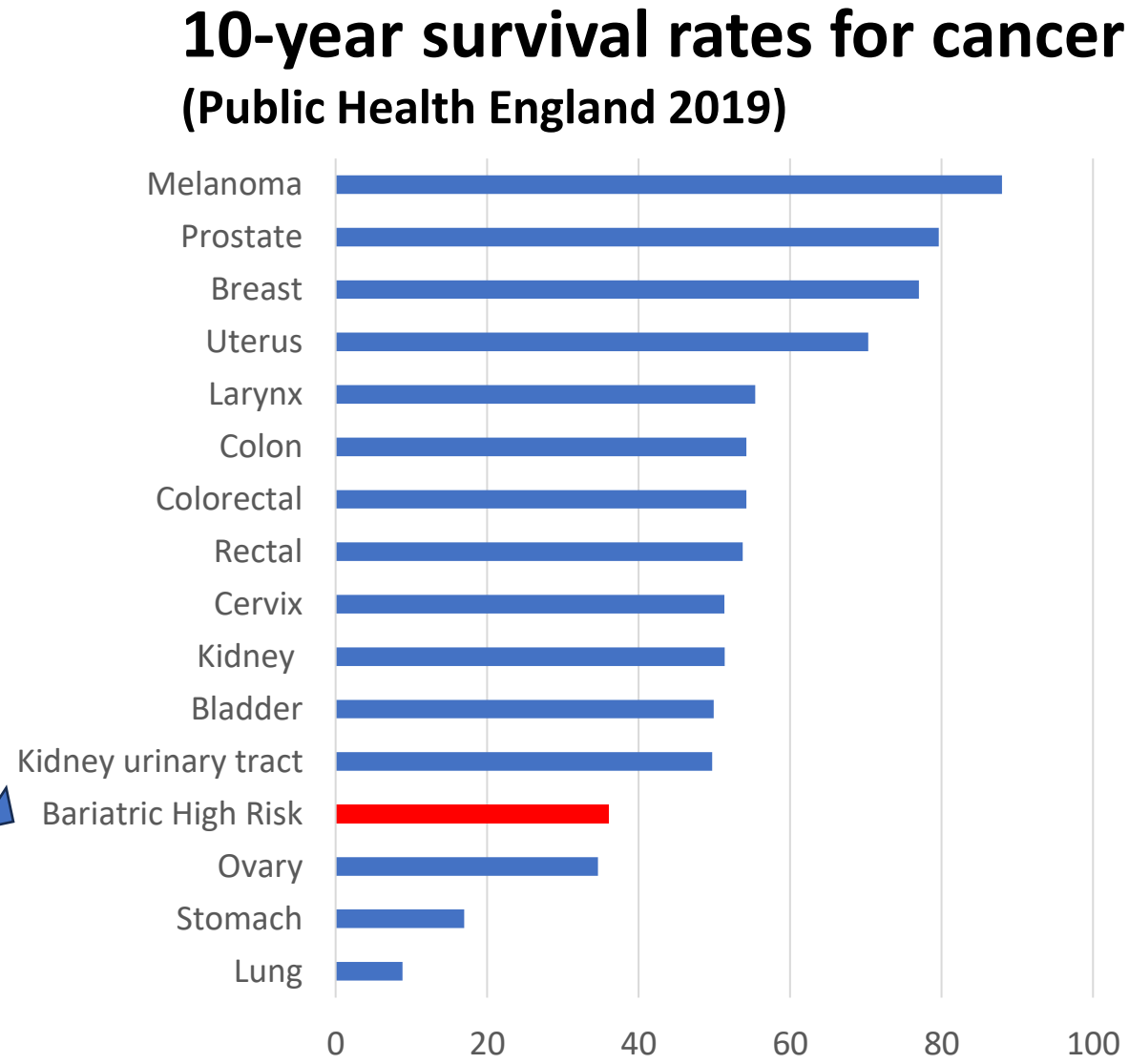
Charlson Comorbidity Index (CCI) Score = 7 points

