



“WITHOUT DATA YOU ARE JUST ANOTHER PERSON WITH AN OPINION”

HOW CAN WE REACH EVIDENCE BASED METABOLIC
BARIATRIC SURGERY?

Ricardo Cohen MD

Director, The Center for Obesity and Diabetes, Hospital Oswaldo Cruz
Sao Paulo Brazil

President, IFSO Global

Past-President, IFSO LAC

Past-President, Brazilian Society for Bariatric and Metabolic Surgery
(2011-2012)



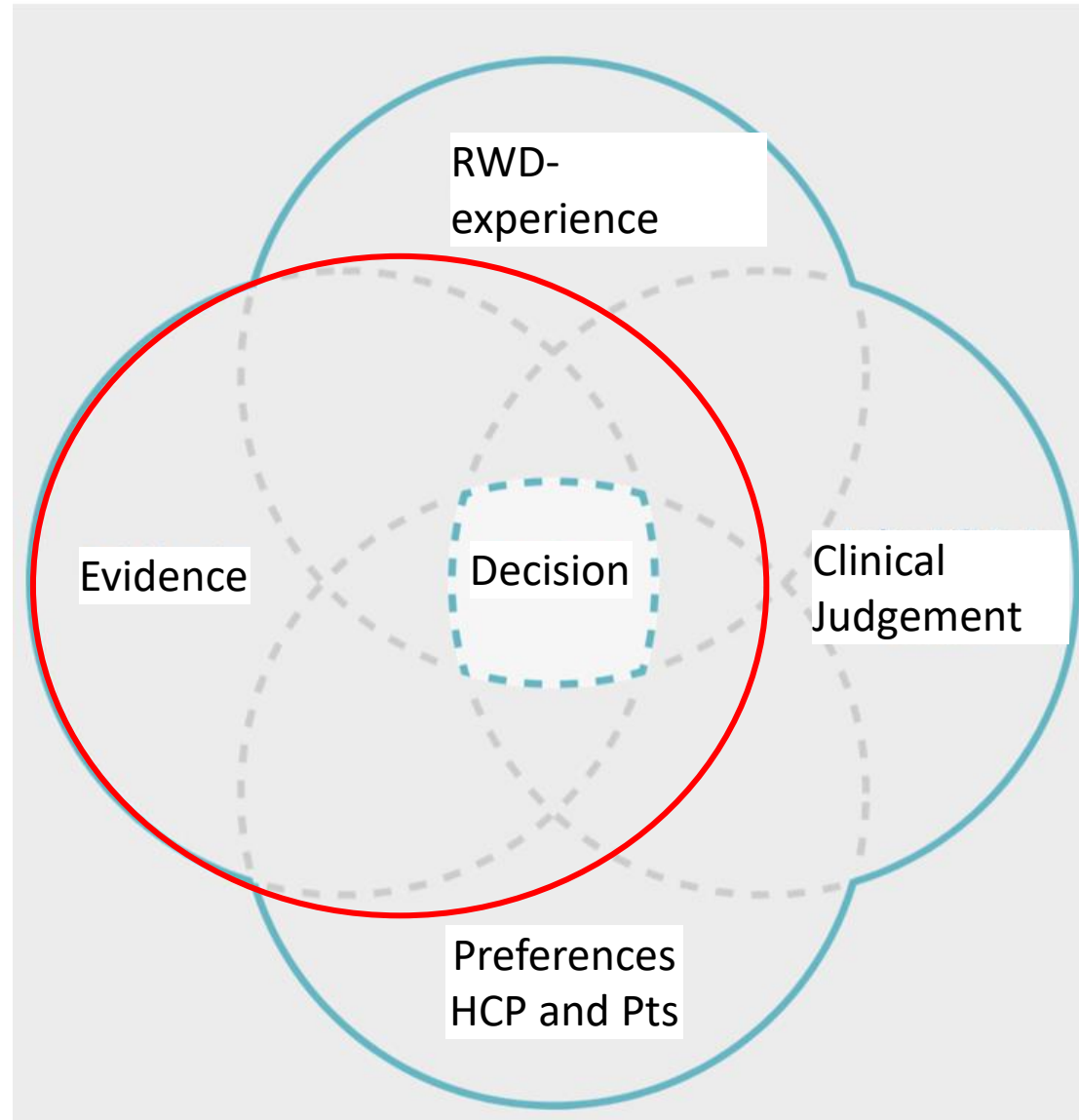
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OSWALDO CRUZ

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- SAB: Morphic Medical, Medtronic, Johnson & Johnson, Regeneron

Evidence based medicine guides clinical decision making



**How do we produce the best evidence?
Observational studies, RWD and RCTs**



ESC

European Society
of Cardiology

European Heart Journal (2019) **40**, 1408–1410

doi:10.1093/eurheartj/ehy874

EDITORIAL

Can we trust observational data for clinical decision-making?

