

Medications vs Metabolic Surgery and Health Gain: What's the Evidence?

Ali Aminian, MD, FACS, FASMBS

Professor of Surgery

Director, Bariatric and Metabolic Institute



Cleveland Clinic
Bariatric and Metabolic Institute



Disclosures

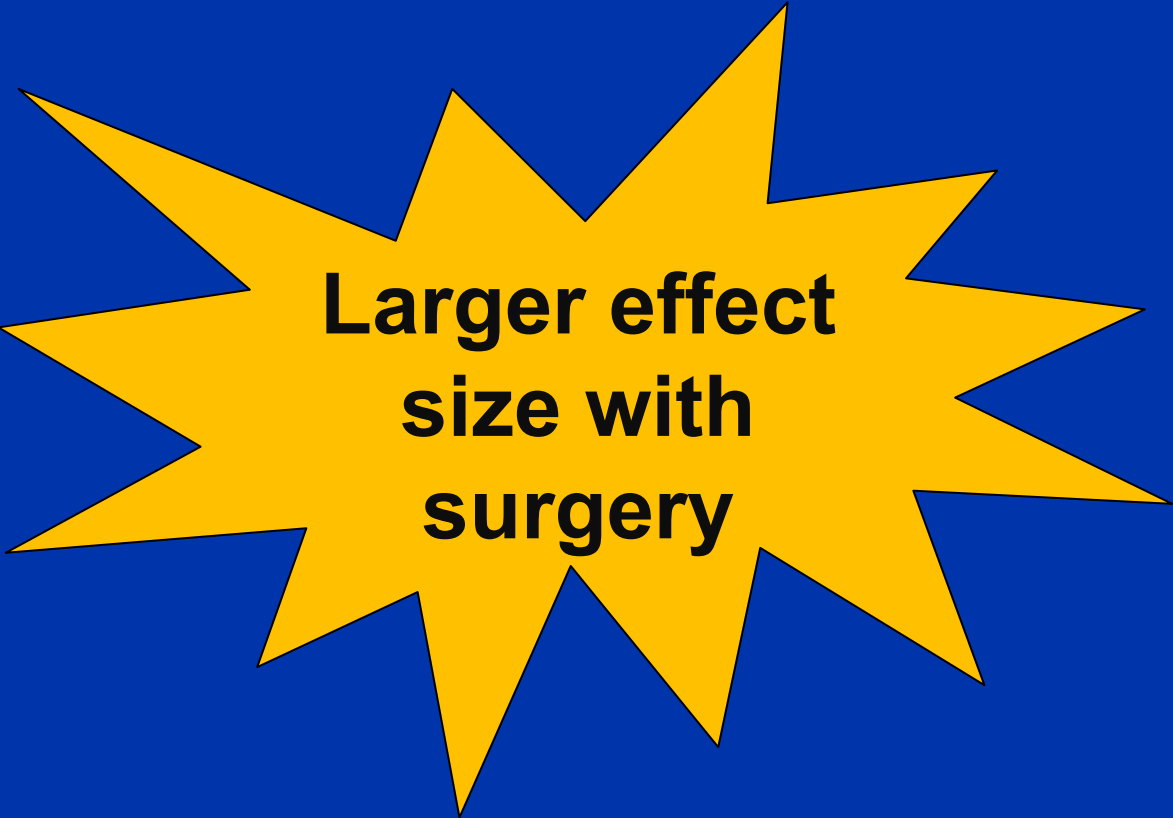
- Amgen (research grant)
- Eli Lilly (member of steering committee of a clinical trial)
- Ethicon (research grant, consulting)
- iRhythm (research grant)
- Medtronic (research grant, consulting)
- NIH (research grant)

Please, Don't Forget:

- **ALL** health benefits of GLP-1RAs have already been shown with metabolic surgery in the past 2 decades:
 - Diabetes
 - CV benefits
 - Renoprotective
 - MASH
 - OSA
 - Osteoarthritis
 - Survival benefits
 - QoL improvement

Please, Don't Forget:

- **ALL** health benefits of GLP-1RAs have already been shown with metabolic surgery in the past 2 decades:
 - Diabetes
 - CV benefits
 - Renoprotective
 - MASH
 - OSA
 - Osteoarthritis
 - Survival benefits
 - QoL improvement



**Larger effect
size with
surgery**

Take Home Message

Losing large amount of weight (by **AOM**, **metabolic surgery**, **etc**) can prevent and/or reverse health consequences of obesity.

Macrovascular and microvascular outcomes of metabolic surgery versus GLP-1 receptor agonists in patients with diabetes and obesity

M6

Macrovascular &
Microvascular
Morbidity &
Mortality after
Metabolic surgery vs
Medicines

Macrovascular and microvascular outcomes of metabolic surgery versus GLP-1 receptor agonists in patients with diabetes and obesity

