

# Will modern pharmacotherapy kill MBS?

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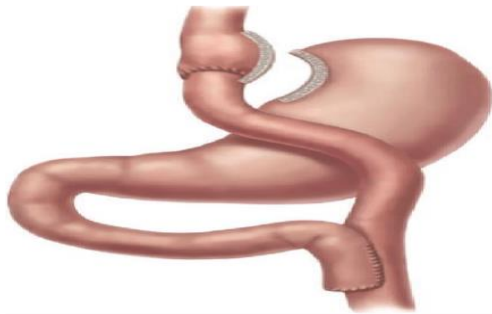
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- **Director, The Center for the treatment of Obesity and Diabetes Oswaldo Cruz German Hospital,**
- **São Paulo Brazil**
  
- **President IFSO Global**
- **Past President SBCBM (2011-2012)**
- **Past President IFSO LAC (2018-2019)**



# Disclosures

- Research Grant, Johnson & Johnson
- Research Grant, Medtronic
- Research Grant, GI Dynamics
- Research Grant, Hospital Oswaldo Cruz Bioscience Institute
- Research Grant, Marlex, Brazil
- Speaker, Johnson & Johnson, Medtronic, Morphic Medical, NovoNordisk, Merck, Boston Scientific
  
- SAB: Morphic Medical, Medtronic, Johnson & Johnson, Regeneron

# **Surgery is great for weight loss and glycemia**



# Prospective matched controlled

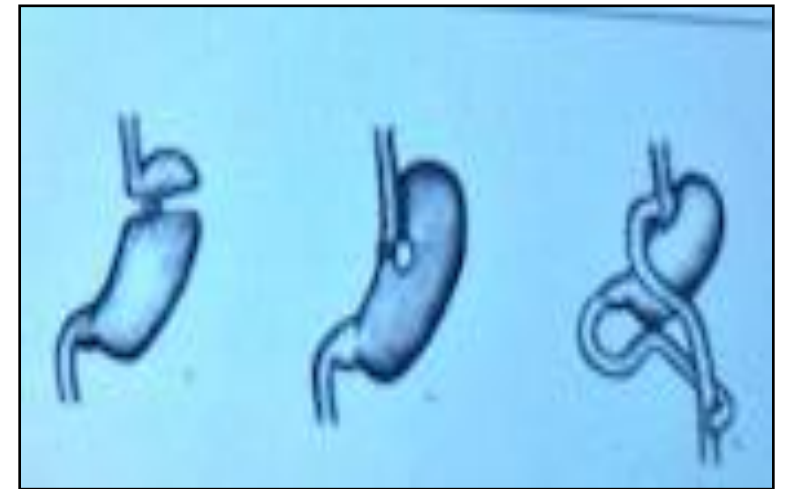
✓ Swedish Obese Subjects (SOS)

✓ Non RCT with over 20 years of follow-up



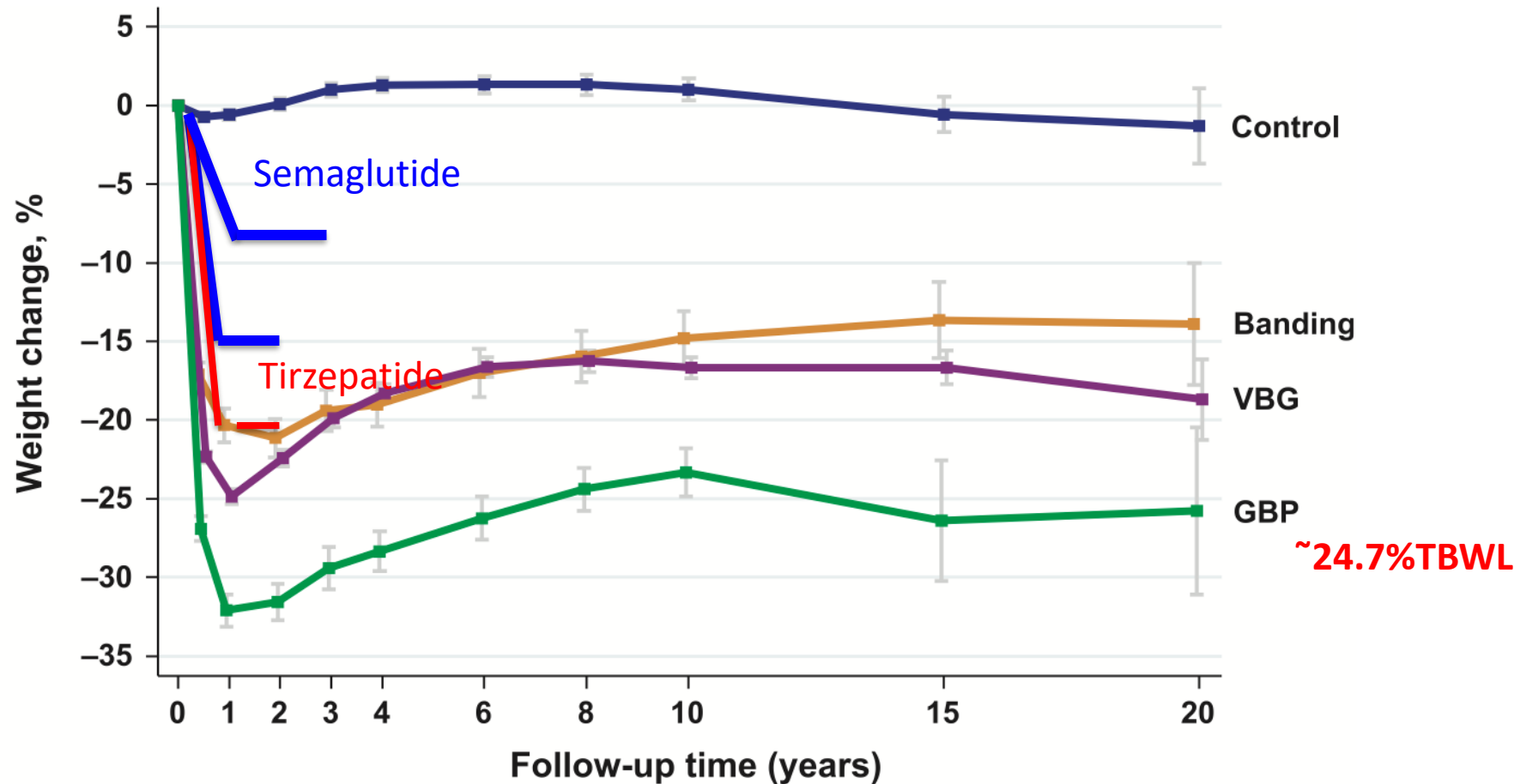
**2039 PTS**

**X**



**2010 PTS, 11% with BMI < 35 kg/m<sup>2</sup>**

# Weight Loss After Bariatric Surgery Is Sustained for at Least 20 years-Superior to all other Treatments



# RCTs of metabolic surgery x BMT, at least 2 years of FU

	Surgical intervention	Follow-up duration, years	Glycaemic target	Proportion reaching glycaemic target (surgical intervention vs current medical treatment), %	Total bodyweight loss (surgical intervention vs current medical treatment), %
Dixon et al <sup>27</sup>	AGB	2	FPG <126 mg/dL and HbA <sub>1c</sub> <6.2% (44.3 mmol/mol), without glucose-lowering agents	73% vs 13%	20% vs 1%
Cohen et al <sup>21</sup>	RYGB	2	HbA <sub>1c</sub> <6.5% (47.5 mmol/mol), regardless of glucose-lowering agents	71% vs 51%	26% vs 5%
Simonson et al <sup>38</sup>	RYGB	3	FPG <126 mg/dL and HbA <sub>1c</sub> <6.5% (47.5 mmol/mol) regardless of glucose-lowering agents	42% vs 0%	25% vs 5%
Ikramuddin et al <sup>39</sup>	RYGB	5	HbA <sub>1c</sub> <7% (53.0 mmol/mol), regardless of glucose-lowering agents	55% vs 14%	22% vs 10%
Courcoulas et al <sup>40</sup>	RYGB vs AGB	5	HbA <sub>1c</sub> <6.5 (47.5 mmol/mol) or FPG <126 mg/dL, without glucose-lowering agents	30% (RYGB) vs 19% (AGB) vs 0%	25% (RYGB) vs 15% (AGB) vs 6%
Wentworth et al <sup>41</sup>	AGB	5	FPG <126 mg/dL and 2 h blood glucose concentration <200 mg/dL (75 g glucose oral challenge test)	23% vs 9%	12% vs 2%
Schauer et al <sup>42</sup>	RYGB vs sleeve gastrectomy	5	HbA <sub>1c</sub> <6% (42.1 mmol/mol), regardless of glucose-lowering agents	29% (RYGB) vs 23% (sleeve gastrectomy) vs 5%	23% (RYGB) vs 19% (sleeve gastrectomy) vs 5%
Mingrone et al <sup>43</sup>	RYGB vs biliopancreatic diversion	10	FPG <100 mg/dL and HbA <sub>1c</sub> <6.5% (47.5 mmol/mol), without glucose-lowering agents	25% (RYGB) vs 50% (biliopancreatic diversion) vs 5%	37% (RYGB) vs 42% (biliopancreatic diversion) vs 7%

HbA<sub>1c</sub>=glycated haemoglobin. FPG=fasting plasma glucose. AGB=adjustable gastric banding. RYGB=Roux-en-Y gastric bypass.