Steven E. Nissen* and **Grant W. Reed**

The Cleveland Clinic Foundation, Desk J2-3, 9500 Euclid Ave, Cleveland, OH 44195, USA

“Observational studies do not prove causation or effect. They generate hypotheses that are best proven via RCTs”

Another Problem with Observational Studies:

Post hoc analysis

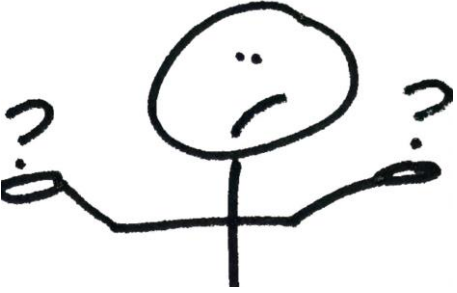
Lack of pre-specified methods allows investigator bias, even if unintentional, to influence results.

Why Bother with Observational Studies?

- ✓ Support evidence-based medicine
 - ✓ RCTs are too costly for every question
 - ✓ Maybe the only evidence to guide practice
-

Why do RCTs
matter?

Why do RCTs matter?



When we don't know

- ✓ Clarify intervention effects, especially under uncertainty
- ✓ Resolve expert disagreements through evidence
- ✓ Account for alternative causes and risk factors

Why do RCTs matter?

When we are wrong



Cautionary Tales Favoring RCTs

- Women's Health Initiative
 - Hormone replacement therapy *unexpectedly increased* cardiovascular events
- ACCORD
 - Tight glycemic control *unexpectedly increased* mortality