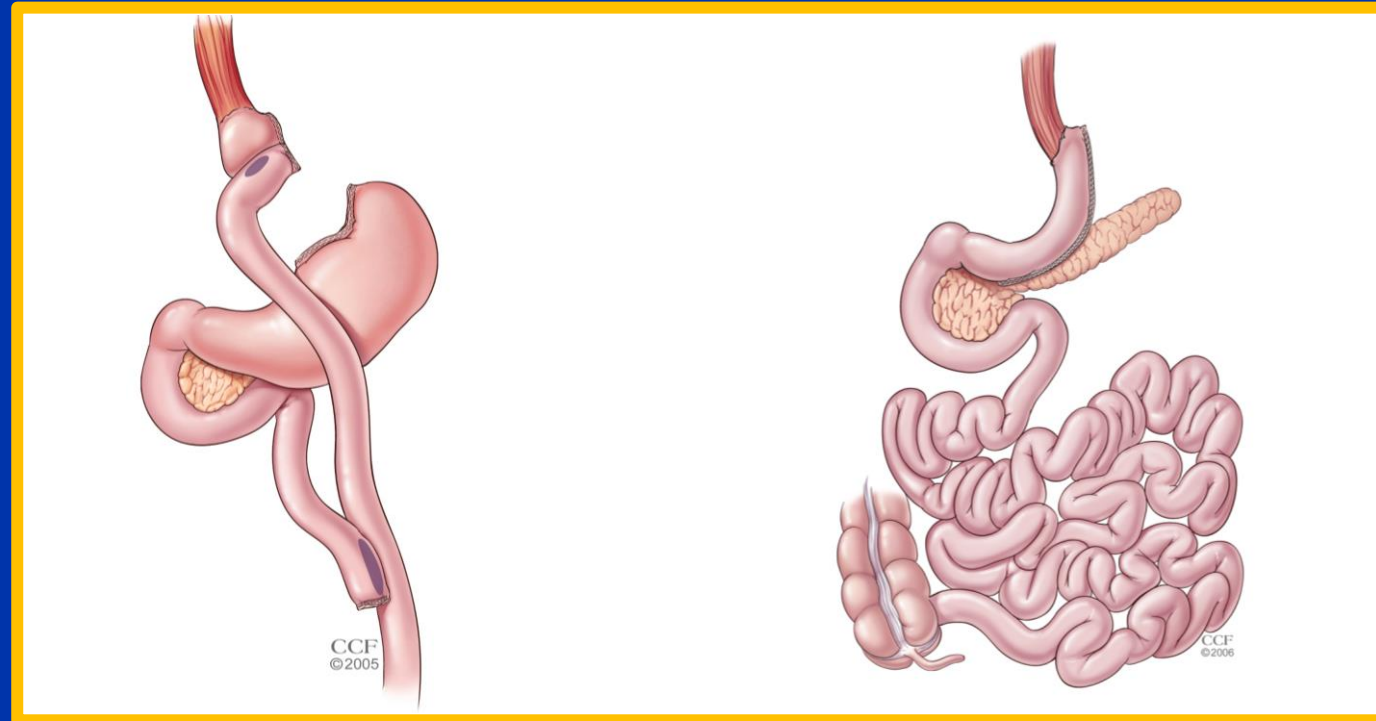
M6

Macrovascular & Microvascular Morbidity & Mortality after Metabolic surgery vs Medicines

- 3932 Cleveland Clinic patients with BMI ≥ 30 and T2DM
- Metabolic surgery (n=1657) vs GLP1-RA (n=2275)
from 2010 to 2017. Follow-up ended in Dec 2022.
- GLP-1RAs during follow-up:

Liraglutide	(65.4%)
Dulaglutide	(48.6%)
Exenatide	(32.5%)
Semaglutide	(26.5%)
Tirzepatide	(4.4%)
Lixisenatide	(2.9%)

Metabolic Surgical Procedures (N=1657)