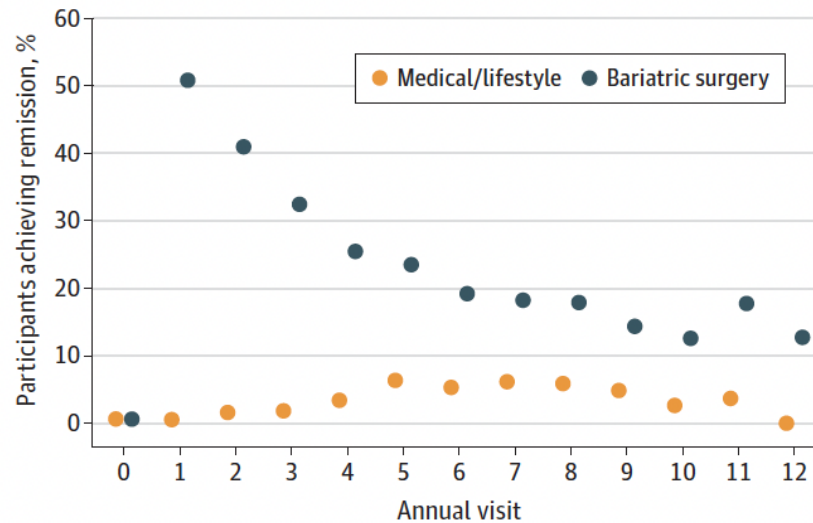
**Table 1: Randomised controlled trials with follow-up duration of at least 2 years comparing bariatric surgery with current medical treatment**

# Long-Term Outcomes of Medical Management vs Bariatric Surgery in Type 2 Diabetes

Anita P. Courcoulas, MD; Mary Elizabeth Patti, MD; Bo Hu, PhD; David E. Arterburn, MD; Donald C. Simonson, MD, ScD; William F. Gourash, PhD; John M. Jakicic, PhD; Ashley H. Vernon, MD; Gerald J. Beck, PhD; Philip R. Schauer, MD; Sangeeta R. Kashyap, MD; Ali Aminian, MD; David E. Cummings, MD; John P. Kirwan, PhD

2024

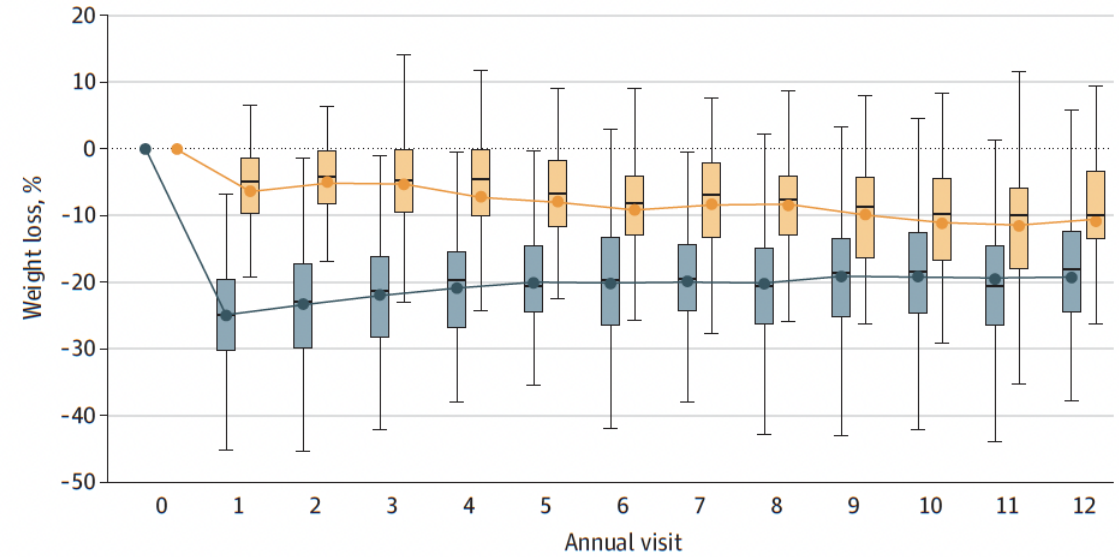
Figure 3. Diabetes Remission



No. of participants													
Medical/lifestyle	96	92	87	82	78	84	76	79	72	70	67	55	31
Bariatric surgery	166	164	151	149	140	146	108	131	116	125	117	99	82

Remission was defined as hemoglobin A<sub>1c</sub> less than 6.5% and not receiving any medications for diabetes.

C Weight loss



No. at risk													
Bariatric surgery	166	164	161	158	144	149	122	139	121	126	121	106	85
Medical/lifestyle	96	91	84	86	79	78	77	75	73	73	70	60	34

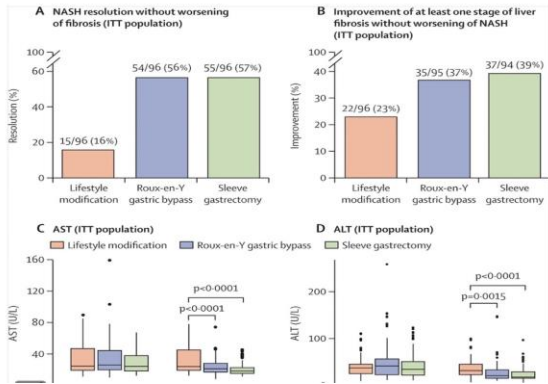
# Non-glucocentric outcomes, CV events and mortality

**Bariatric-metabolic surgery versus lifestyle intervention plus best medical care in non-alcoholic steatohepatitis (BRAVES): a multicentre, open-label, randomised trial**

Ornella Venastro<sup>1</sup>, Simona Panunzi<sup>2</sup>, Lidia Castagneto-Gissy, Andrea De Gaetano, Erminia Lembo, Esmeralda Capristo, Caterino Guidone, Giulia Angelini, Francesco Pennestrì, Luca Sessa, Fabio Maria Vecchio, Laura Riccardi, Maria Assunta Zocco, Ivo Boskoski, James R Casella-Mariolo, Pierluigi Marini, Maurizio Pompili, Giovanni Casella, Enrico Fiori, Francesco Rubino, Stefan R Bornstein, Marco Roffiaelli, Goltzde Mingrone



Lancet, 2023



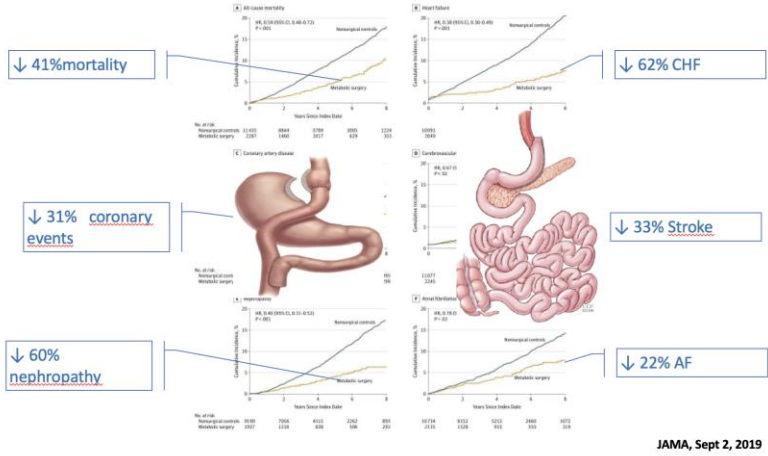
VL 11, 83, 4, 2024

ORIGINAL RESEARCH

## Randomized Trial of Effect of Bariatric Surgery on Blood Pressure After 5 Years

Carles A. Schiavon, MD,<sup>1,3</sup> Alexandre B. Cavalcanti, MD,<sup>1</sup> Juliana D. Oliveira, CN,<sup>1,3</sup> Rachel H.V. Machado, CN,<sup>1</sup> Eliana V. Santucci, Pr,<sup>1</sup> Renato N. Santos, Sr,<sup>1</sup> Julia S. Oliveira, Sr,<sup>1</sup> Lucas P. Damiani, Sr,<sup>1</sup> Débora Junqueira, MD,<sup>1</sup> Helio Halpern, MD,<sup>1</sup> Frederico de L.L. Monteiro, MD,<sup>1</sup> Patricia M. Noujaim, MD,<sup>1</sup> Ricardo V. Cohen, MD,<sup>1</sup> Marcio G. de Sousa, MD,<sup>1</sup> Luiz A. Bortolotto, MD,<sup>1</sup> Otavio Berwanger, MD,<sup>1</sup> Luciano F. Drager, MD<sup>1,3</sup>