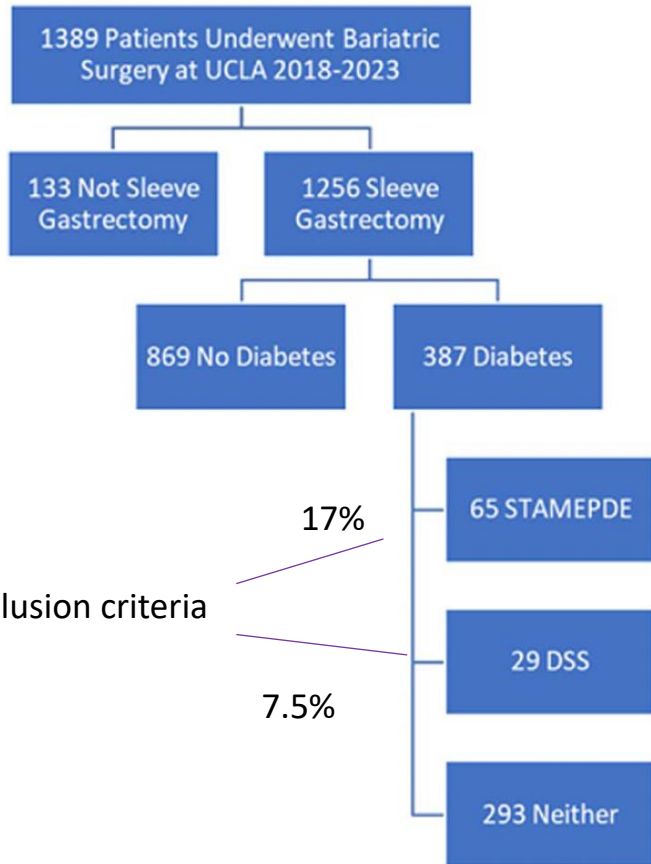


RCTs results **are**
reproducible

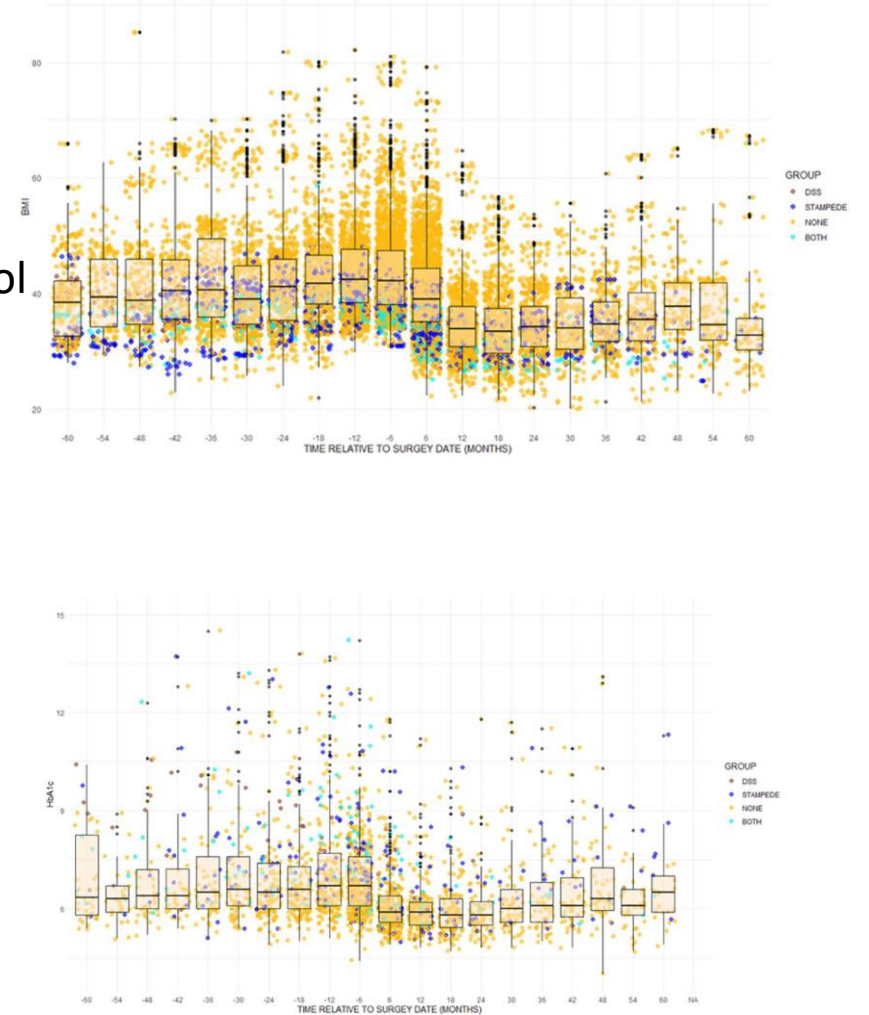
Generalizability of Randomized Clinical Trial Outcomes for Diabetes Control Resulting From Bariatric Surgery

2024

Edward H. Livingston, MD, FACS, AGAF,* Hila Zelicha, RD, PhD,* Erik P. Dutson, MD,* Zhaoping Li, MD, PhD,†† Matthew L. Maciejewski, PhD,§ || ¶ and Yijun Chen, MD*



Similar WL and glucose control UCLA x Stampede and DSS



Real-world data and evidence

1. RWD comes from routine practice — EHRs, claims, registries, patient-generated data

2. RWE is the clinical evidence generated by aggregating and analyzing RWD

3. Together, they inform real-world effectiveness, safety, and treatment use

RCTs x RWD

- **Population:** Strict criteria (RCT) vs. diverse real-world (RWD)
- **Setting:** Controlled research sites (RCT) vs. routine care (RWD)
- **Outcomes:** Prespecified/short-term (RCT) vs. broader/long-term (RWD)
- **Data:** Protocol-driven (RCT) vs. routine records & claims (RWD)
- **Size:** Smaller (RCT) vs. very large (RWD)
- **Bias:** Randomized, causal inference (RCT) vs. observational, no randomization (RWD)

Randomized Trials vs Real-world Evidence How Can Both Inform Decision-making?

R. Christopher Sheldrick, PhD

JAMA, 2024

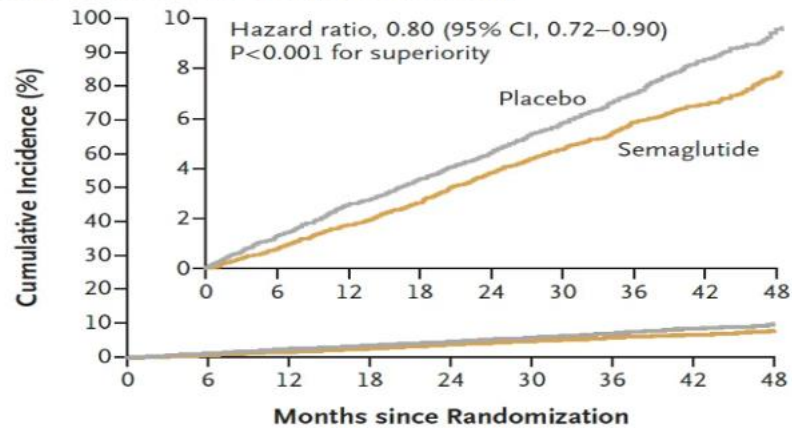
- ✓ **RWE is an instrument of external validations of RCTs**
- ✓ **RWE does not replace RCTs**

Do RCTs change indications of interventions (drugs, devices, operations)?

Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes

A. Michael Lincoff, M.D., Kirstine Brown-Frandsen, M.D., Helen M. Colhoun, M.D., John Deanfield, M.D., Scott S. Emerson, M.D., Ph.D., Sille Esbjerg, M.Sc., Søren Hardt-Lindberg, M.D., Ph.D., G. Kees Hovingh, M.D., Ph.D., Steven E. Kahn, M.B., Ch.B., Robert F. Kushner, M.D., Ildiko Lingvay, M.D., M.P.H., Tugce K. Oral, M.D., Marie M. Michelsen, M.D., Ph.D., Jorge Plutzky, M.D., Christoffer W. Tornøe, Ph.D., and Donna H. Ryan, M.D.,
 for the SELECT Trial Investigators* **NEJM, Nov 2023**

A Primary Cardiovascular Composite End Point



No. at Risk

Placebo	8801	8652	8487	8326	8164	7101	5660	4015	1672
Semaglutide	8803	8695	8561	8427	8254	7229	5777	4126	1734

Select RCT



20% CV events risk

YES !!

- The FDA approved an expanded label for semaglutide 2.4 mg for prevention of CV events in patients with overweight/obesity and prior CVD.
- The approval was based on positive results of the SELECT trial.



HOW WAS THE PERCEPTION ABOUT
RESEARCH IN SURGERY IN A RECENT PAST

**Surgical research or comic opera:
questions, but few answers**

*Richard Horton, Editor-in-Chief,
The Lancet, 1996*

“The repeated reports of biased data or poorly designed trials give an illusion of success because they are numerous. The numbers seem impressive on paper, but they add up ZERO to science.”

WHERE IS MBS STANDING TODAY



RCTs of metabolic surgery x BMT, at least 2 years of FU, gluco-centric outcomes

	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 ²⁷	AGB	2	FPG <126 mg/dL and HbA _{1c} <6.2% (44.3 mmol/mol), without glucose-lowering agents	73% vs 13%	20% vs 1%
Cohen et al ²¹	RYGB	2	HbA _{1c} <6.5% (47.5 mmol/mol), regardless of glucose-lowering agents	71% vs 51%	26% vs 5%
Simonson et al ³⁸	RYGB	3	FPG <126 mg/dL and HbA _{1c} <6.5% (47.5 mmol/mol) regardless of glucose-lowering agents	42% vs 0%	25% vs 5%
Ikramuddin et al ³⁹	RYGB	5	HbA _{1c} <7% (53.0 mmol/mol), regardless of glucose-lowering agents	55% vs 14%	22% vs 10%
Courcoulas et al ⁴⁰	RYGB vs AGB	5	HbA _{1c} <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 ⁴¹	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 ⁴²	RYGB vs sleeve gastrectomy	5	HbA _{1c} <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 ⁴³	RYGB vs biliopancreatic diversion	10	FPG <100 mg/dL and HbA _{1c} <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_{1c}=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

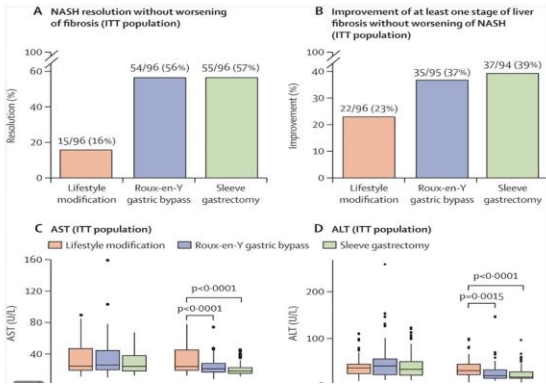
Non-glucocentric outcomes, CV events and mortality

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

Ornella Venastro¹, Simona Panunzi², 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, Goltzude Mingrone



Lancet, 2023



VL 11, 83, 4, 2024

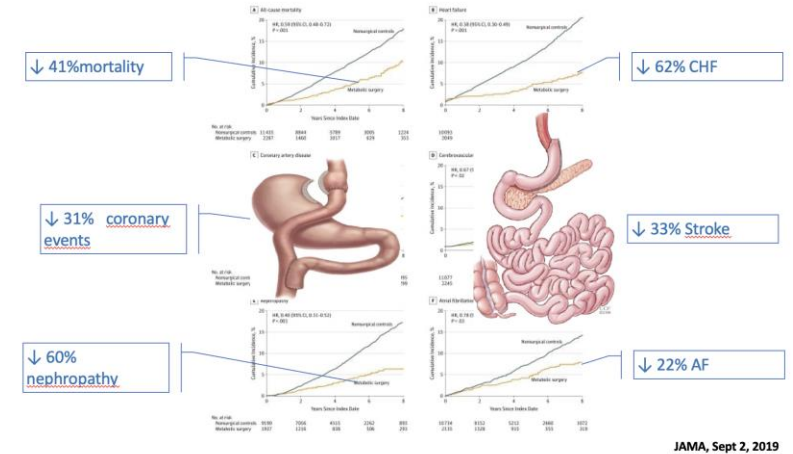
ORIGINAL RESEARCH

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



Carlos A. Schiavon, MD,^{1,3} Alexandre B. Cavalcanti, MD,¹ Juliana D. Oliveira, CN,^{1,3} Rachel H.V. Machado, CN,¹ Eliana V. Santucci, Pr,¹ Renato N. Santos, Sr,¹ Julia S. Oliveira, Sr,¹ Lucas P. Damiani, Sr,¹ Débora Junqueira, MD,¹ Helio Halpern, MD,¹ Frederico de L.L. Monteiro, MD,¹ Patricia M. Noujaim, MD,¹ Ricardo V. Cohen, MD,¹ Marcio G. de Sousa, MD,¹ Luiz A. Bortolotto, MD,¹ Otavio Berwanger, MD,¹ Luciano F. Drager, MD^{1,4}