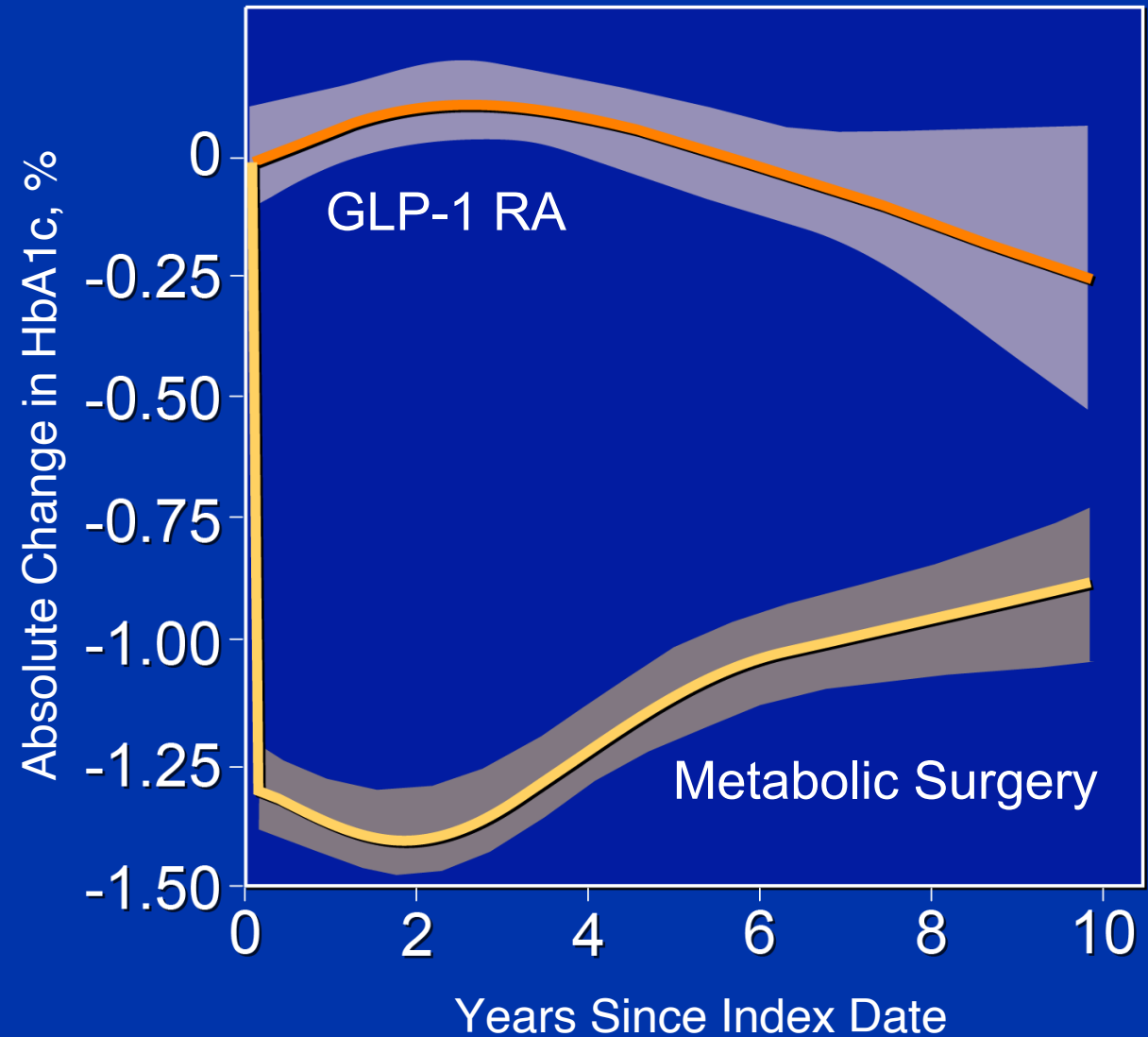
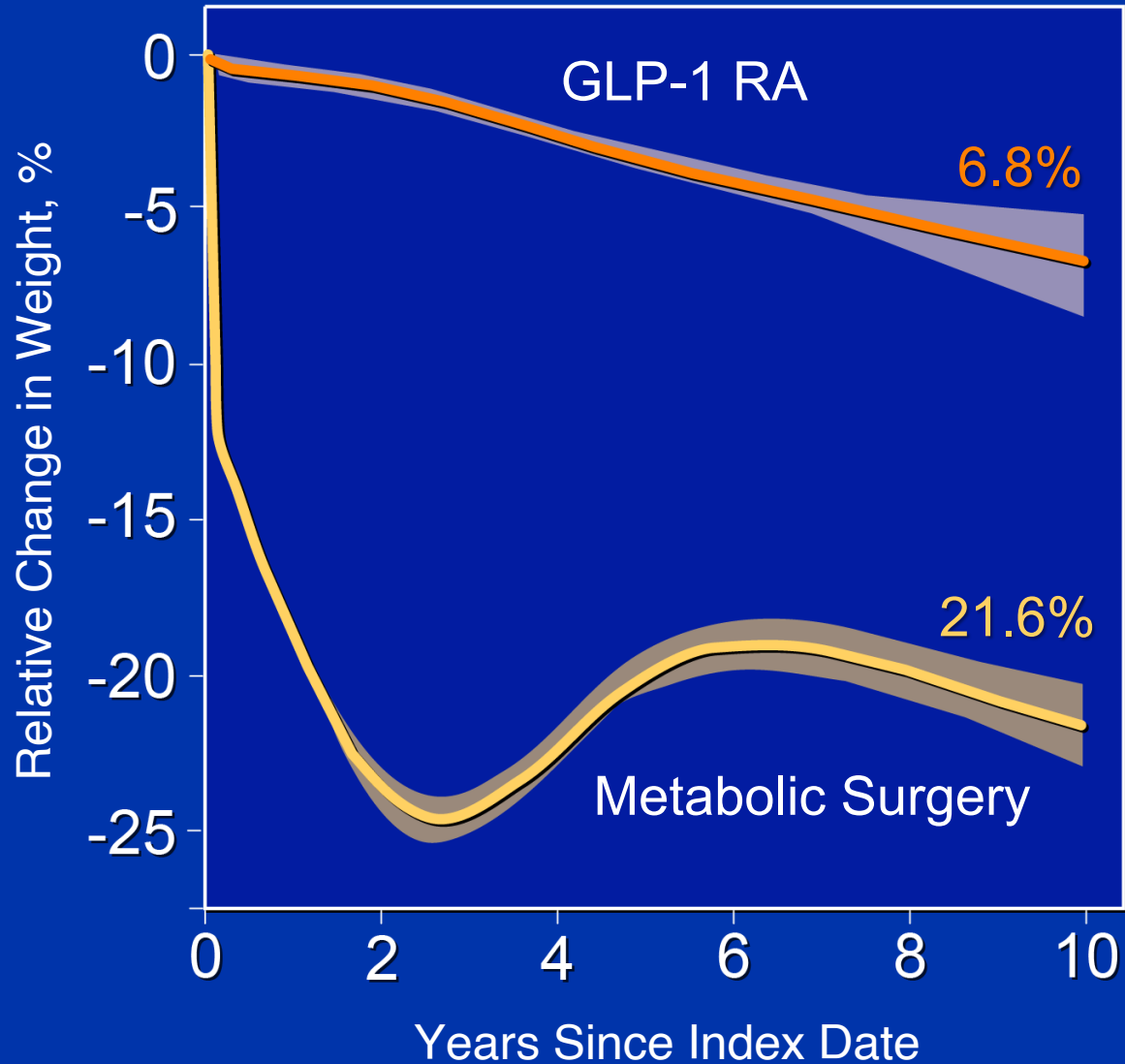
Gastric Bypass

N=1015 (61%)