JACC, 2024



JAMA, Sept 2, 2019



## Gastric bypass versus best medical treatment for diabetic kidney disease: 5 years follow up of a single-centre open label randomised controlled trial

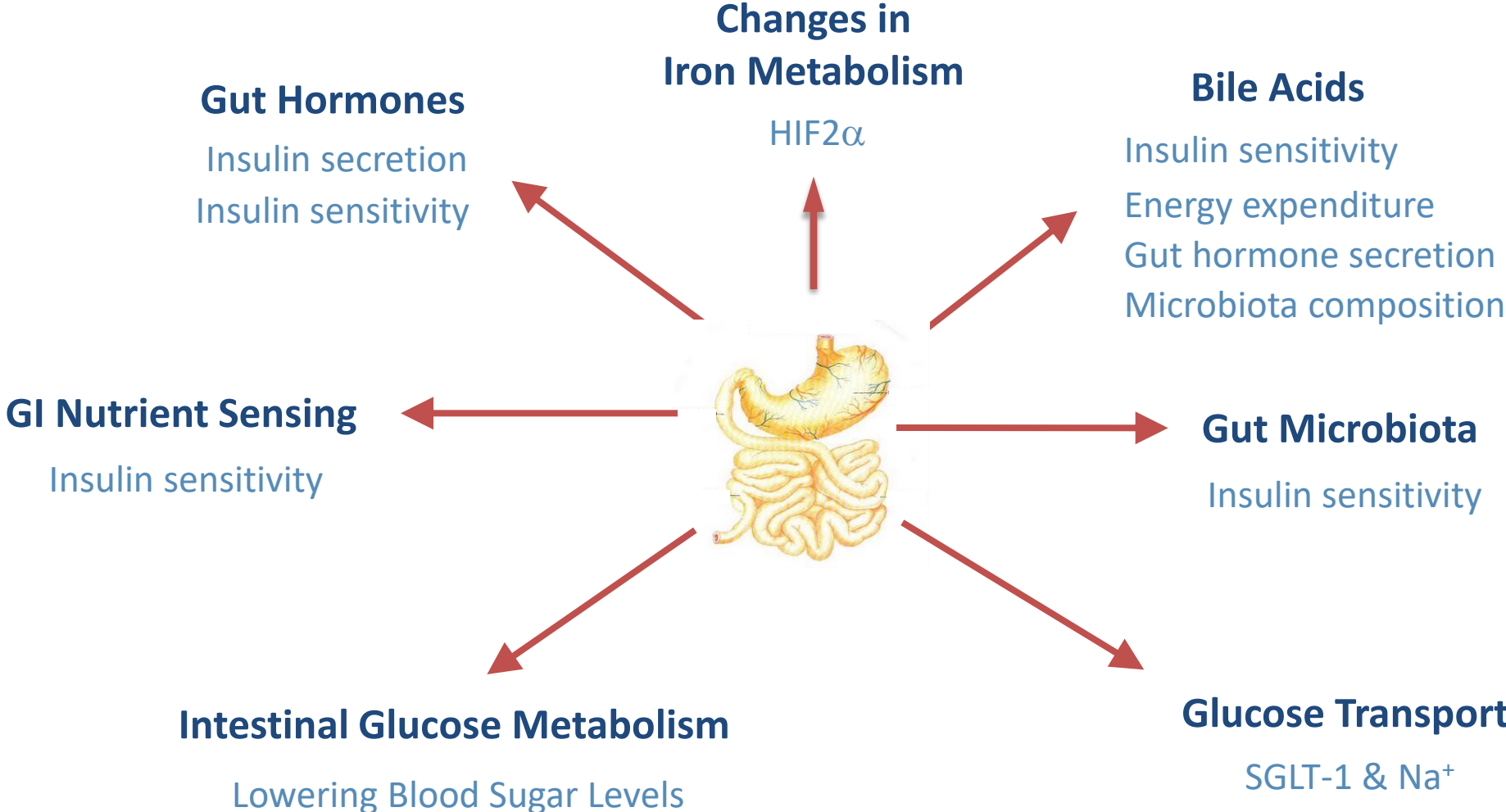
Ricardo V. Cohen,<sup>1,4</sup> Tiago Veiga Pereira,<sup>1,2</sup> Cristina Mamede Abad,<sup>1</sup> Tereza Beatriz Zanata Petry,<sup>1</sup> José Luis Lopes Cortes,<sup>1</sup> Carlos Antonio Schiavon,<sup>1</sup> Carlos Eduardo Pompili,<sup>1</sup> Fernando Nogueira Quirino Petry,<sup>1</sup> Aline Carolina Calmon da Costa Silva,<sup>1</sup> Lívia Porto Cunha dos Siveira,<sup>1</sup> Pedro Paulo de Paes Caravatta,<sup>1</sup> Helio Halpern,<sup>1</sup> Frederica de Lima Jacy Monteiro,<sup>1</sup> Bruno da Costa Martins,<sup>1</sup> Rogério Kuga,<sup>1</sup> Thais Mantovani Saxon Pulumbo,<sup>1</sup> Allan N. Friedman,<sup>1</sup> and Cael W. Le Roux<sup>1,5</sup>