JACC, 2024



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

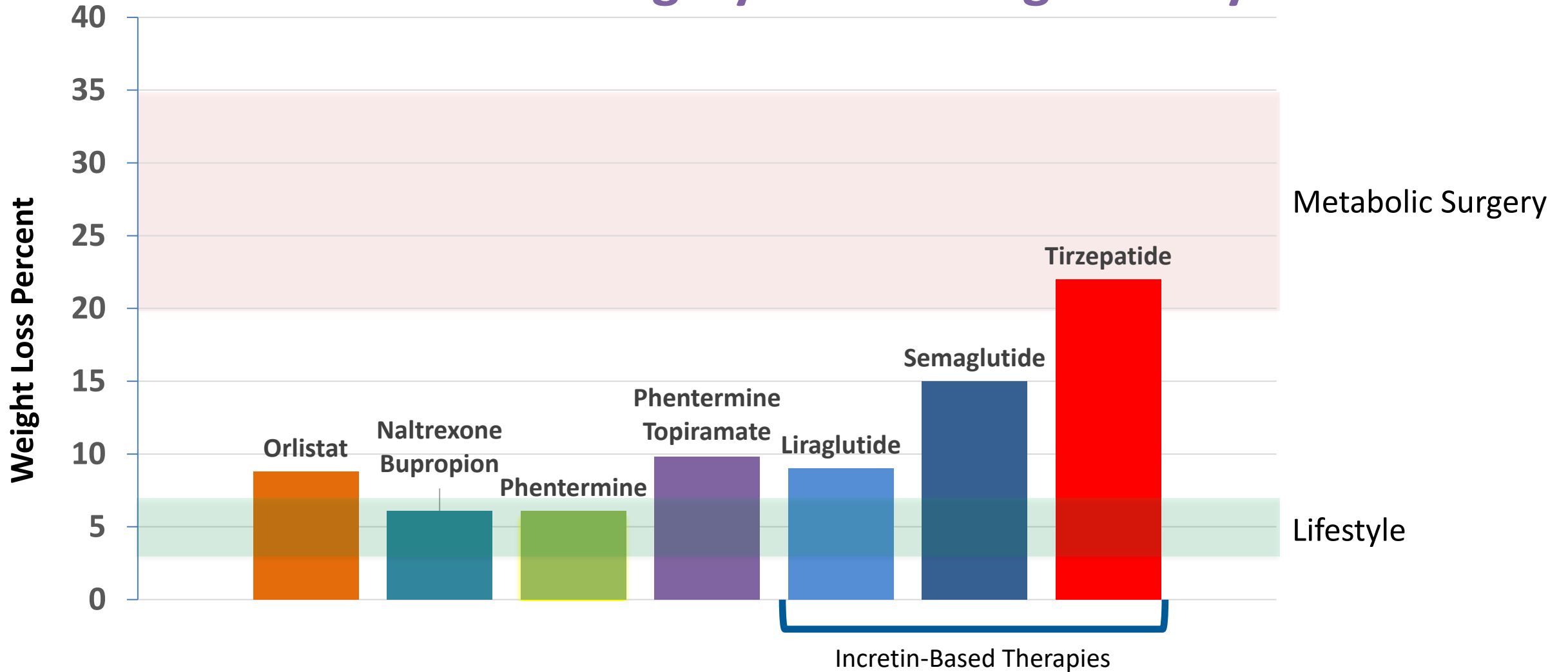
Ricardo V. Cohen,^{1,4} Tiago Veiga Pereira,^{1,2} Cristina Mamede Abad,^{1,2} Tereza Beatriz Zanata Petry,^{1,2} José Luis Lopes Cortes,¹ Carlos Augusto Schiavon,¹ Carlos Eduardo Pompili,¹ Fernando Nogueira Quirino Peçhy,¹ Aline Carolina Calmon da Costa Silva,¹ Lívia Porto Cunha dos Siveira,¹ Pedro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

The Lancet Eclin, online Nov 11, 2022



Outperforms the medical Tx

Effectiveness of Anti-obesity Medications vs. Lifestyle and Bariatric Surgery for Treating Obesity