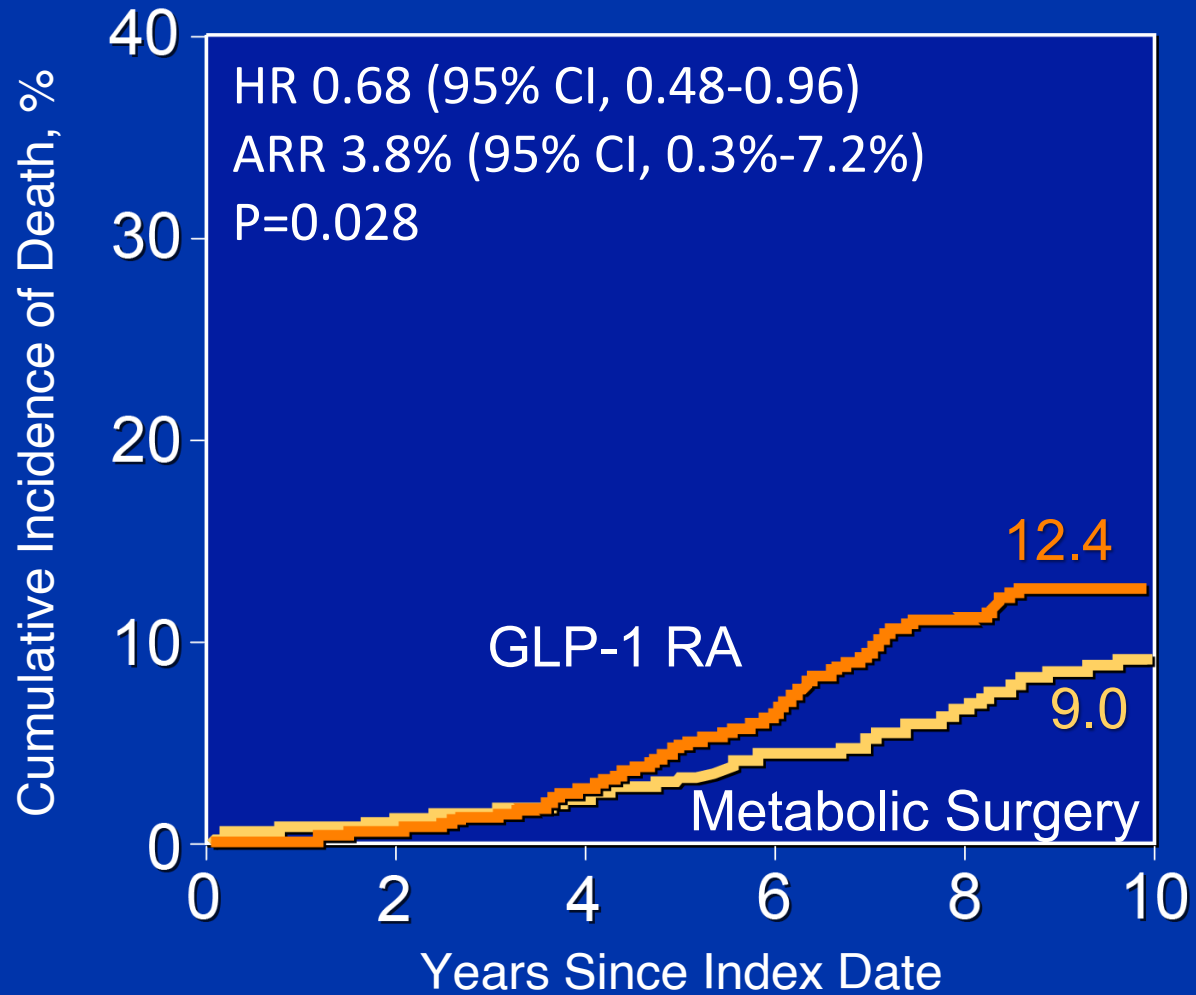
Sleeve Gastrectomy

N=642 (39%)