The Lancet Eclin, online Nov 11, 2022



Outperforms the medical Tx

# Mechanisms of Metabolic Surgery



# Complications and mortality continuous decrease

Campos et al

Annals of Surgery • Volume 271, Number 2, February 2020

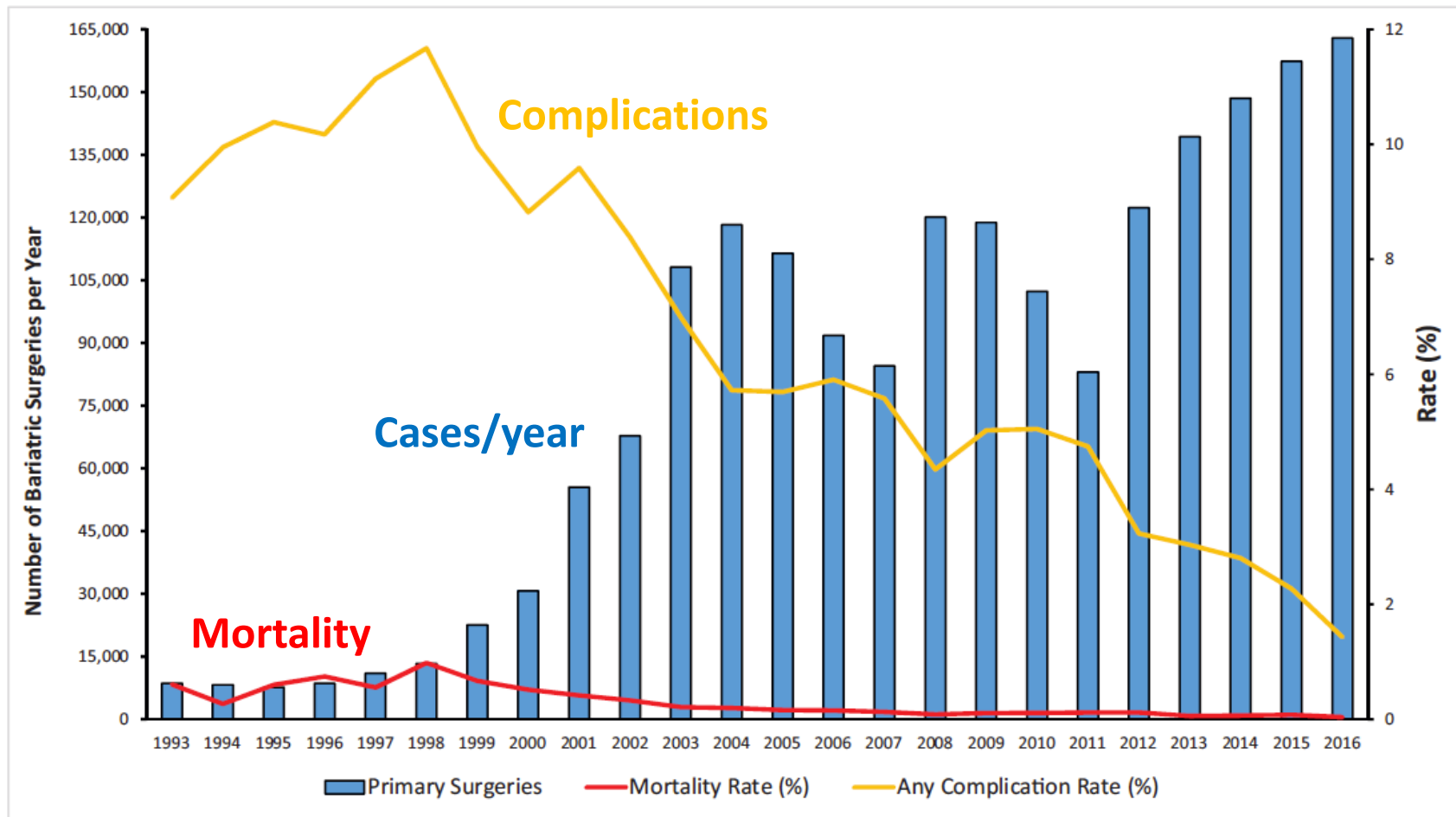


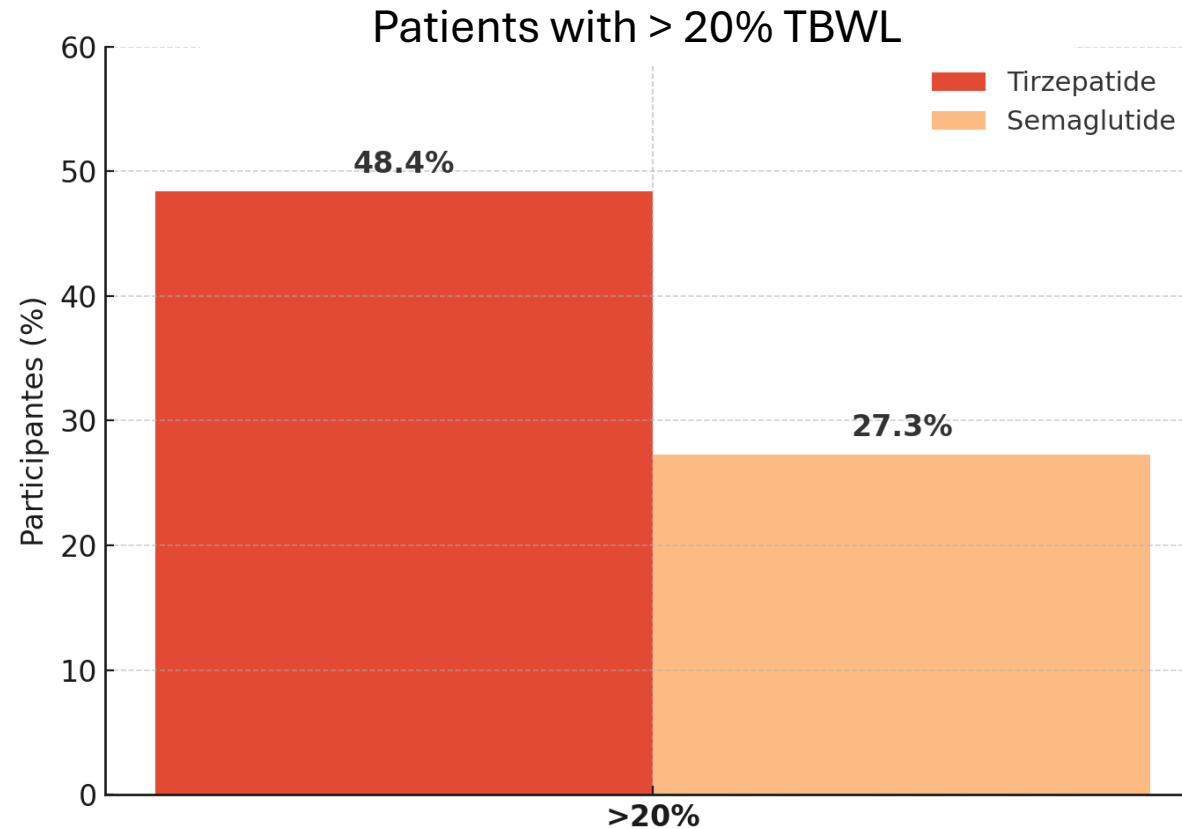
FIGURE 2. Number of inpatient primary bariatric surgery procedures and initial admission complication and mortality rates in the United States from 1993 to 2016.

ORIGINAL ARTICLE

# Tirzepatide as Compared with Semaglutide for the Treatment of Obesity

Louis J. Aronne, M.D.,<sup>1</sup> Deborah Bade Horn, D.O.,<sup>2</sup>  
Carel W. le Roux, M.D., Ph.D.,<sup>3,4</sup> Wayne Ho, M.D.,<sup>5,6</sup> Beverly L. Falcon, Ph.D.,<sup>7</sup>  
Elisa Gomez Valderas, M.Sc.,<sup>7</sup> Sagar Das, M.Sc.,<sup>7</sup> Clare J. Lee, M.D., M.H.S.,<sup>7</sup>  
Leonard C. Glass, M.D.,<sup>7</sup> Cagri Senyucel, M.D., Ph.D.,<sup>7</sup> and Julia P. Dunn, M.D.,<sup>7</sup>  
for the SURMOUNT-5 Trial Investigators\*

May /25





The Death of Julius Caesar (1806) by Vincenzo Camuccini in the National Museum of Capodimonte, in Naples

# First-Line Therapy for Type 2 Diabetes With Sodium– Glucose Cotransporter-2 Inhibitors and Glucagon-Like Peptide-1 Receptor Agonists:

A Cost-Effectiveness Study



ICER= \$327 000 per QALY



ICER= \$823 000 per QALY.

Above the WTP threshold

To be cost-effective, GLP1 RA should cost under \$6 per day

# Cost-Effectiveness of Newer Pharmacologic Treatments in Adults With Type 2 Diabetes: A Systematic Review of Cost-Effectiveness Studies for the American College of Physicians

John T. Schousboe, MD, PhD; Adrienne Landsteiner, PhD, MPH; Tyler Drake, MD; Shahnaz Sultan, MD, MHSc; Lisa Langsetmo, PhD; Anjum Kaka, MD; Maylen Anthony, MPH; Charles J. Billington, MD; Caleb Kalinowski, MS; Kristen Ullman, MPH; and Timothy J. Wilt, MD, MPH