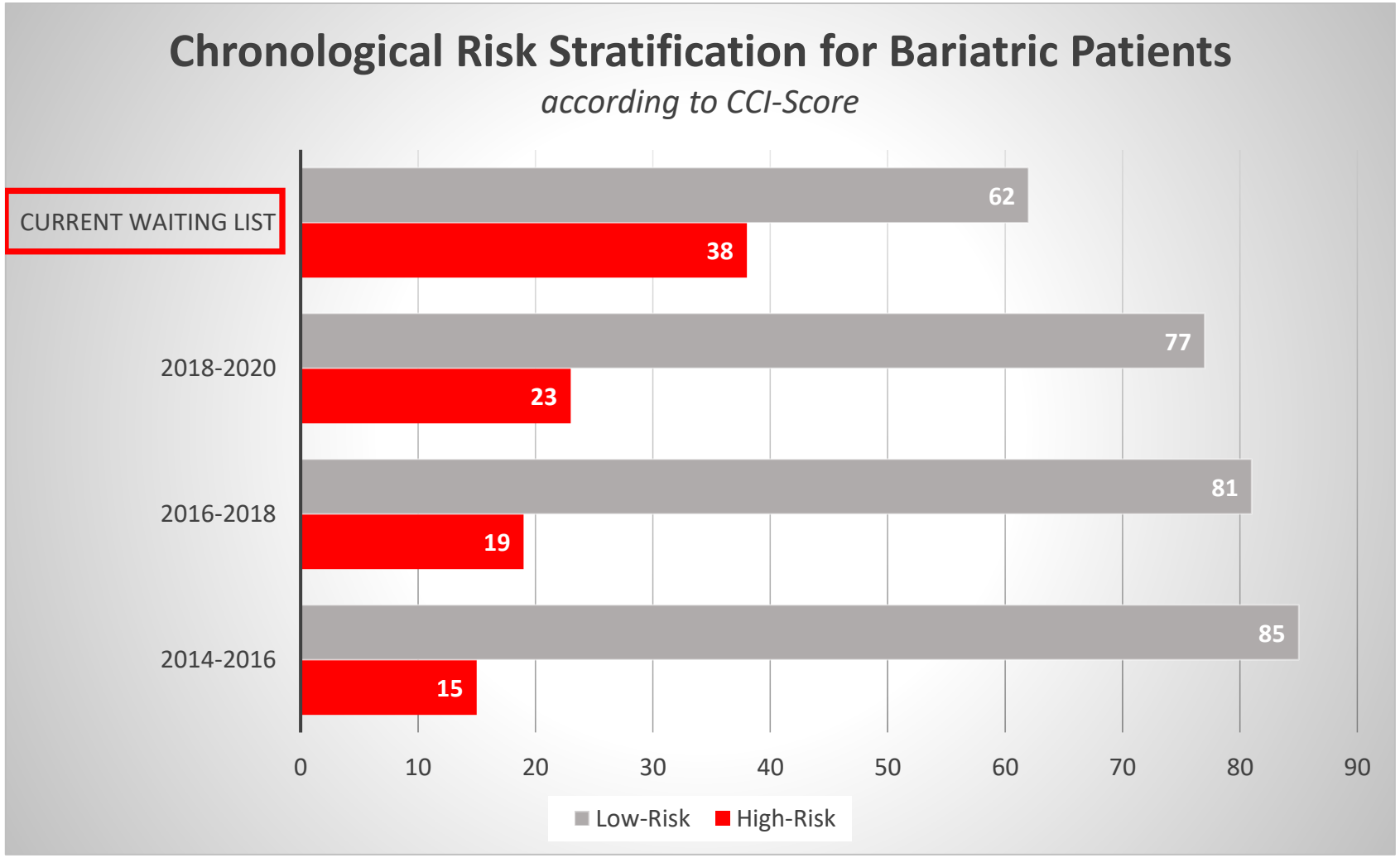
>>Estimated 10-year survival = 0 %

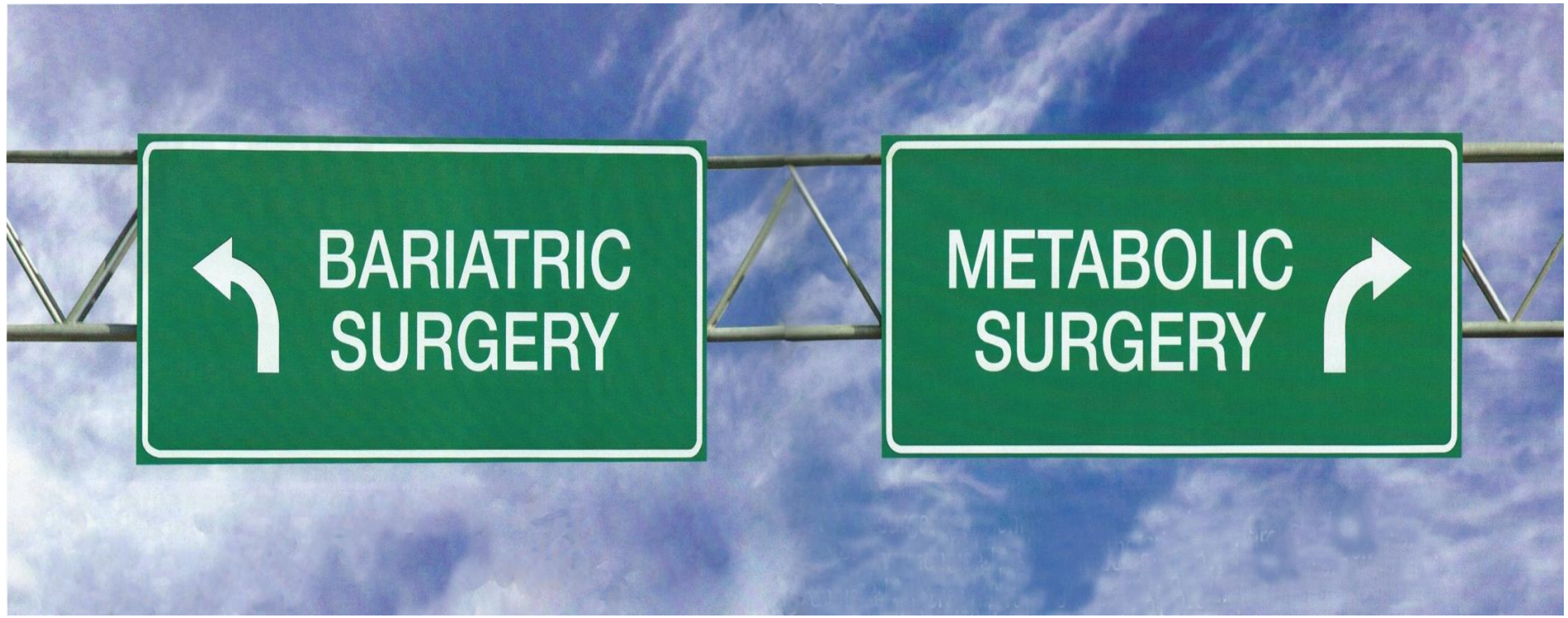
Prognosis (estimated 10-year survival based on CCI-Score)



About 4 in 10 patients on WL have high mortality risk from their disease status (average 10-year survival 36%)