M6: Change in Weight and Hemoglobin A1c



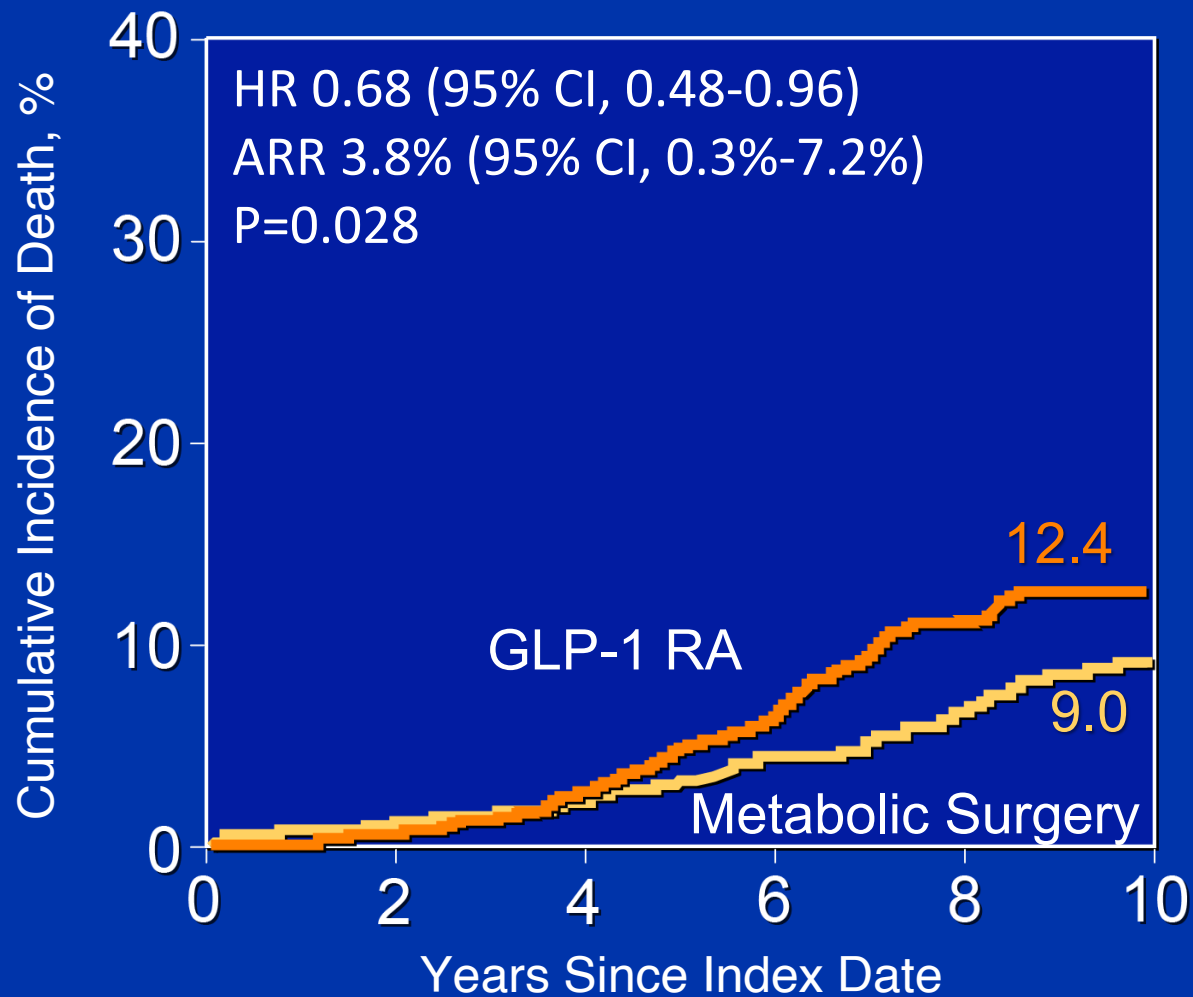
All-Cause Mortality



No. at Risk

2275	2114	1885	1025	249	58
1657	1341	1201	913	605	287