April 19, 2024

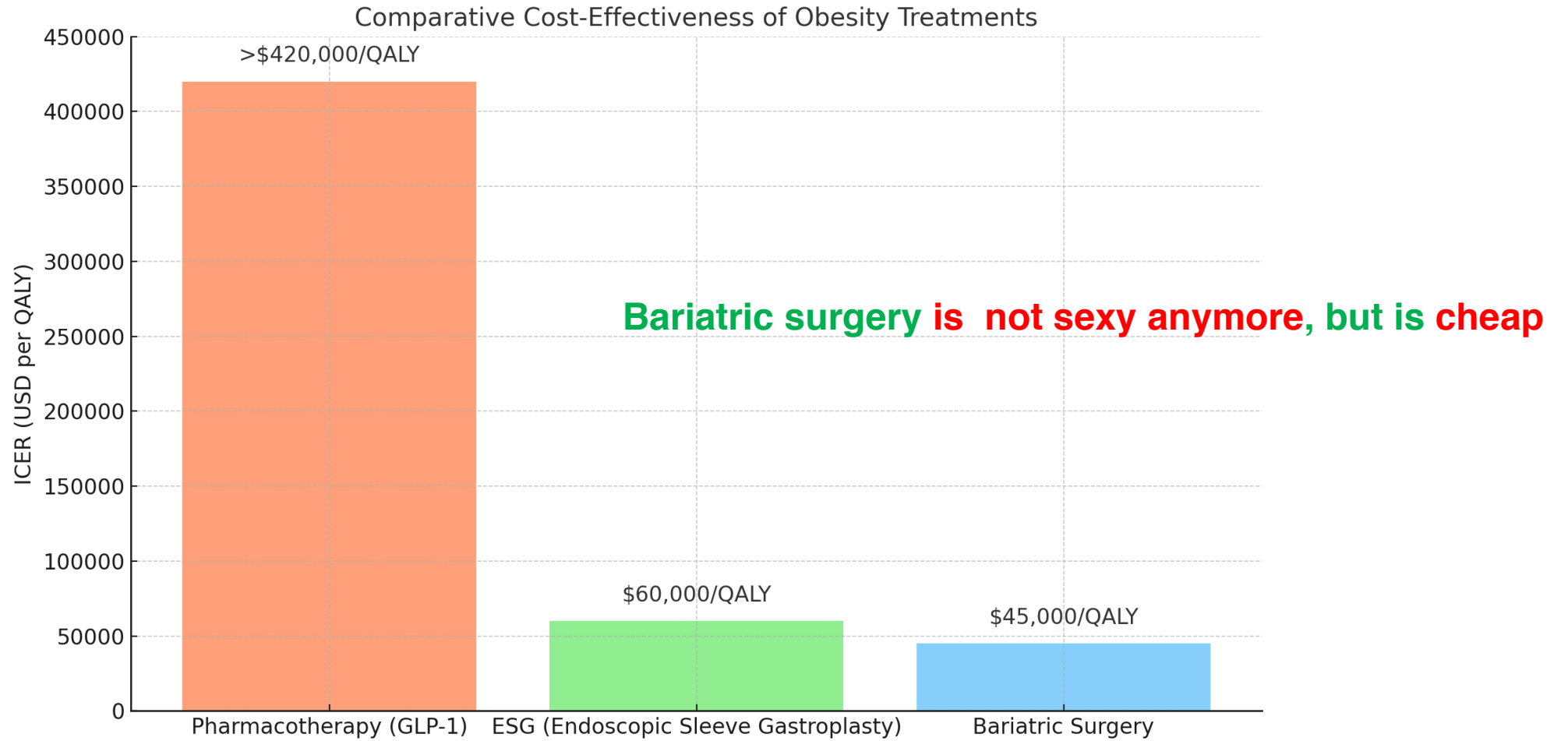
1st line GLP1 RA, oral or injectable, *had an incremental cost-effectiveness ratio of \$1 089 000 per QALY*



WTP threshold

To fit in the WTP of worldwide health systems, we need a decrease in 70% (oral) to 90% (injectables) of GLP1RA cost

# Cost/QALY



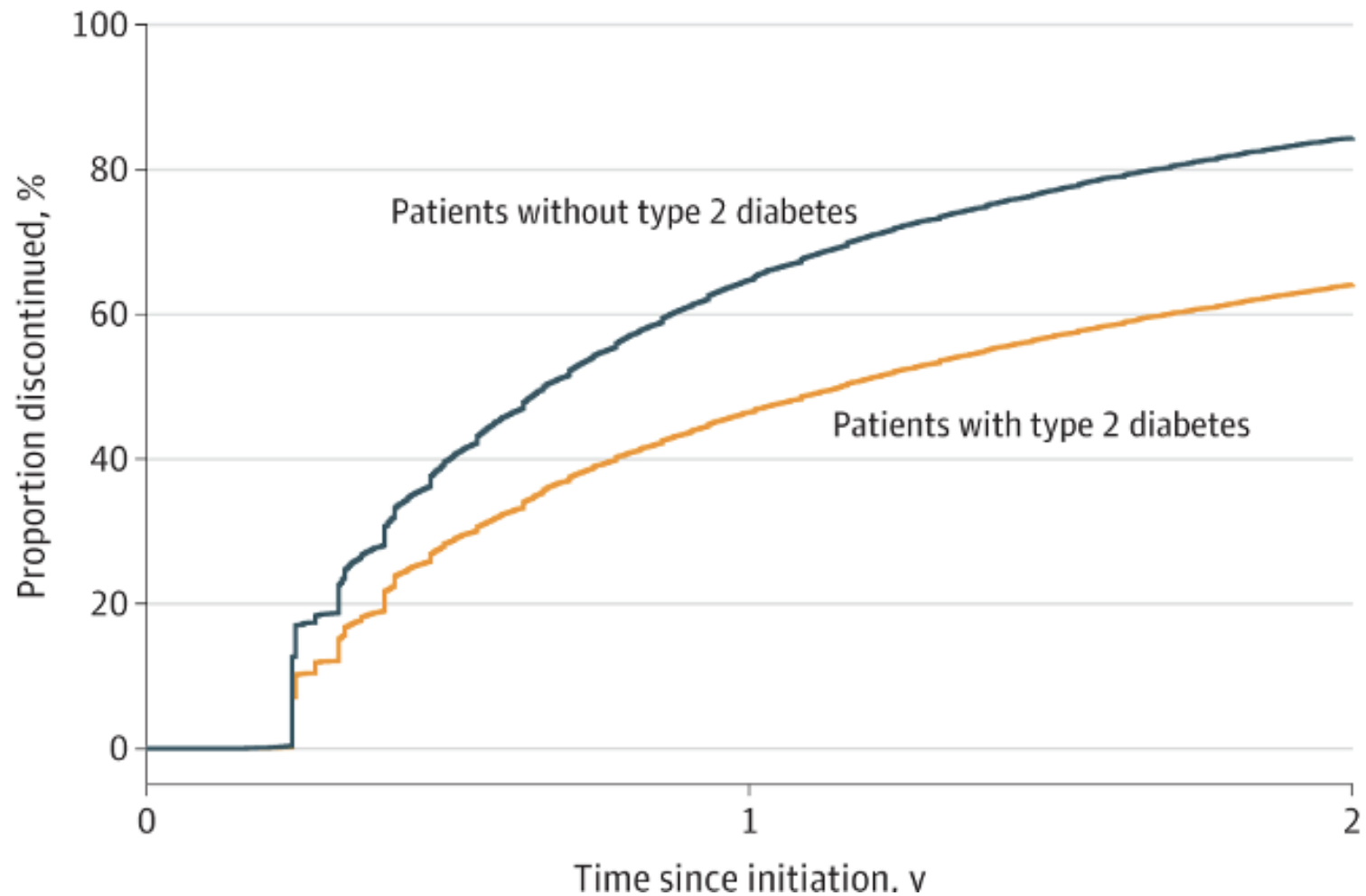
**Few individuals continue using GLP-1RAs long-term, despite their proven benefits.**

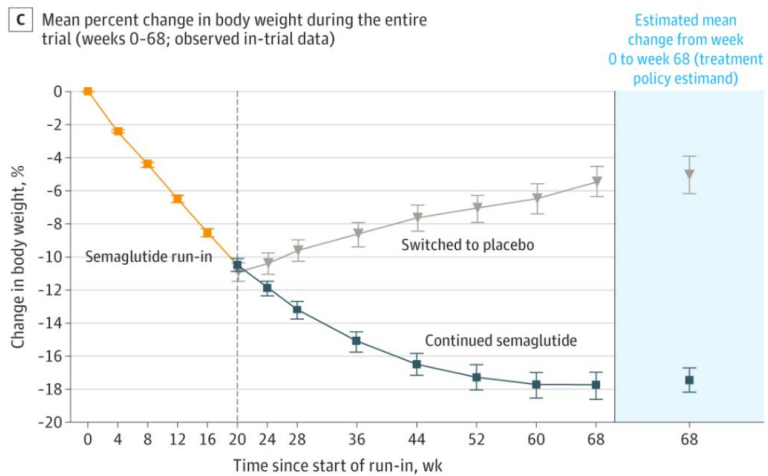
@ 1 year:  
**25%** still on  
medication

