

# Combining Surgery and best medical treatment for obesity and T2D

**RICARDO COHEN**  
**Past President, IFSO LAC**

Director, The Center for Obesity and  
Diabetes Oswaldo Cruz German Hospital, São  
Paulo - Brazil



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

# Disclosures

- Research Grant, J&J Medical, Brasil
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- Research Grant, GI Dynamics
- Research Grant, Hospital Oswaldo Cruz Bioscience Institute
- SAB: GI Dynamics, JJ Medical,, Medtronic, Bariatek
- Speaker: J&J Medical, Medtronic



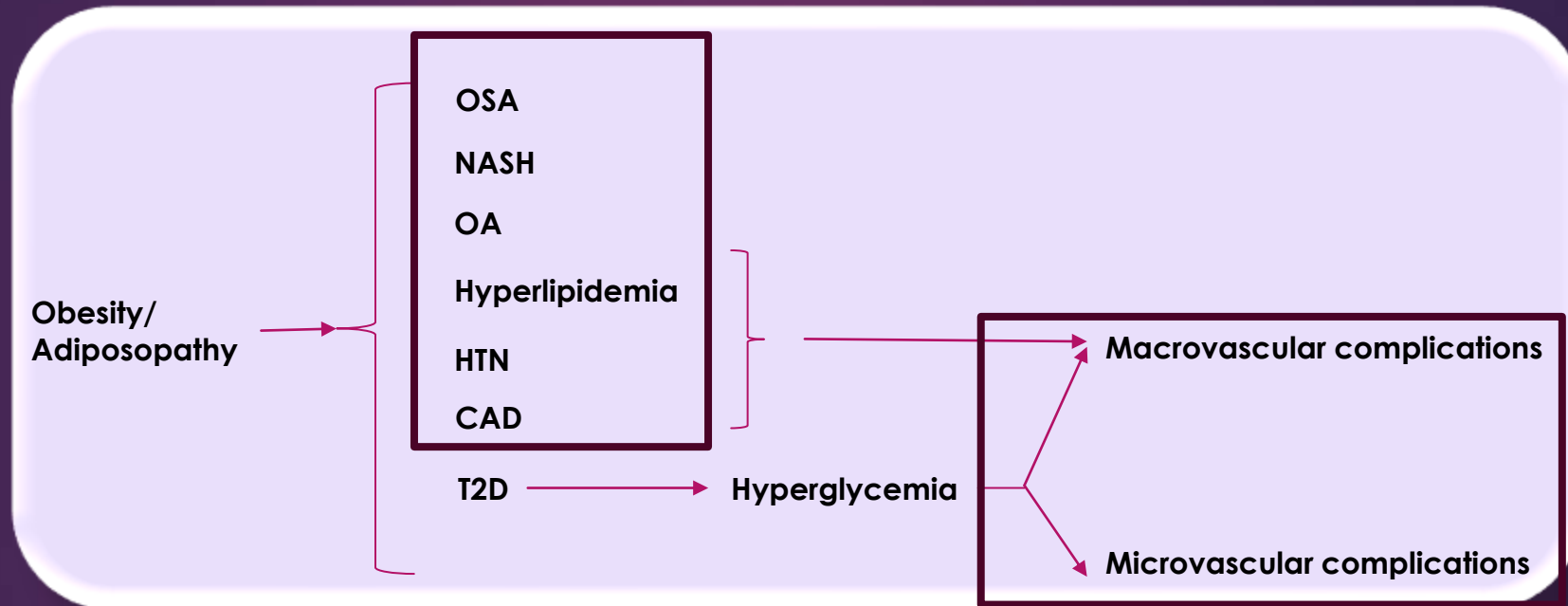
Obesity, Diabetes under  
control

# Obesity management as a primary treatment goal for type 2 diabetes: time to reframe the conversation



The Lancet 2022

Ildiko Lingvay, Priya Sumithran, Ricardo V Cohen, Carel W le Roux

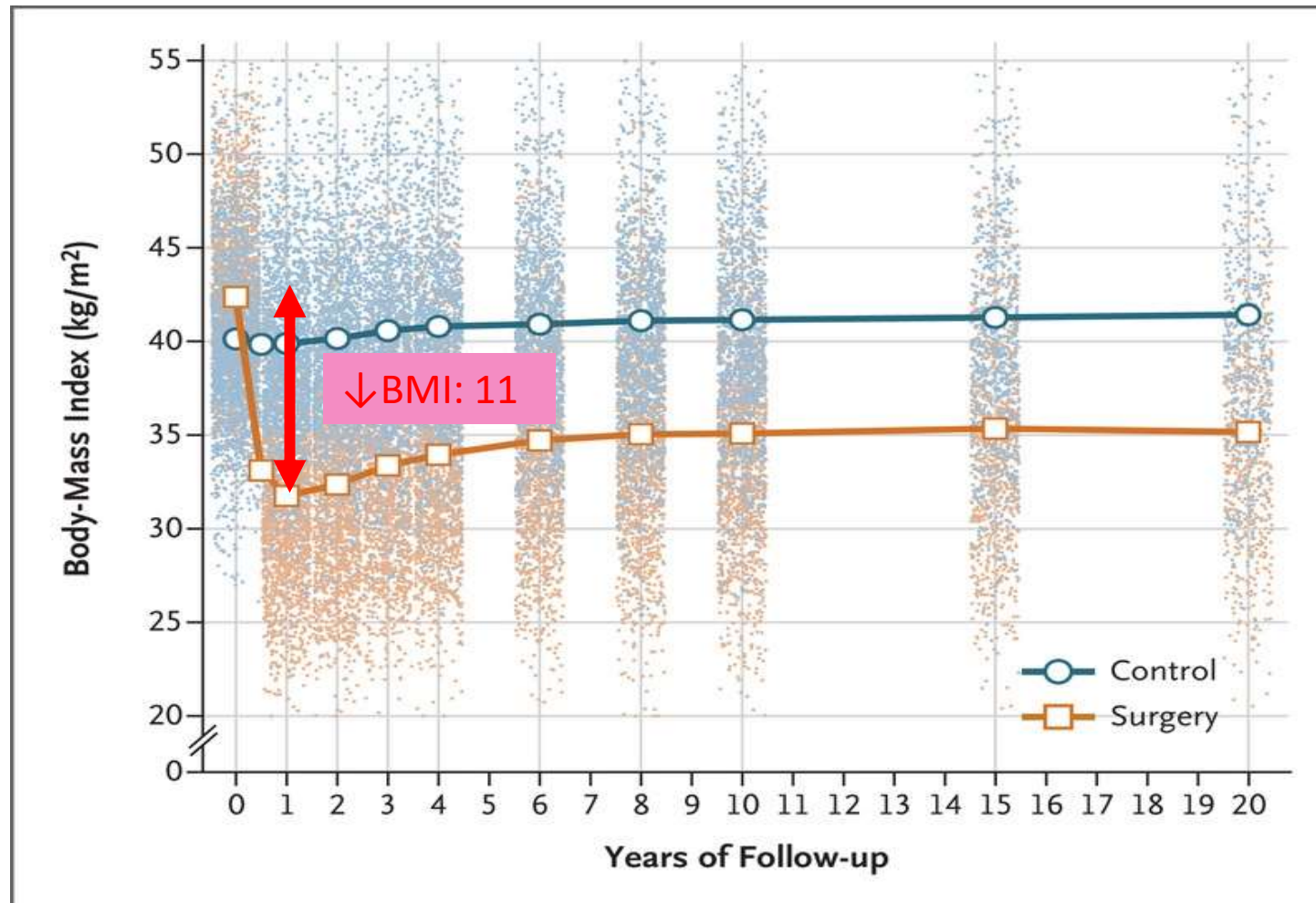


**Weight-centric Approach  
Upstream Intervention**

**Glucocentric approach  
Downstream intervention**

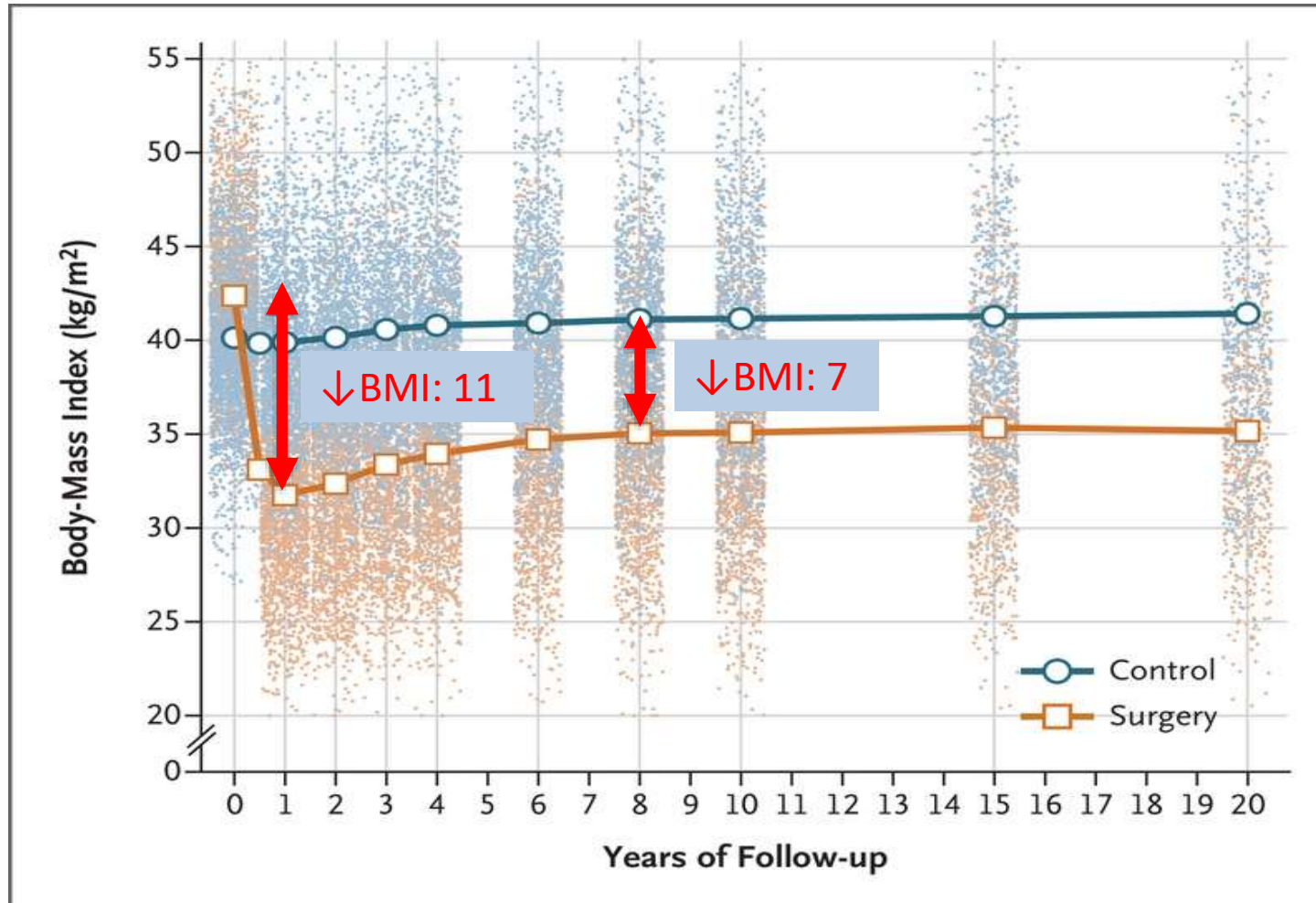
# SOS: Results

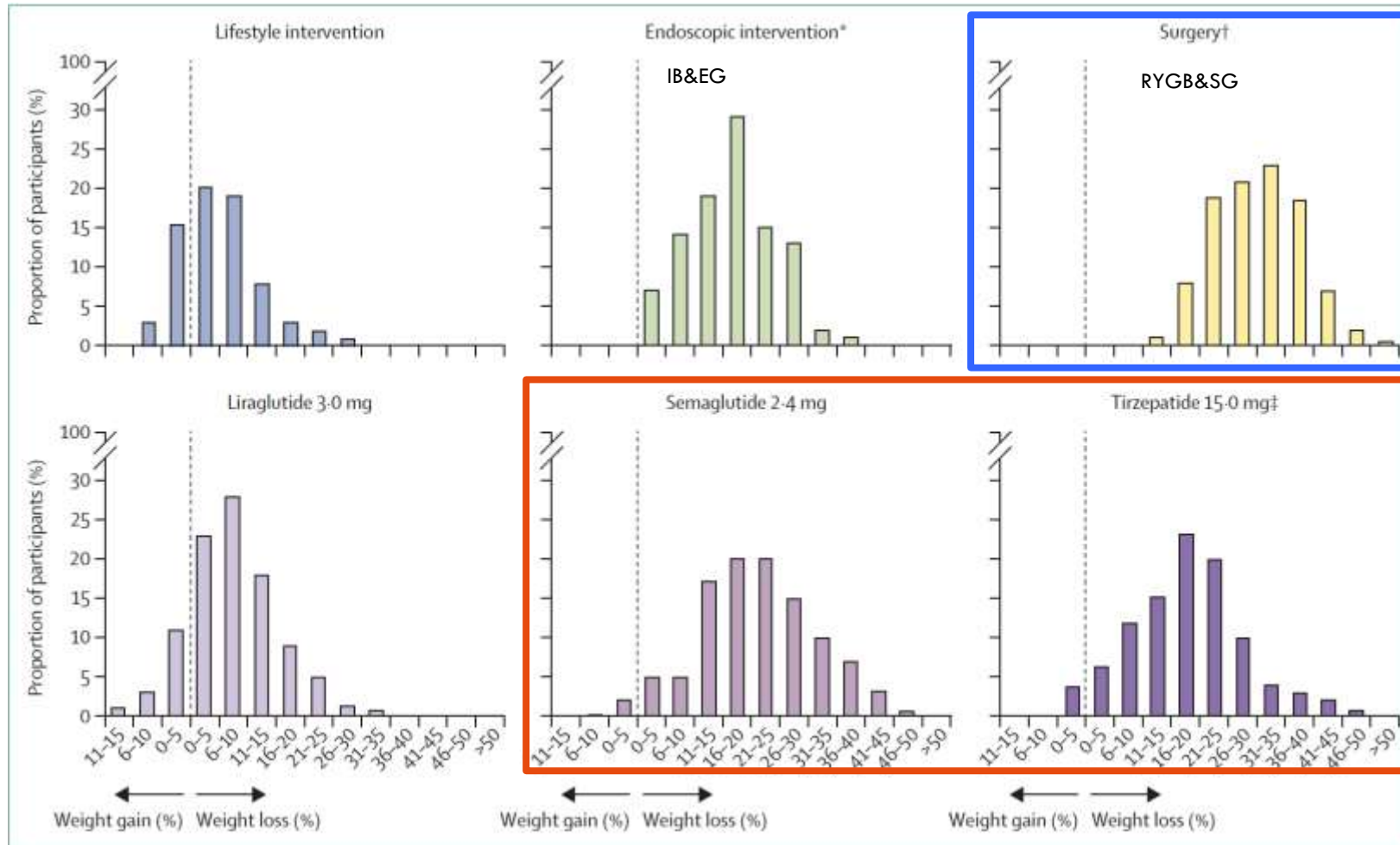
Surgery Group (N=2007) X Control Group (N=2040)