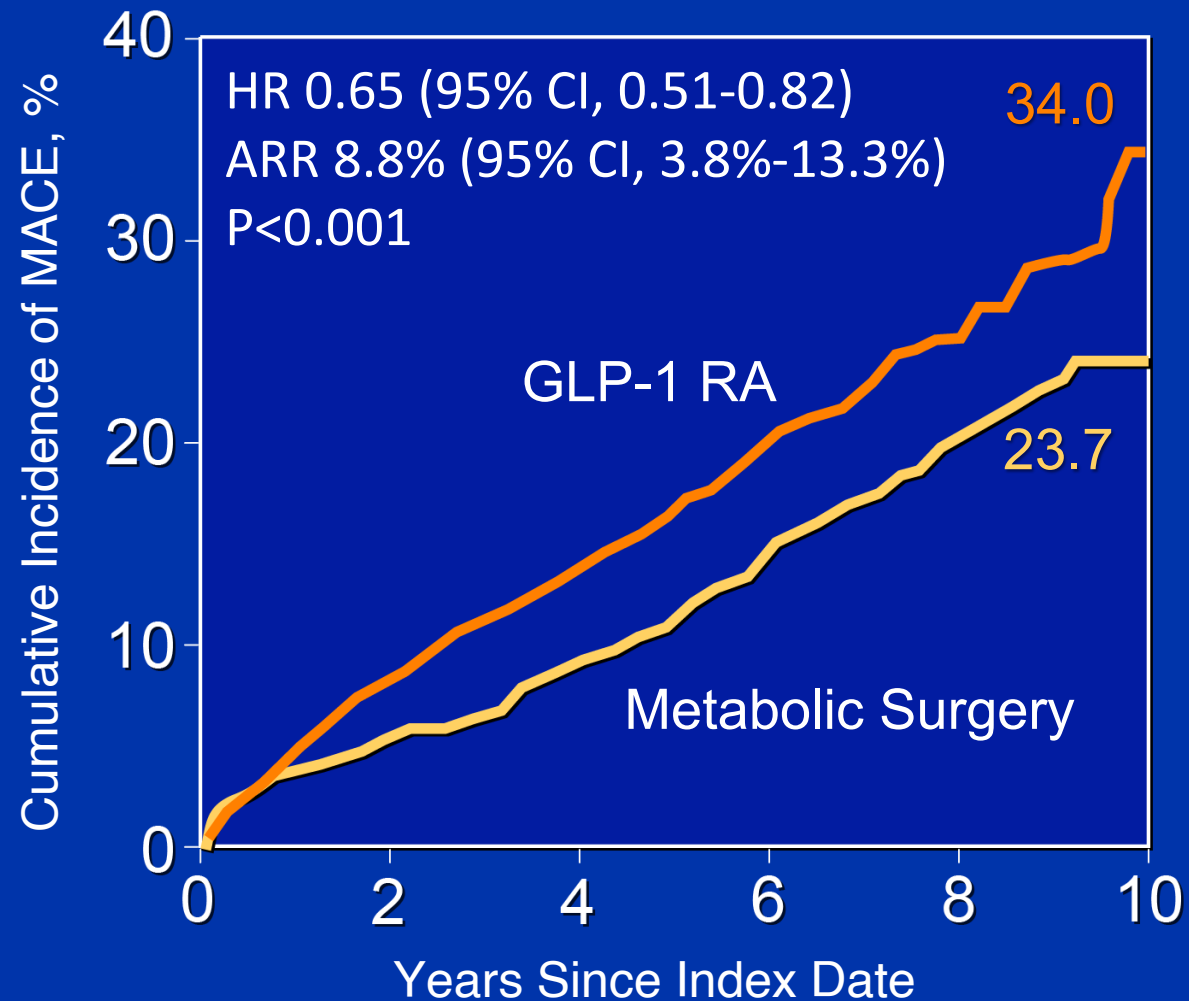
All-Cause Mortality



No. at Risk

2275	2114	1885	1025	249	58
1657	1341	1201	913	605	287

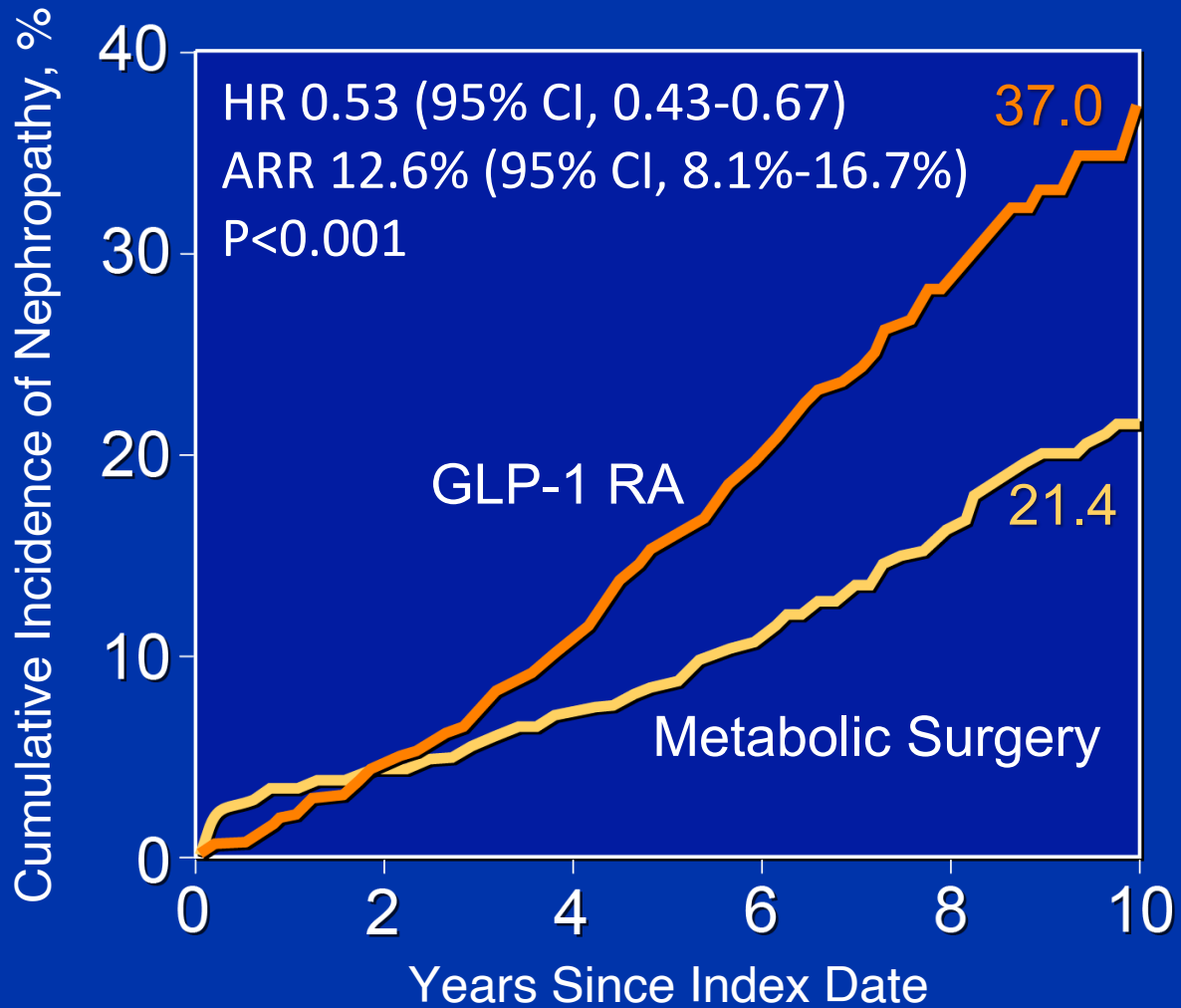
MACE-4