@ 2 years :  
**15%** still on  
medication

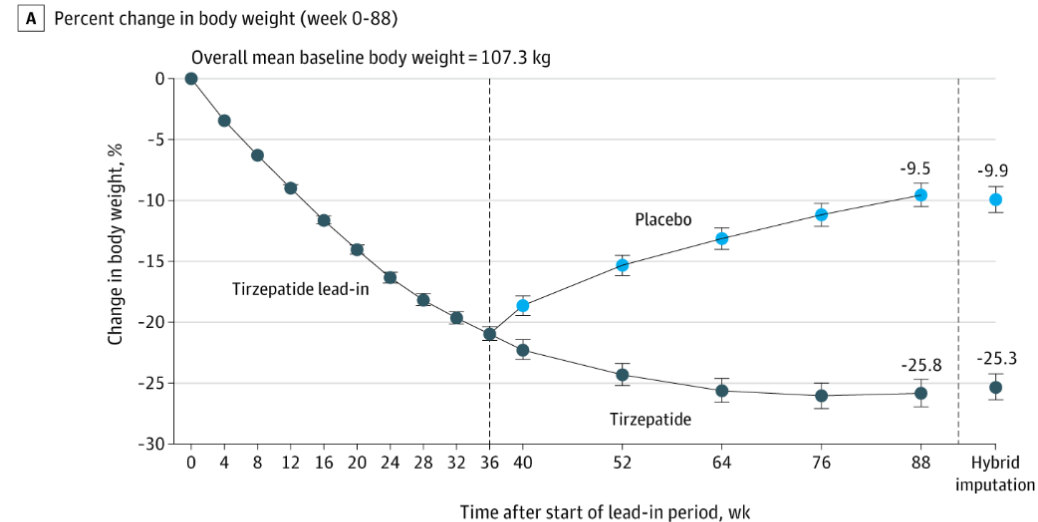
# Discontinuation of GLP1RA

Time to discontinuation of GLP-1 RA



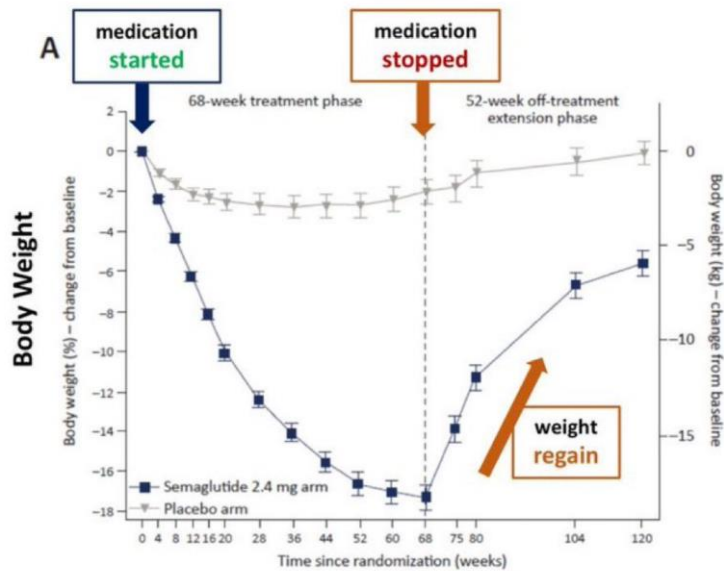


No. of participants									
Semaglutide run-in									
	803	803	803	802	801				
Continued semaglutide	535	527	531	525	523	521	516	520	535
Switched to placebo	268	267	265	258	260	254	246	250	268



No. at risk													
Tirzepatide lead-in	670	666	669	668	667	667	669	663	659	670			
Tirzepatide							335	333	328	317	310	310	335
Placebo							335	330	317	303	292	289	335