# SOS: Results

Surgery Group (N=2007) X Control Group (N=2040)





The Lancet, Perdomo C, Cohen RV et al, 2023



## Bariatric Surgery: There Is a Room for Improvement to Reduce Mortality in Patients with Type 2 Diabetes

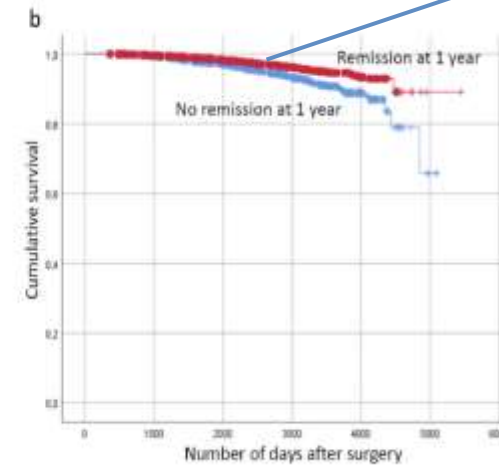
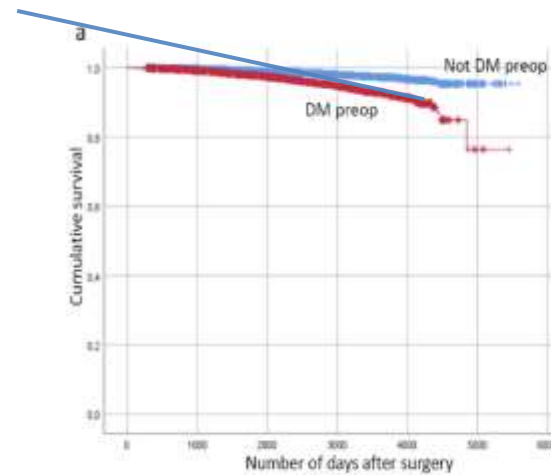
Carel W. le Roux<sup>1</sup> · Johan Ottosson<sup>2,3</sup> · Erik Näslund<sup>2,4</sup> · Ricardo V. Cohen<sup>5</sup> · Erik Stenberg<sup>2,3</sup> · Magnus Sundbom<sup>2,6</sup> · Ingmar Näslund<sup>2,3</sup>

Received: 6 July 2020 / Revised: 13 August 2020 / Accepted: 14 August 2020  
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### SoReg, Scandinavian Obesity Surgery Registry 65,345 pts up tp 10y FU

Operated pts with  
uncontrolled T2D have  
higher mortality @ 1  
year

Adjuvant  
pharmacotherapy





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## **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>a,\*</sup> Tiago Veiga Pereira,<sup>b,c</sup> Cristina Mamédio Aboud,<sup>a</sup> Tarissa Beatrice Zanata Petry,<sup>a</sup> José Luis Lopes Correa,<sup>a</sup> Carlos Aurélio Schiavon,<sup>d</sup> Carlos Eduardo Pompilio,<sup>a</sup> Fernando Nogueira Quirino Pechy,<sup>a</sup> Ana Carolina Calmon da Costa Silva,<sup>a</sup> Livia Porto Cunha da Silveira,<sup>a</sup> Pedro Paulo de Paris Caravatto,<sup>a</sup> Helio Halpern,<sup>a</sup> Frederico de Lima Jacy Monteiro,<sup>b</sup> Bruno da Costa Martins,<sup>a</sup> Rogerio Kuga,<sup>a</sup> Thais Mantovani Sarian Palumbo,<sup>a</sup> Allon N. Friedman,<sup>e</sup> and Carel W. le Roux<sup>f,g</sup>*

The Lancet eClin Med , online Nov 11,2022

# MOMS TRIAL

100 pts



+ BMT

T2D

uACR > 30 mg/g

BMI 30-35 kg/m<sup>2</sup>

Early stage kidney disease

# MOMS trial



- **Best Medical Treatment**

- ✓ Metformin
- ✓ **GLP1 RA**
- ✓ **SGLT-2 i**
- ✓ **Insulin**
- ✓ Glitazones
- ✓ DPP4 i
- ✓ ACEi/ARB
- ✓ Statins
- ✓ Diuretics



- **RYGB + BMT**

- ✓ ACE/ARB
- ✓ Statins
- ✓ Metformin
- ✓ Multivitamins

# MOMS trial

## MOMS trial

### Endpoints

- **Primary endpoint**

- uACR < 30 mg/g

- **Secondary endpoints**

- CKD remission

- Metabolic control ( A1c < 6%; FPG < 100 mg/dl; LDL < 100 mg/dl (< 70 if CV+); HDL > 50; TG < 150 mg/dl; SBP < 130 mmHg ; DBP < 80 mmHg

- Weight-loss

- Use of T2D medications

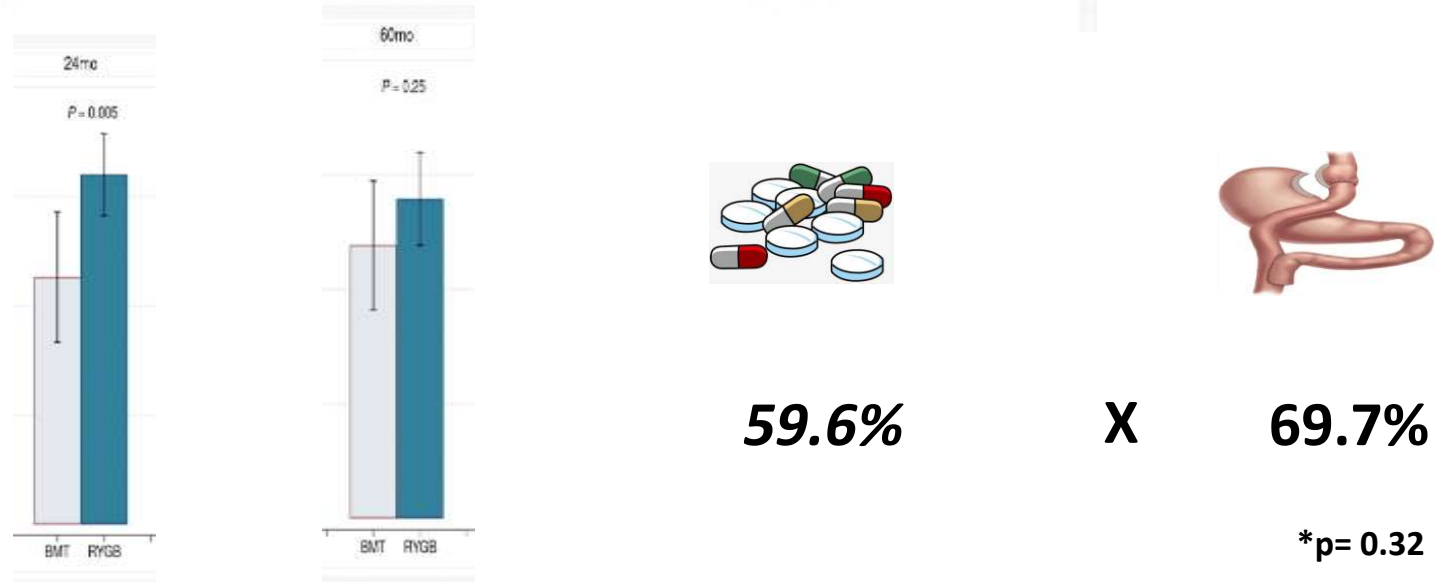
- Neuropathy/Retinopathy

- QOL

# MOMS trial – 5 years outcomes

Dicothomous primary outcome  
uACR <30

Proportion of albuminuria remission (%)