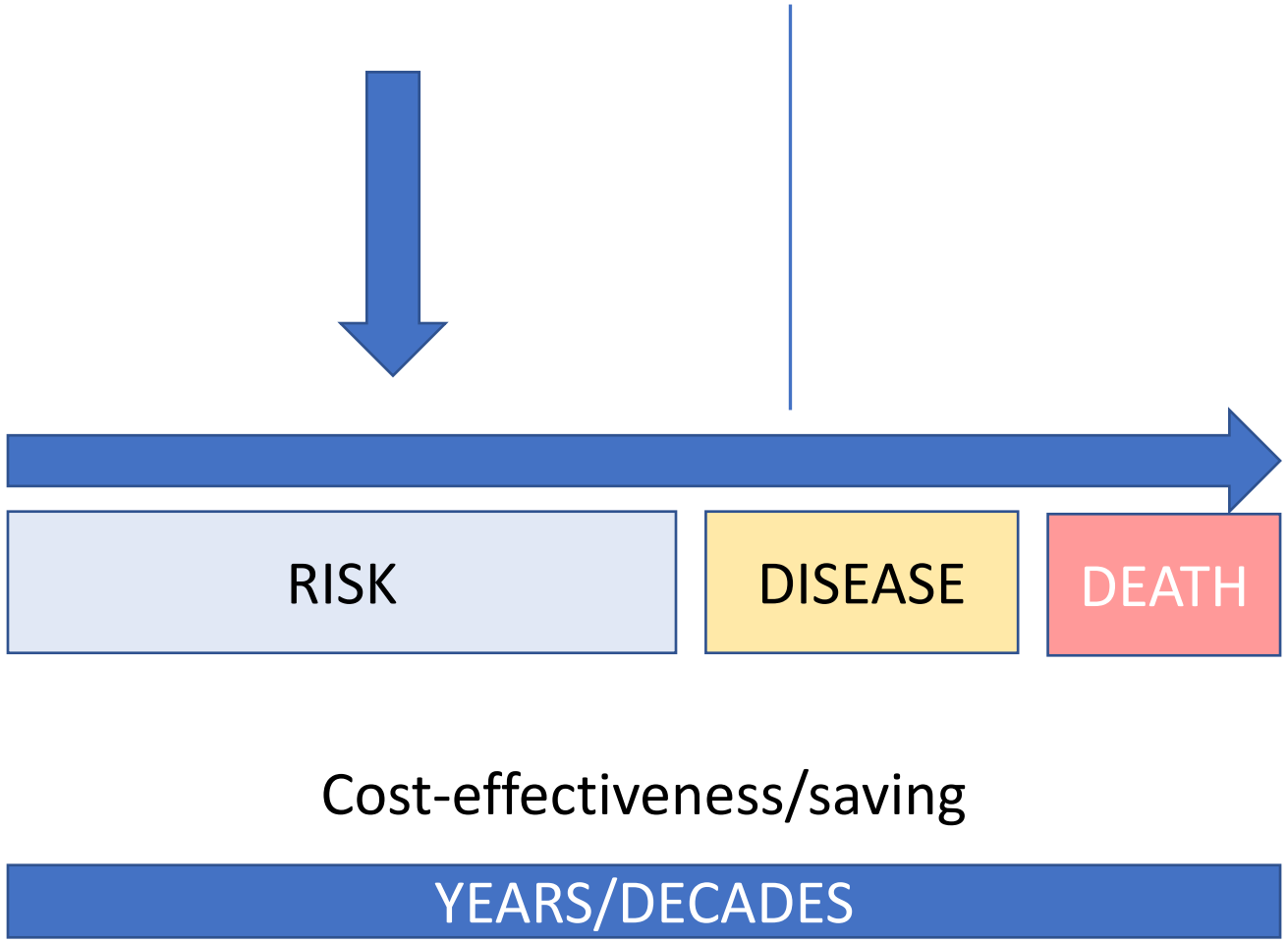



Chronological Risk Stratification for Bariatric Patients
according to CCI-Score
CURRENT WAITING LIST
2018-2020
2016-2018
2014-2016
62
38
77
23
81
19
85
15
0
10
20
30
40
50
60
70
80
90
Low-Risk
High-Risk