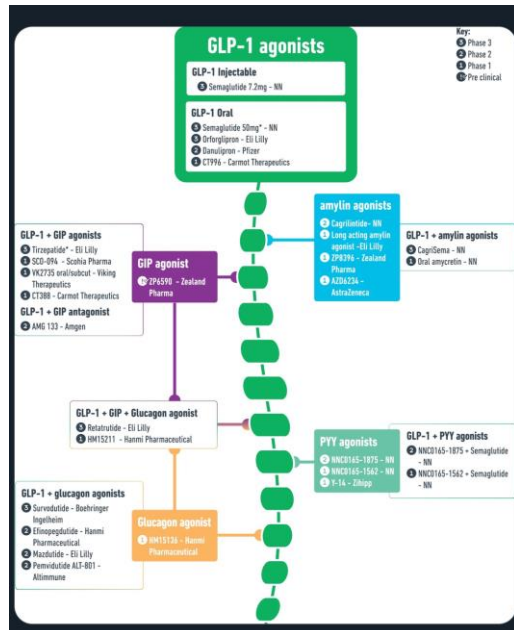




Is Metabolic Surgery Having an Identity Crisis?

Ricardo V. Cohen¹ · Ildiko Lingay² · Carel Le Roux³ · Priya Sumithran⁴

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- ✓ Tablets (with >25% TBWL)
- ✓ Monthly/3 months/6months injections
- ✓ Decreased CV risk
- ✓ Decreased kidney disease
- ✓ Hepatic fibrosis reversal
- ✓ WL>30% 40-50 weeks



Novel surgical proposals WITHOUT robust evidence

Safety/efficacy



How metabolic/bariatric surgery is sometimes practiced



Eminence based medicine.

Webvidence based medicine .

Everybody-does-so-I'll do it based medicine

In-my-hand it works evidence based medicine.

Eloquence based medicine.

Conference based medicine.

Clarevidence based medicine .

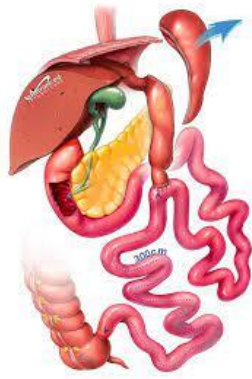
Beliefs based medicine.

Trend based medicine

Efficacy and safety of single-anastomosis duodeno-ileal bypass with sleeve gastrectomy versus Roux-en-Y gastric bypass in France (SADISLEEVE): results of a randomised, open-label, superiority trial at 2 years of follow-up

*Maud Robert, Tigran Poghosyan, Nicolas Romain-Scelle, Sebastien Czernichow, Dominique Delaunay, Adrien Sterkers, Litavan Khamphommala, Andrea Lazzati, Claire Blanchard, Robert Caiazzo, François Pattou, Emmanuel Disse, and the SADISLEEVE Collaborative Group**

Lancet, Aug 2025



190 patients



191 patients

SADI-S vs RYGB: Is the Hype Justified for Index MBS?

The Weight Loss Paradox

Superior weight loss with SADI-S (76.0% vs 68.1% EWL) **did not translate** into better diabetes remission (57% vs 62%) or health gains

Study Limitations

High dropout rate: 20% missing data (46 in SADI-S vs 32 in RYGB)

Short follow-up: 2 years insufficient for long-term assessment

Key Findings after SADI-S

Statistically greater weight reduction (76% vs 68%)

SAME metabolic outcomes AS RYGB, **no further health gain**

Fewer dietary constraints

The Complication Trade-Off

SADI-S: Higher early complications
(6% vs 2%) including anastomotic leaks

SADI-S: More GI side effects
(diarrhea , steatorrhea)