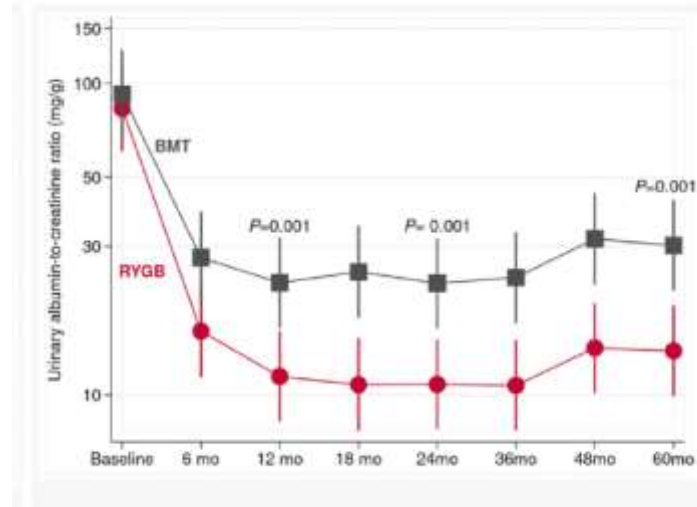
# MOMS trial – 5 years outcomes

Primary outcome – uACR- continuous variable

**B**



+ BMT



***The geometric mean for albuminuria levels  
was 46%  
lower after RYGB (P = 0.001)***

# MOMS trial – 5 years outcomes

## Early stage CKD remission

Remission of albuminuria with eGFR > 60 ml/min



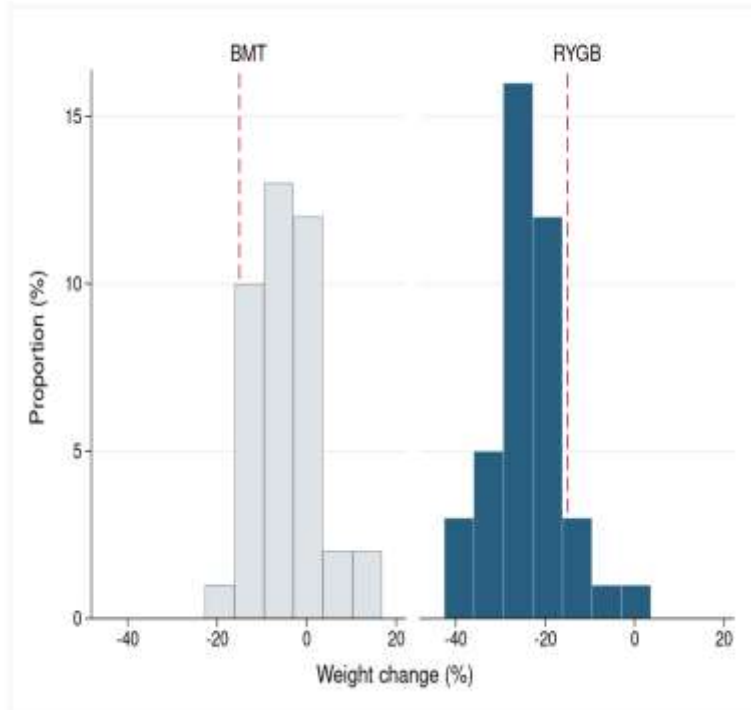
**52.8%**

**X**



**63.1%**

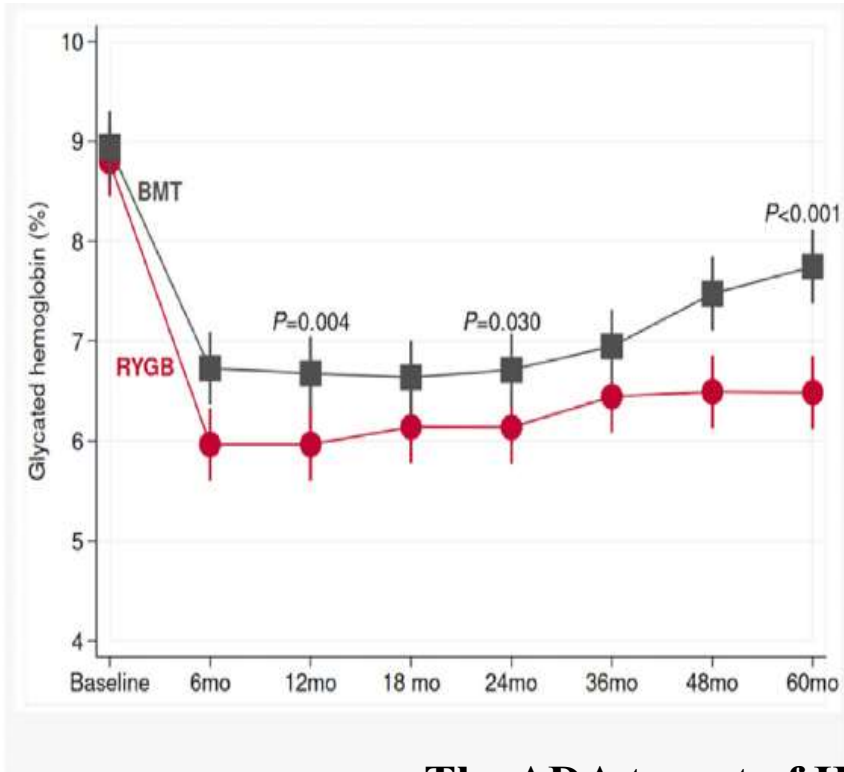
\*p= 0.32



**Only 22.5% BMT achieved >15% TBWL**  
**90% RYGB >15% TBWL**

**NO BMT pt reached normal BMI**  
**53% after RYGB ( $P < 0.001$ )**





# Glycemic control

The ADA target of HbA1c  $\leq$  6.5%

25.4%



x

60.2%

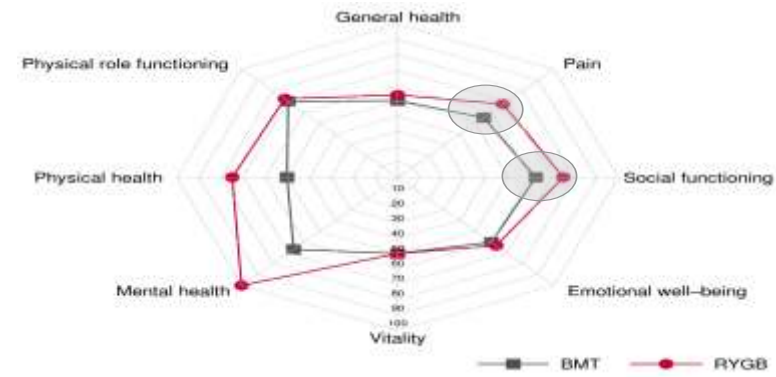


$P < 0.001$

# Quality of Life

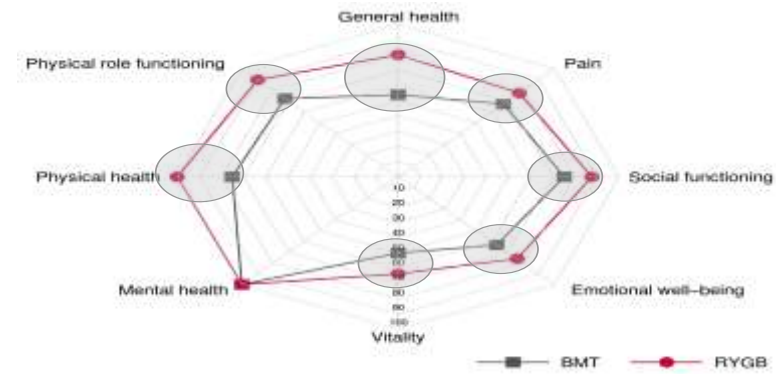
## QOL

A



Baseline

B



60 mo FU

# MOMS trial AEs & Safety

| Safety outcomes        | RYGB (n = 46) | BMT (n = 46) | OR (95% CI)       | P     |
|------------------------|---------------|--------------|-------------------|-------|
| Serious adverse events | 11 (24)       | 7 (15)       | 1.74 (0.55-5.92)  | 0.80  |
| Grade I                | 46 (100)      | 45 (98)      | 1.00 (0.03, +inf) | >0.99 |
| Grade II               | 28 (61)       | 36 (78)      | 0.44 (0.15-1.18)  | 0.11  |
| Grade III              | 5 (11)        | 2 (4.3)      | 2.66 (0.41-29.3)  | 0.43  |
| Grade IV               | 2 (4.3)       | 2 (4.3)      | 1.00 (0.07, 14.4) | >0.99 |

Summary of treatment-emergent adverse events (safety population, 46 participants per treatment group) after 5 years of follow-up. BMT - best medical treatment; RYGB - Roux-en-Y gastric bypass; OR - odds ratio. 95% CI denotes a 95% confidence interval. P values refer to two-sided tests based on exact logistic regression models. Grades I to IV refers to Clavien-Dindo for grading adverse events. +inf denotes that the upper bound cannot be computed (+infinity).