No. at Risk

2275	1935	1622	822	186	45
1657	1266	1091	776	475	221

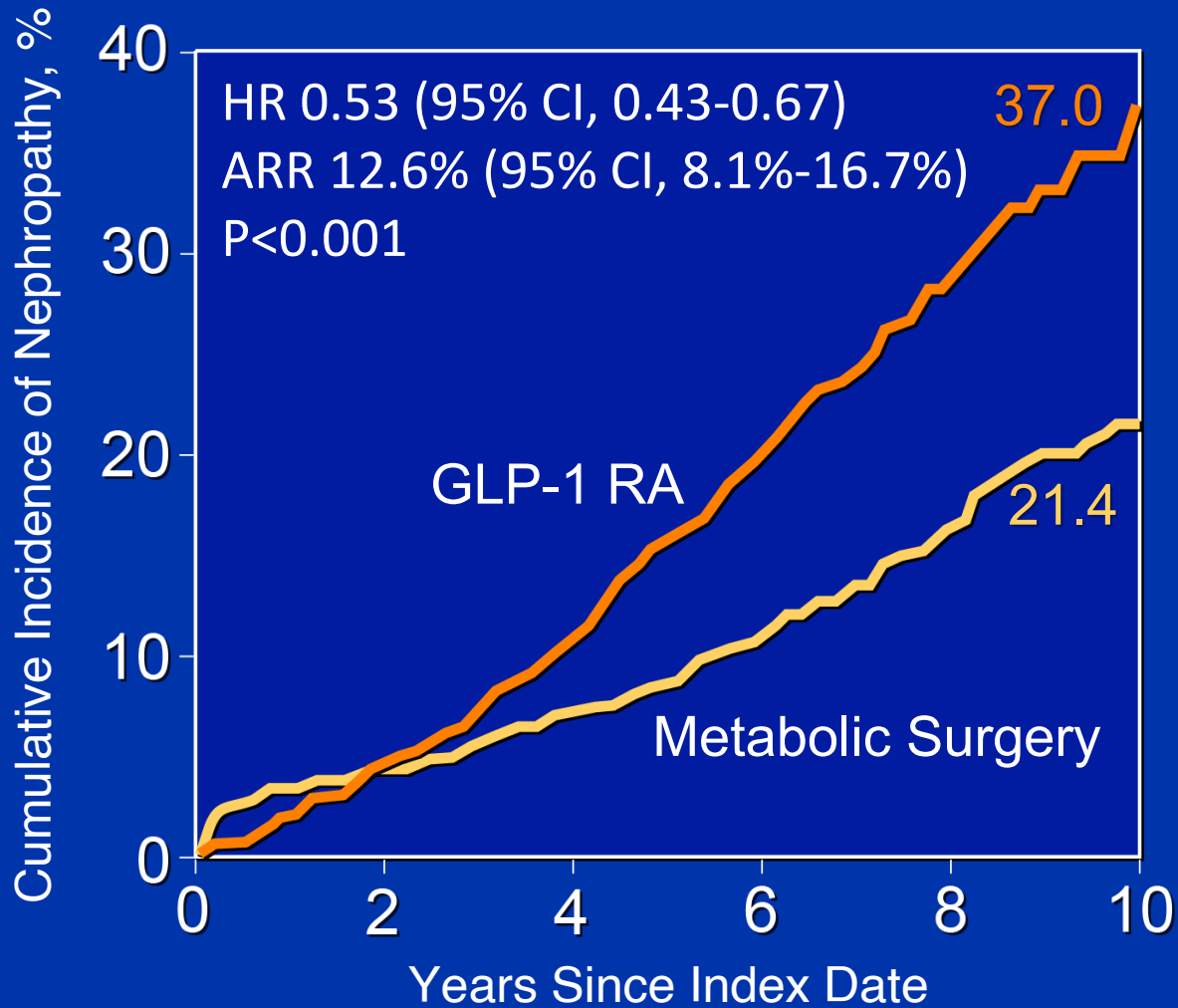
Nephropathy



No. at Risk

2275	2010	1675	845	196	49
1657	1281	1117	817	506	225