Aaron, JAMA, 2023



Aronne, NEJM, 2023

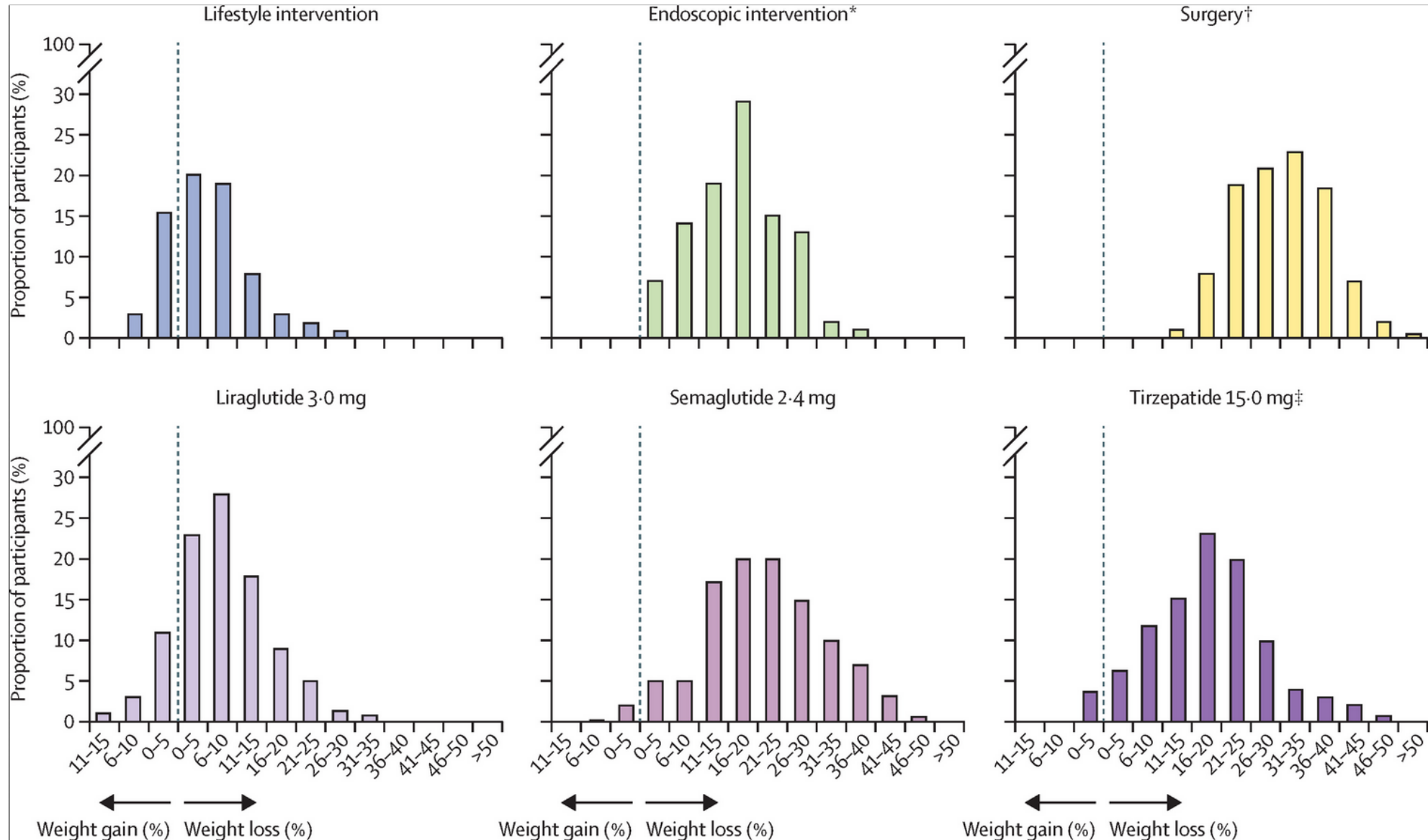
Wilding, 2022

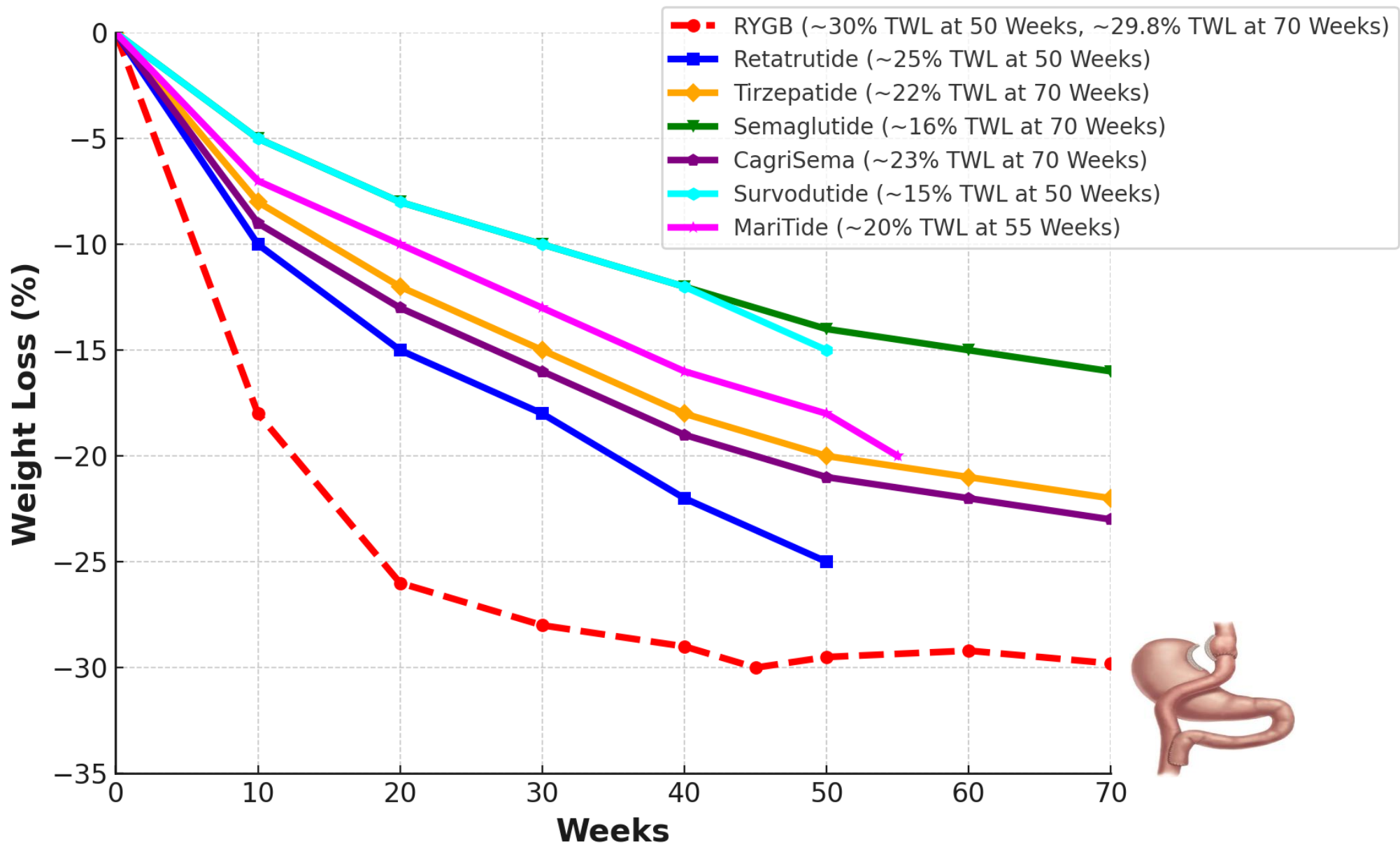


**NO!**



# Heterogeneous response to obesity treatments





Indirect comparison with Cohen R last 122 cases of RYGB in people with obesity, no T2D

# Metabolic surgery in era of modern pharmacotherapy

- ✓ Advancements in CV medications and PCI did not kill CABG
- ✓ Advancements in chemo, radio and immunotherapy did not kill cancer surgery
- ✓ Multifactorial disease, no magic bullet



2023  
2024  
2025  
2026  
2027

# Candidates in the new obesity treatment era

Pts preference

Extreme Obesity BMI > 45-50

Suboptimal response to med tx

Intolerance to pharmacotherapy

Candidates in  
the new  
obesity  
treatment  
era

Contraindications to  
medicines

Cost

# International Federation for the Surgery of Obesity statement on metabolic bariatric surgery after pharmacotherapy-induced weight loss in clinical obesity

Lancet Diabetes Endocrinol 2021

Published Online

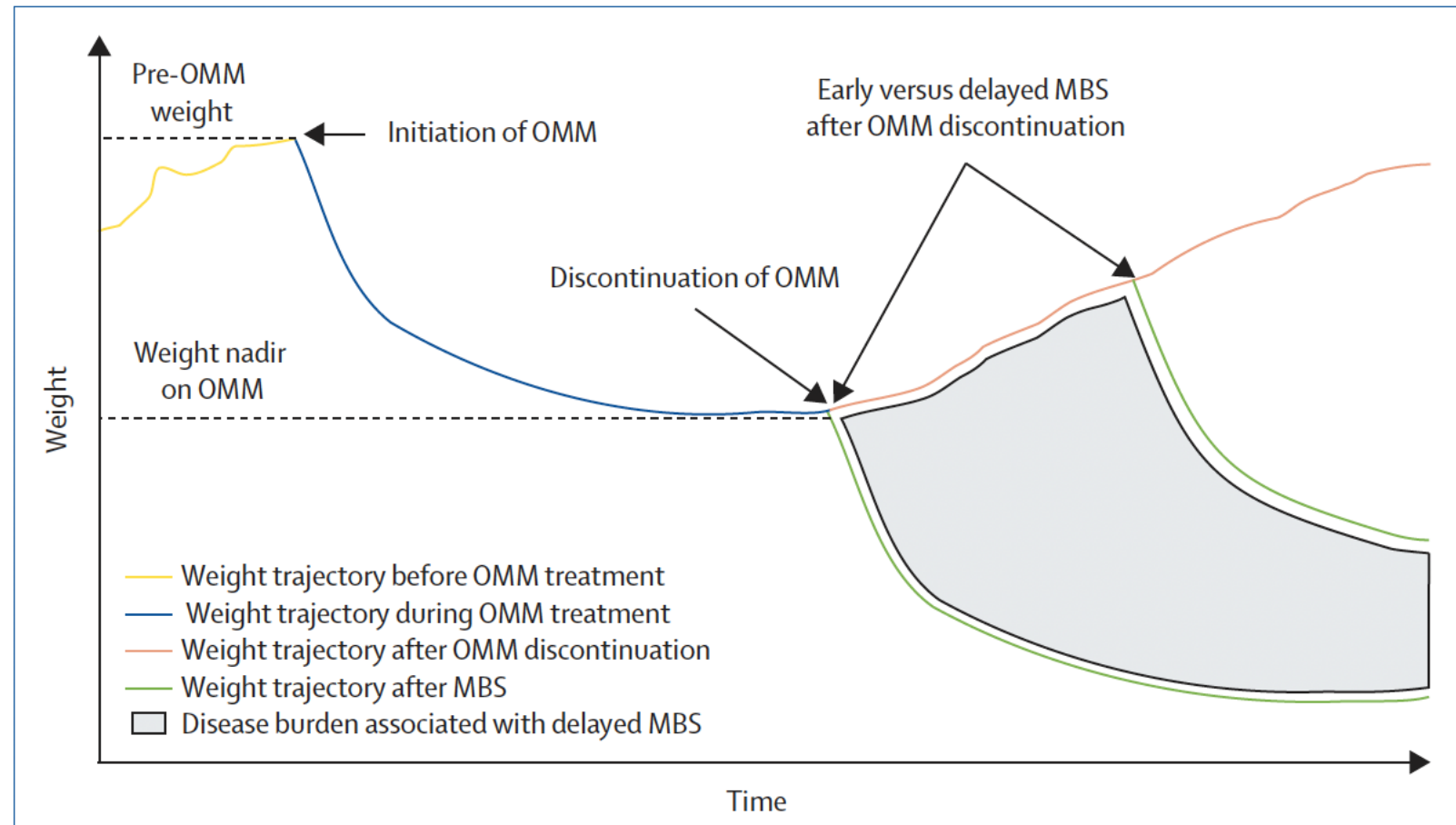
July 22, 2025

[https://doi.org/10.1016/](https://doi.org/10.1016/S2213-8587(25)00198-6)