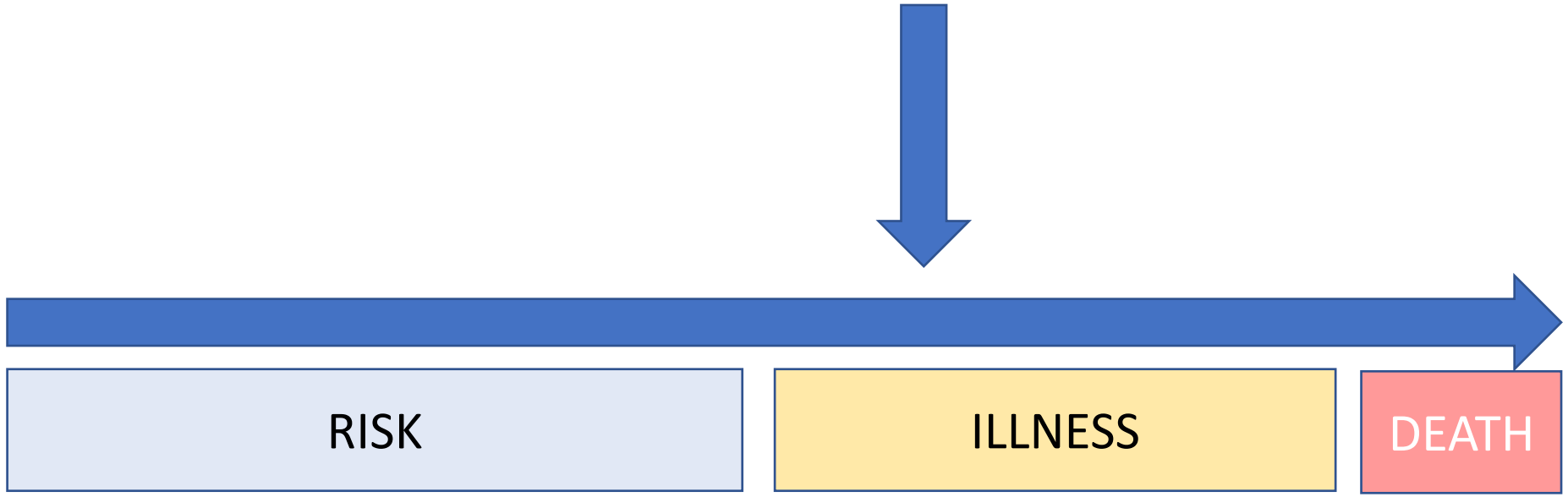

BARIATRIC
SURGERY
METABOLIC
SURGERY

TRADITIONAL “BARIATRIC” (WEIGHT-LOSS) SURGERY

BMI



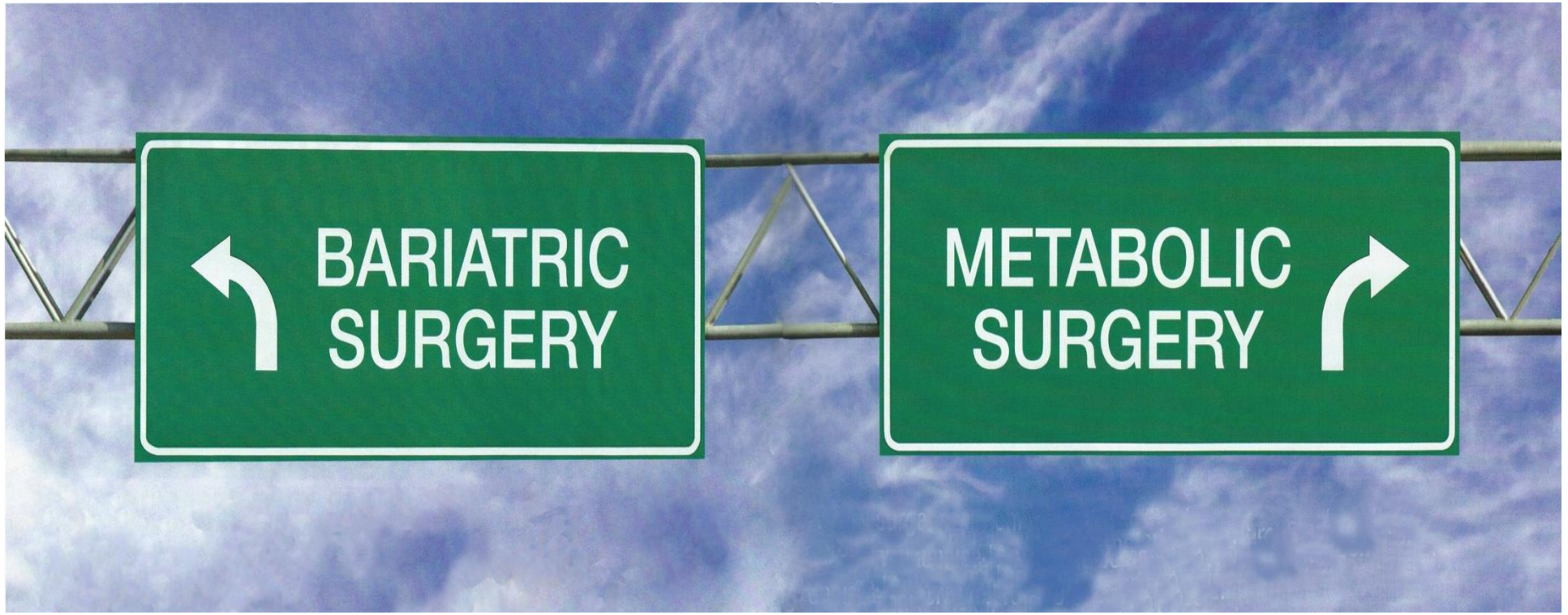
METABOLIC SURGERY



Cost-effectiveness/saving

MONTHS/YEARS

From Bariatric to Metabolic Surgery:
= “Prophylactic” vs “Therapeutic” Intervention



Lancet Commission on Clinical Obesity (coming up soon)
Reframing Obesity to Improve Care and Policy

Causes of Adipose Tissue Expansion

- Genetic
- Environmental
- Psychological
- Other (Unknown)

Obesity

Clinical Obesity

Risk Factor >>>> Illness

Primary Prevention

Prophylactic Interventions

Therapeutic Intervention (Disease Treatment)