Table 3: Safety outcomes (safety population, n = 92).

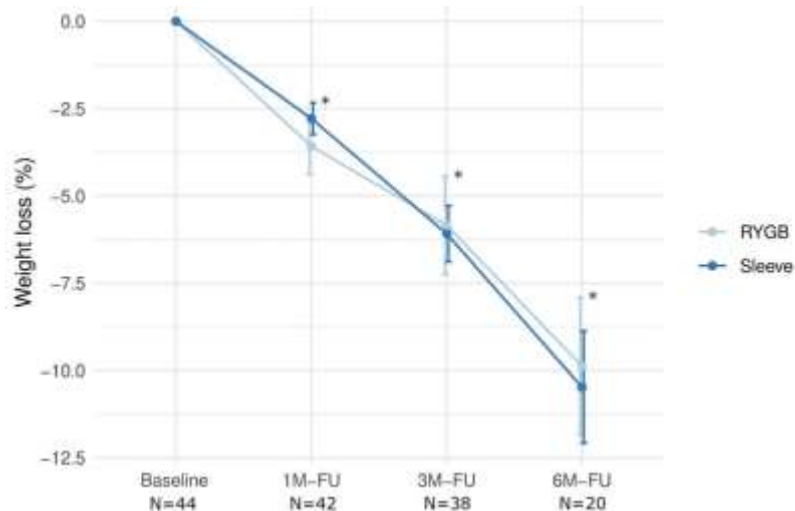
- ✓ 1 surgical complication managed by endoscopy
- ✓ No serious hypoglycemia
- ✓ No malnutrition
- ✓ No excessive weight-loss



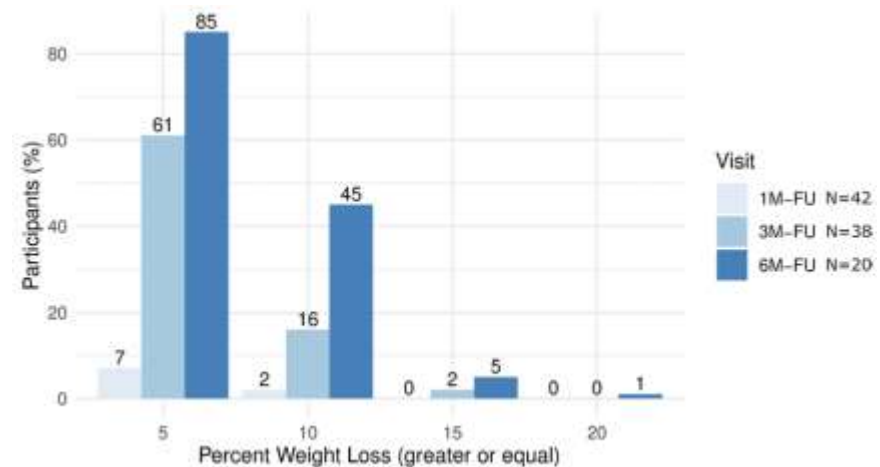
# The Potential of Semaglutide Once-Weekly in Patients Without Type 2 Diabetes with Weight Regain or Insufficient Weight Loss After Bariatric Surgery—a Retrospective Analysis

Received: 24 April 2022 / Revised: 10 July 2022 / Accepted: 14 July 2022

Anne Lautenbach<sup>1</sup>  · Marie Wernecke<sup>1</sup> · Tobias B. Huber<sup>1</sup> · Fabian Stoll<sup>1</sup> · Jonas Wagner<sup>2</sup> · Sebastian M. Meyhöfer<sup>3,4</sup> · Svenja Meyhöfer<sup>3,4,5</sup> · Jens Aberle<sup>1</sup>



RYGB (N = 15)  
SG (N = 29)  
Total (N = 44)



# Adjunctive liraglutide treatment in patients with persistent or recurrent type 2 diabetes after metabolic surgery (GRAVITAS): a randomised, double-blind, placebo-controlled trial

Alexander Dimitri Miras\*, Belén Pérez-Pevida\*, Madhawi Aldhwayan, Anna Kamocka, Emma Rose McGlone, Werd Al-Najim, Harvinder Chahal, Rachel L Batterham, Barbara McGowan, Omar Khan, Veronica Greener, Ahmed R Ahmed, Aviva Petrie, Samantha Scholtz, Stephen R Bloom, Tricia M Tan

80 pts RYGB or SG with persistent or recurrent T2D

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graph TD; A[80 pts RYGB or SG with persistent or recurrent T2D] --> B[Liraglutide (n=53) or placebo (n=27)]; B --> C[At least 1 year after surgery]; C --> D[Follow-up: 24 weeks];
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Liraglutide (n=53) or placebo (n=27)