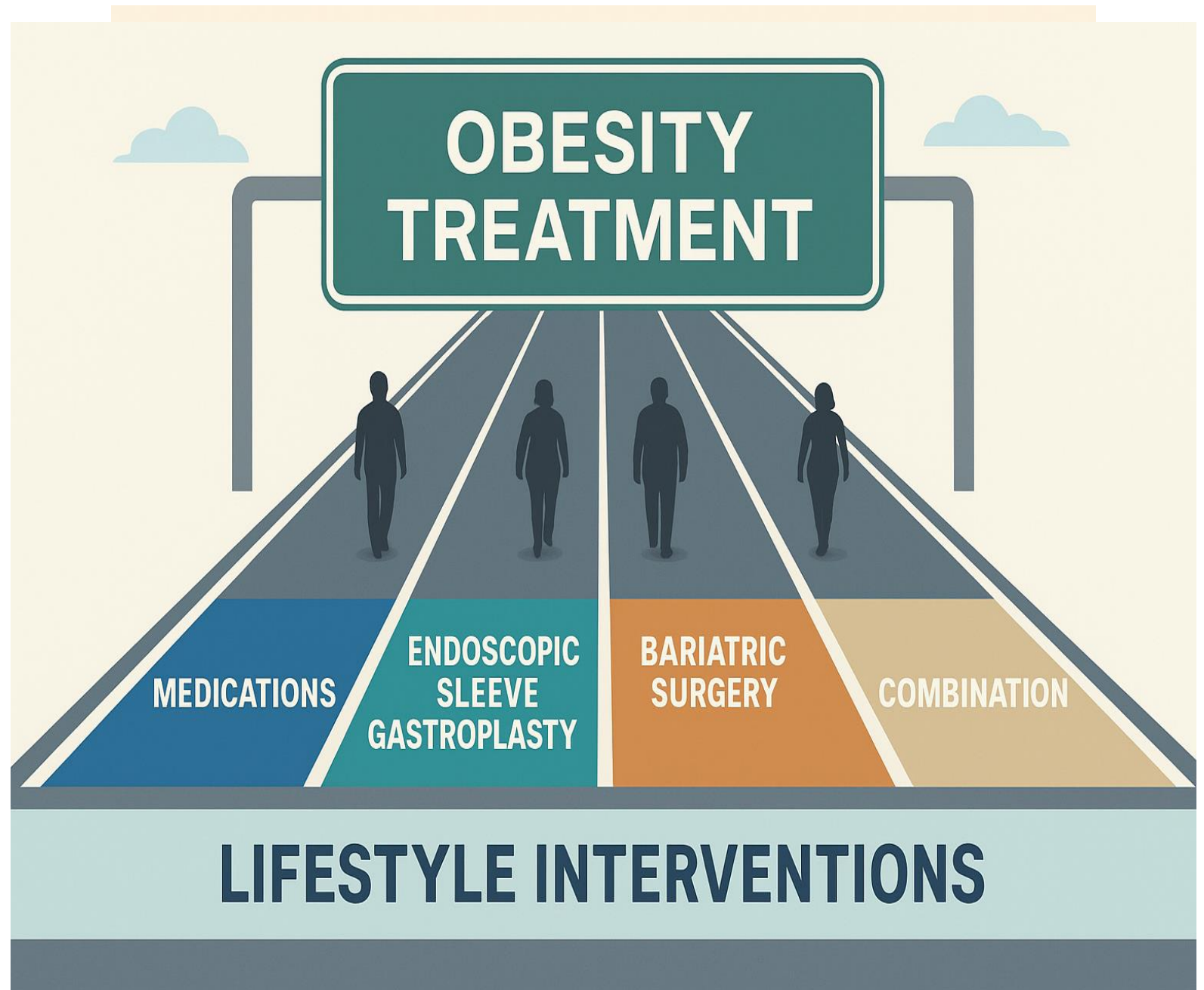
[S2213-8587\(25\)00198-6](https://doi.org/10.1016/S2213-8587(25)00198-6)

\*Ricardo V Cohen, Gerhard Prager, Carel W le Roux,  
Ildiko Lingvay, Paulina Salminen  
[ricardo.cohen@haoc.com.br](mailto:ricardo.cohen@haoc.com.br)

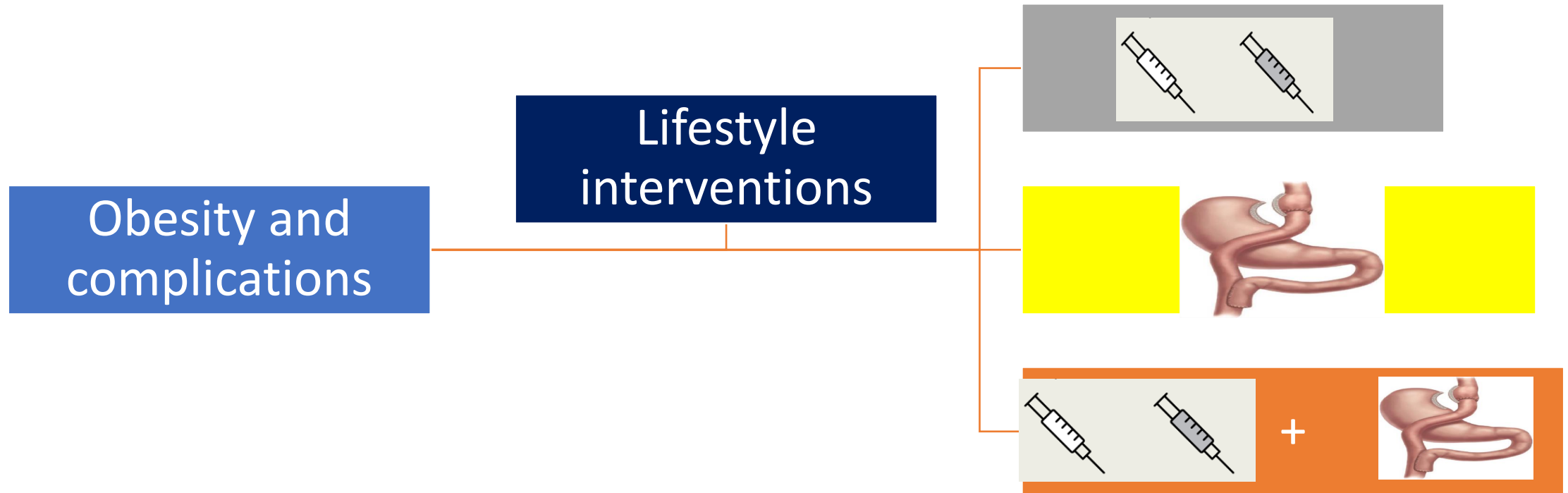
- Good outcomes, however:
- Lack of access
- Long-term side effects
- Cost of continued Tx
- "I don't want it anymore"



**Evidence-  
based**



# Individualized Strategy





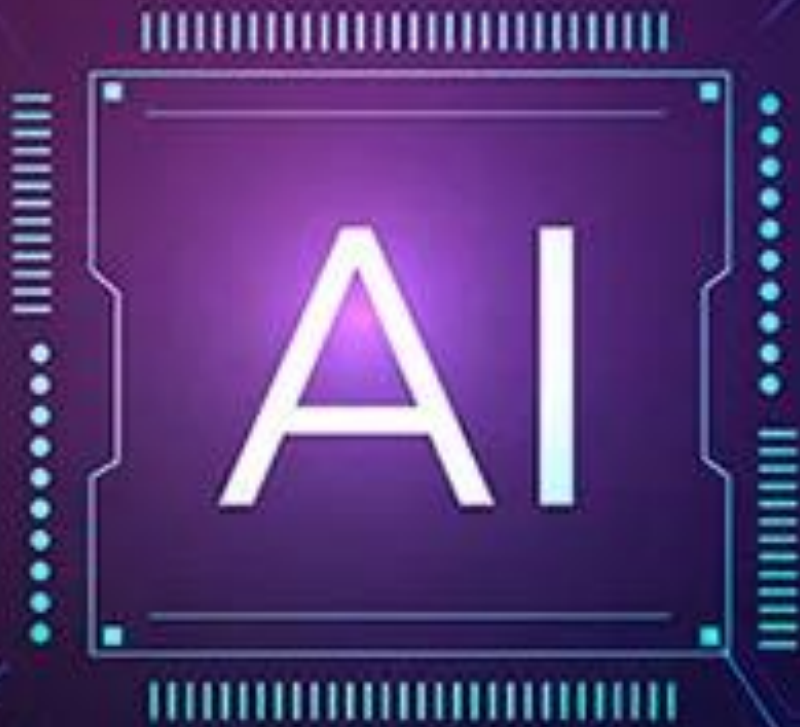
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[@rvcohen](https://twitter.com/rvcohen)(twitter)



**OSWALDO CRUZ**  
CENTRO ESPECIALIZADO EM **OBESIDADE E DIABETES**

# Personalized Treatment Selection



AI Analyzes medical history, exams and past treatments to recommend the best intervention

Predicts which patients will respond best to surgery, pharmacotherapy or combined strategies

AI Risk Stratification:

- Categorizes patients into low-, moderate-, and high-risk groups based on organ dysfunction and prioritization to treatments