RYGB: Higher late complications
(10% vs 2%) internal hernias

Important Trade-offs

Increased complication risk with SADI-S

Potential nutritional deficiencies, malabsorption

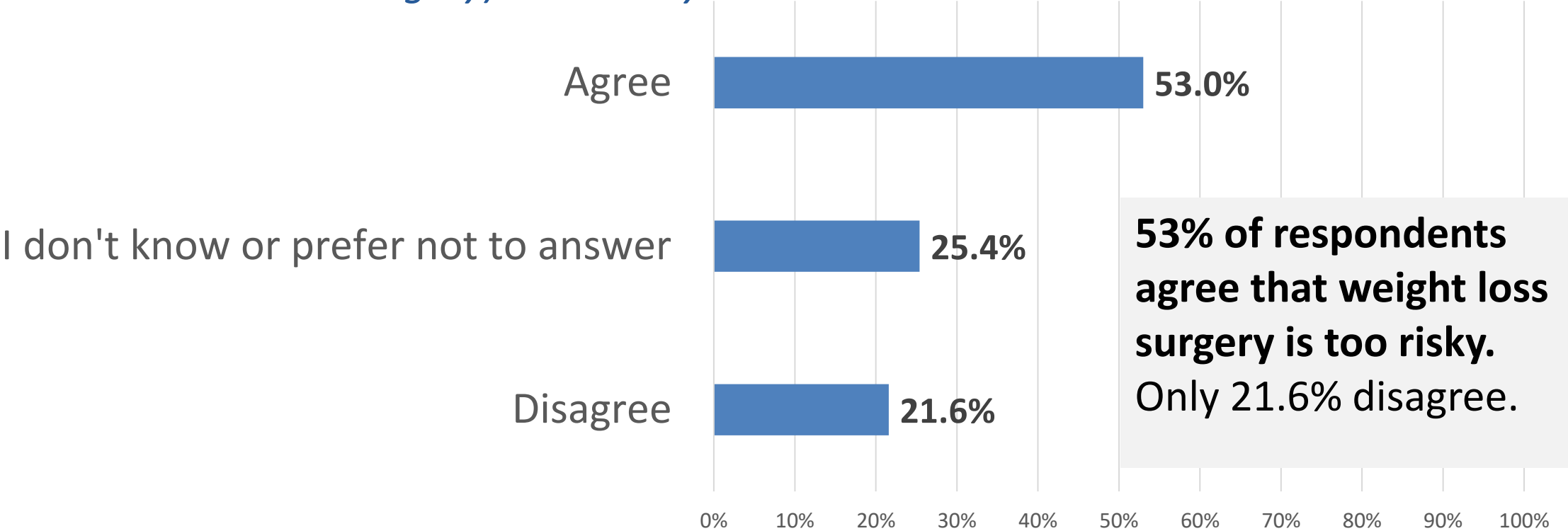
Complexity of procedure

*"If the extra weight loss doesn't improve the most critical health problems associated with obesity, its clinical significance can be questioned."
Cohen RV*

The hype is not justified – statistical WL superiority with significant trade-offs and no clear benefits

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.”



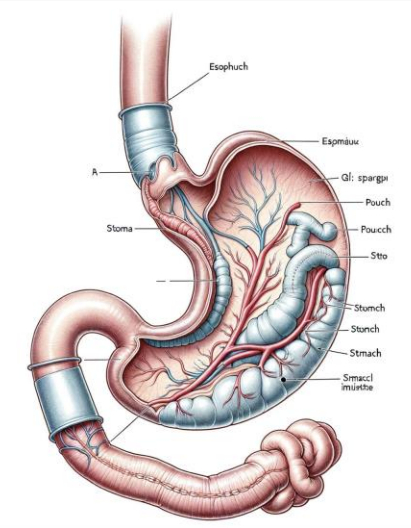
■ US Adults 18+ with Self-Reported Weights and Heights Resulting in BMIs of 30 and Greater

Innovation is important..



Courtesy of Paulina Salminen

While we waste time
discussing techniques with
NO ROBUST DATA, pharmas
are moving fast with science



A flow-chart how to choose study type:

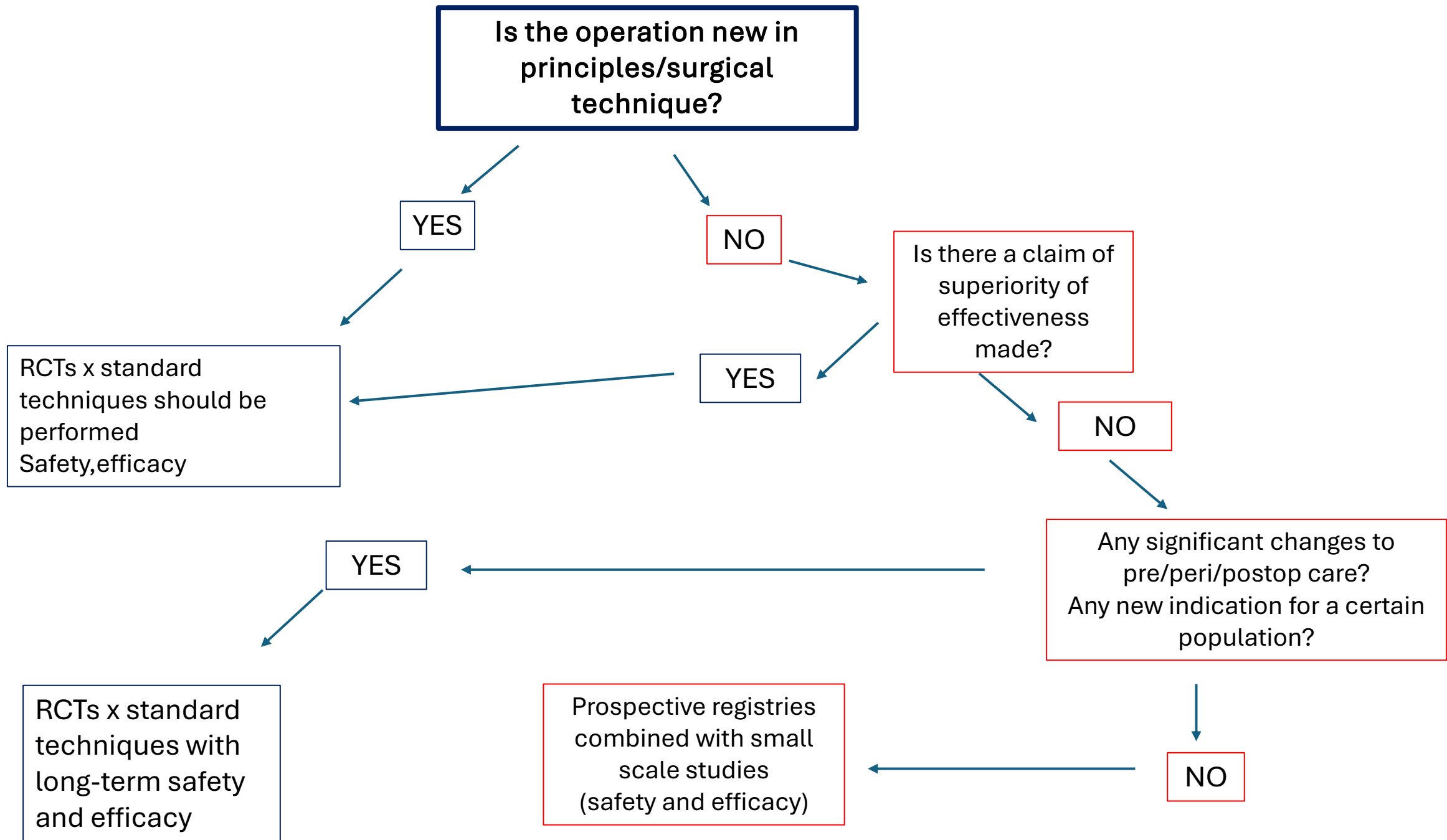
Is it possible to randomize?