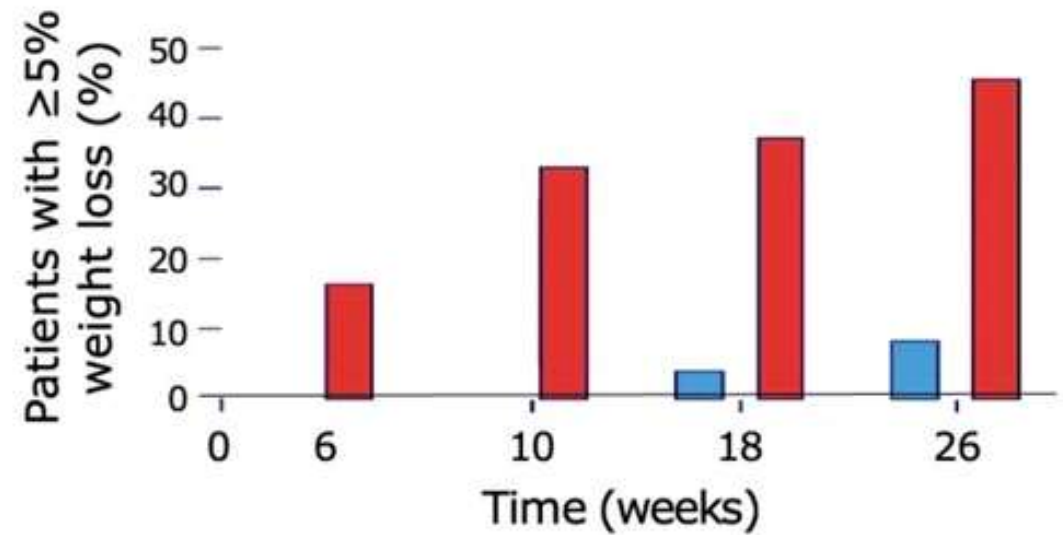
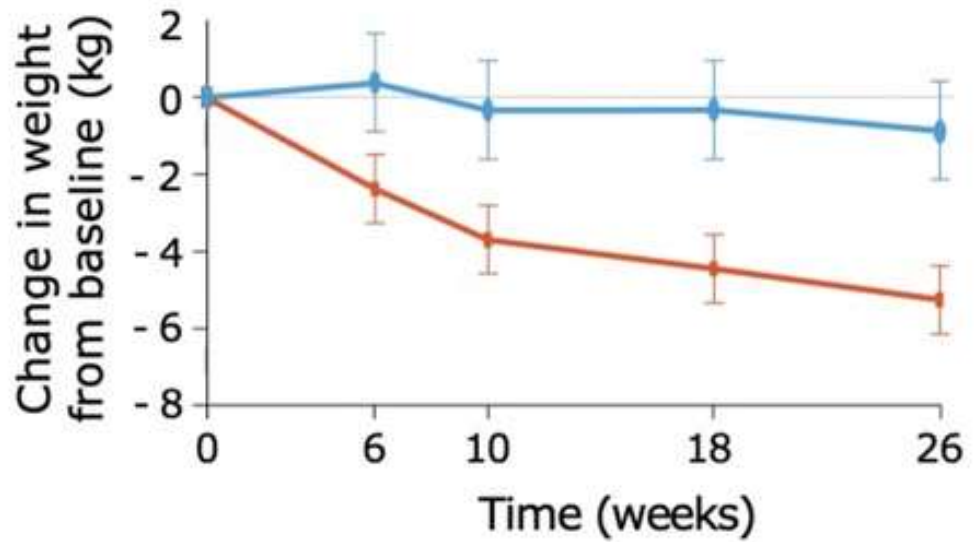
At least 1 year after surgery

Follow-up: 24 weeks

# Postoperative pharmacotherapy augments surgical weight loss

## GRAVITAS Study

Liraglutide after Gastric Bypass in T2D



- Placebo
- Liraglutide

JAMA Surgery | **Original Investigation**

# Safety and Efficacy of Liraglutide, 3.0 mg, Once Daily vs Placebo in Patients With Poor Weight Loss Following Metabolic Surgery

## The BARI-OPTIMISE Randomized Clinical Trial

Aug 2023

Jessica Mok, BMBS, MPhil; Mariam O. Adeleke, PhD; Adrian Brown, PhD; Cormac G. Magee, MBBChir, MA; Chloe Firman, MRes; Christwishes Makahamadze, MRes; Friedrich C. Jassil, PhD; Parastou Marvasti, PhD; Alisia Carnemolla, PhD; Kalpana Devalia, MBBS, MS; Naim Fakih, MD; Mohamed Elkalaawy, MRCSEd, MS, MD; Andrea Pucci, MD, PhD; Andrew Jenkinson, MBBS, MS; Marco Adamo, MD; Rumana Z. Omar, PhD; Rachel L. Batterham, MBBS, PhD; Janine Makaronidis, MBChB, PhD

**POPULATION**

**18 Men,**  
**52 Women**



Adults  $\geq 1$  y after metabolic surgery with poor weight loss ( $\leq 20\%$ ) and a suboptimal GLP-1 response

**Mean age, 47.6 y**

**INTERVENTION**

**70** Patients randomized,  
**57** Analyzed



**31 Liraglutide, 3.0 mg**  
Self-administration once daily of a subcutaneous injection of liraglutide, 3.0 mg, for 24 wk



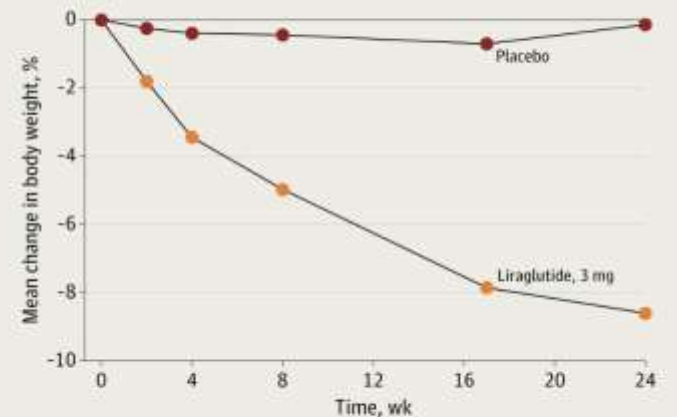
**26 Placebo**  
Self-administration once daily of placebo saline solution for the same period

**PRIMARY OUTCOME**

Change in percentage body weight from baseline to end of 24-wk study period

**FINDINGS**

Liraglutide, 3.0 mg once daily, resulted in a significantly greater reduction in body weight from baseline to week 24 compared with placebo

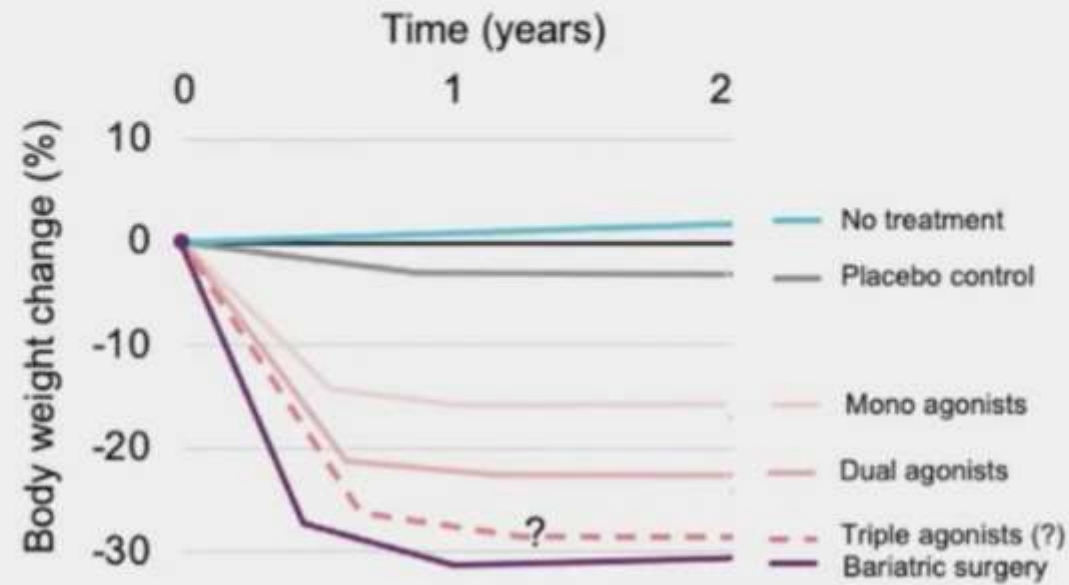


**Mean difference: -8.0%; 95% CI, -10.4 to -5.7;  $P < .001$**

# Controlling Obesity with Multi Receptor Drugs



## Closing the Gap



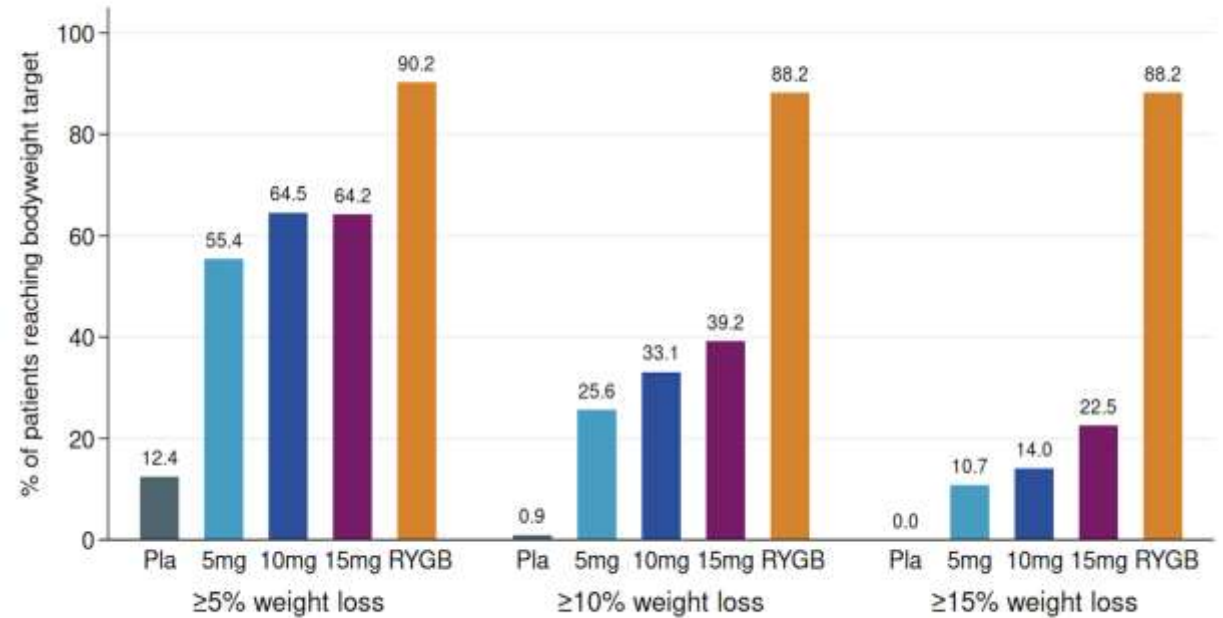
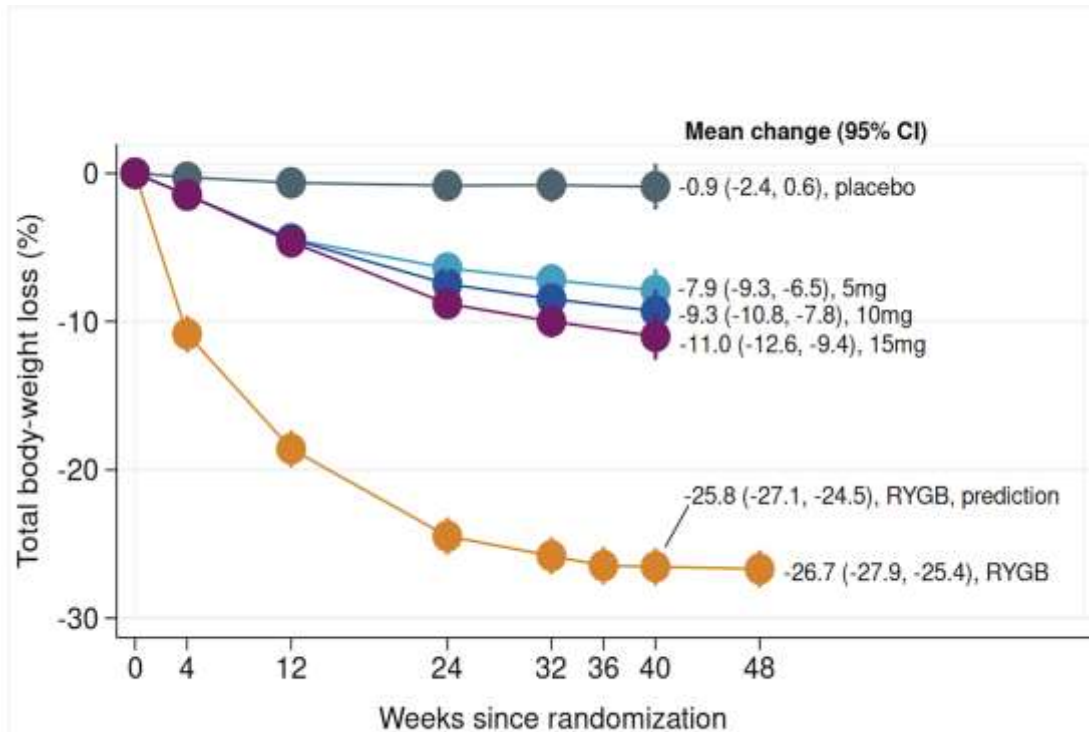


# MOMS

# X

# SURPASS 1

(Tirzepatide in people with obesity and T2D)