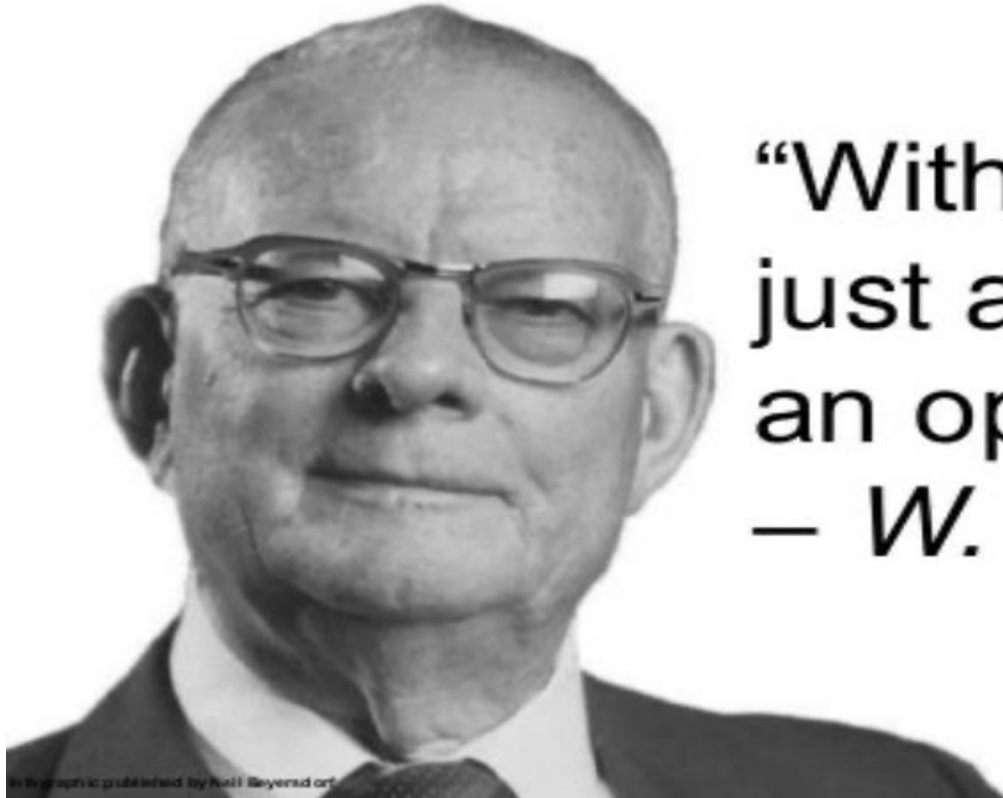
Do Randomized Controlled Study!



*When are
Randomized
Trials
Unnecessary in
MBS ?*



Thank You



“Without data you’re
just another person with
an opinion.”
– *W. Edwards Deming*

ricardo.cohen@haoc.com.br

[X= @rvcohen](#)