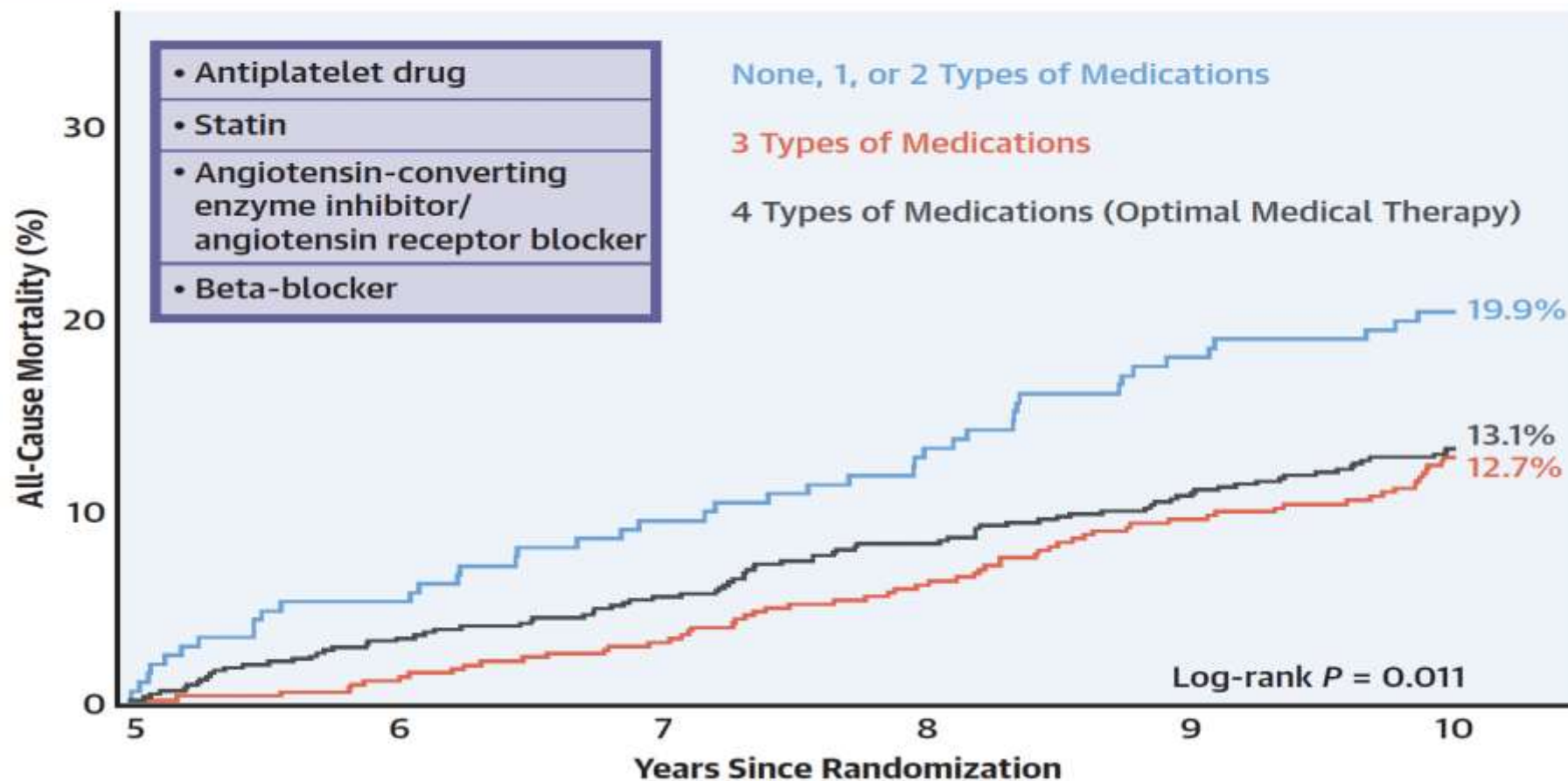


## Impact of Optimal Medical Therapy on 10-Year Mortality After Coronary Revascularization



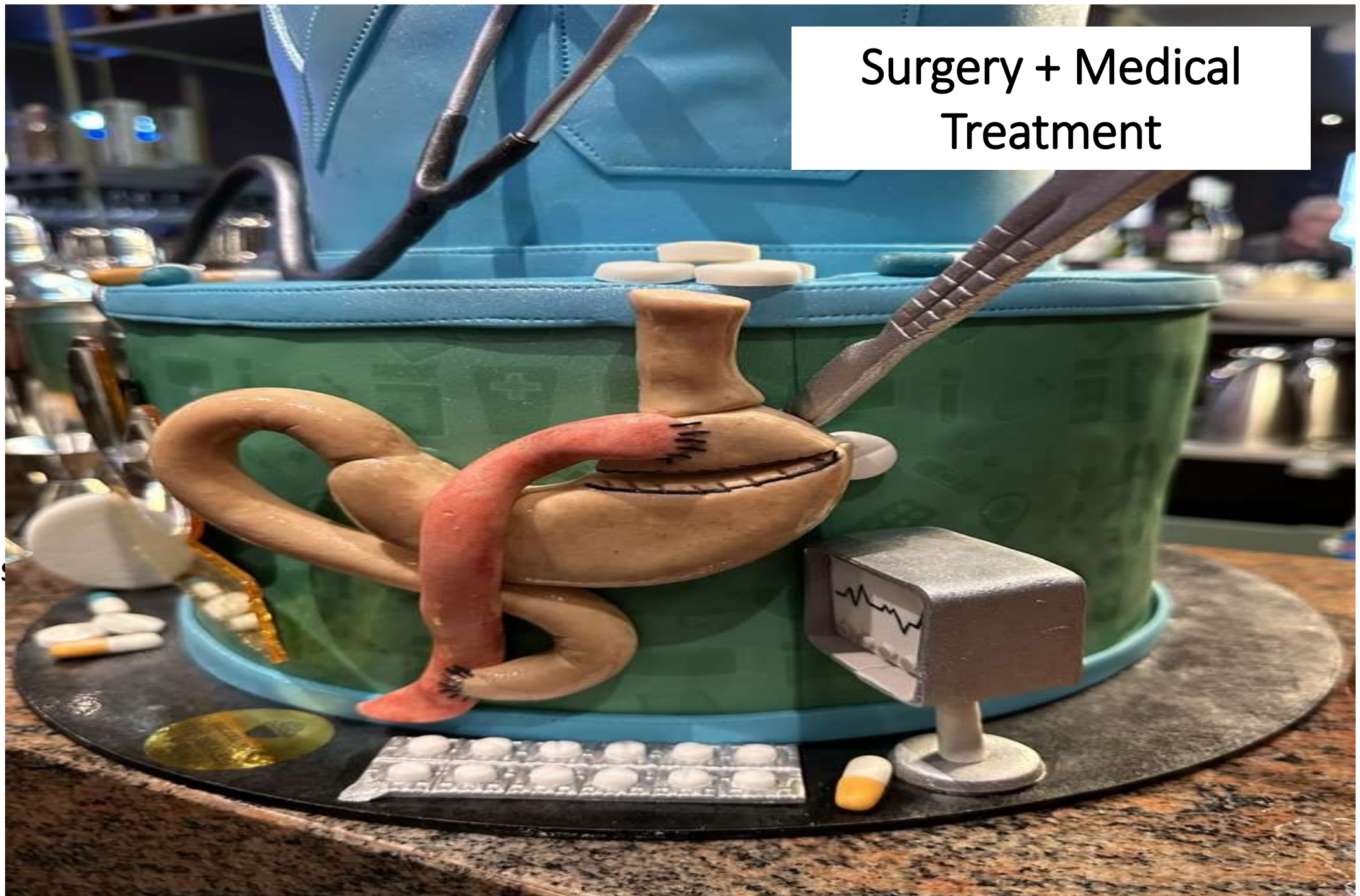
Hideyuki Kawashima, MD,<sup>a,b</sup> Patrick W. Serruys, MD, PhD,<sup>a,c</sup> Masafumi Ono, MD,<sup>a,b</sup> Hironori Hara, MD,<sup>a,b</sup> Neil O'Leary, PhD,<sup>a</sup> Michael J. Mack, MD,<sup>b</sup> David R. Holmes, MD,<sup>c</sup> Marie-Claude Morice, MD,<sup>f</sup> Stuart J. Head, MD, PhD,<sup>g</sup> Arie Pieter Kappetein, MD, PhD,<sup>h</sup> Daniel J.F.M. Thuijs, MD, PhD,<sup>h</sup> Milan Milojevic, MD, PhD,<sup>i,j</sup> Thilo Noack, MD,<sup>f</sup> Friedrich-Wilhelm Mohr, MD, PhD,<sup>f</sup> Piroze M. Davierwala, MD,<sup>f</sup> Faisal Sharif, MD, PhD,<sup>g</sup> John W. McEvoy, MB, BCH, MHS,<sup>g</sup> Yoshinobu Onuma, MD, PhD,<sup>g</sup> on behalf of the SYNTAX Extended Survival Investigators

### CENTRAL ILLUSTRATION Kaplan-Meier Curves of All-Cause Mortality From 5 to 10 Years



Patient number at risk

# Surgery + Medical Treatment



[ricardo.cohen@haoc.com.br](mailto:ricardo.cohen@haoc.com.br)

@rvcohen(twitter)

Thank you



Hospital Alemão  
OSWALDO CRUZ