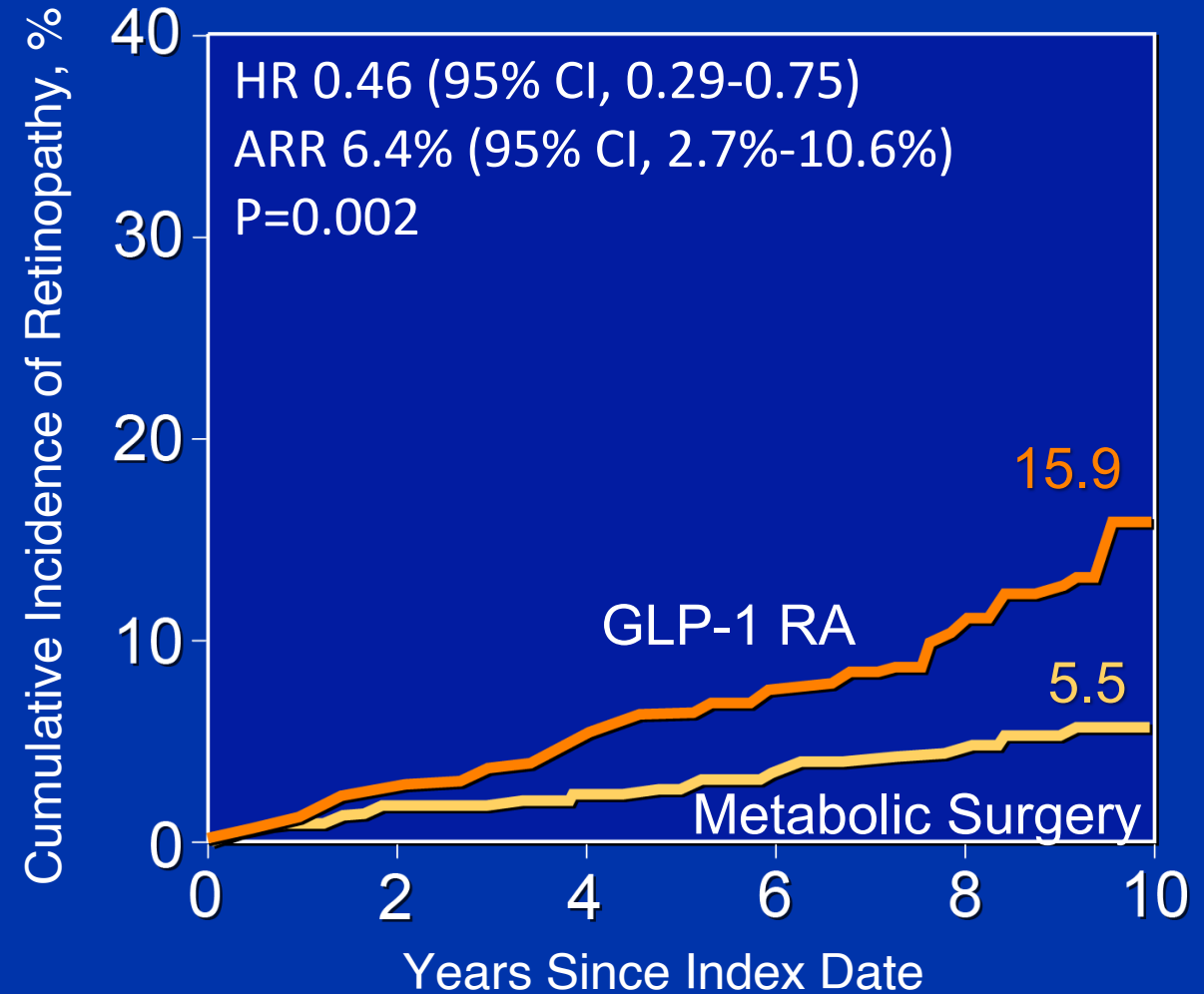
Nephropathy



No. at Risk

2275	2010	1675	845	196	49
1657	1281	1117	817	506	225

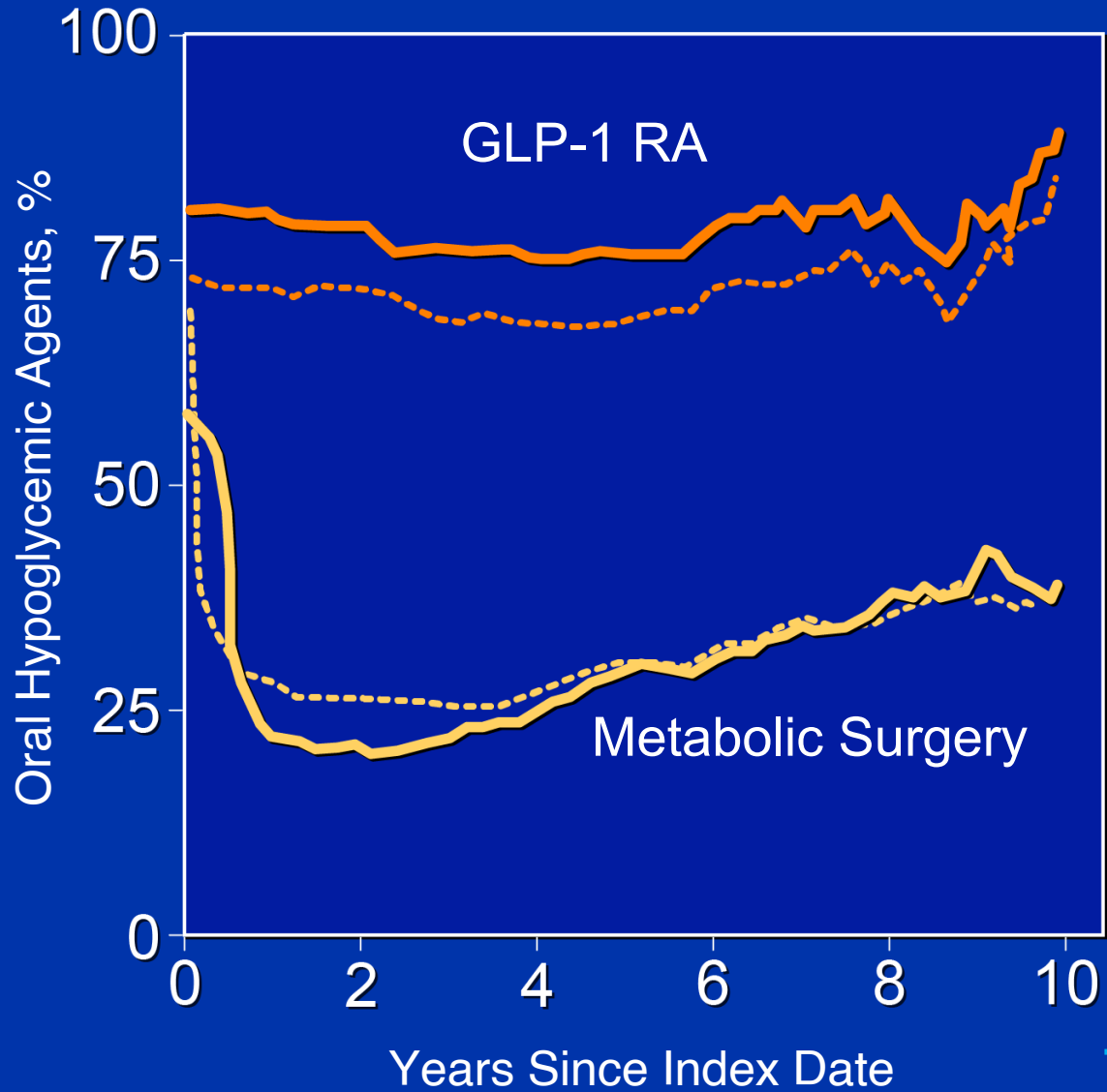
Retinopathy



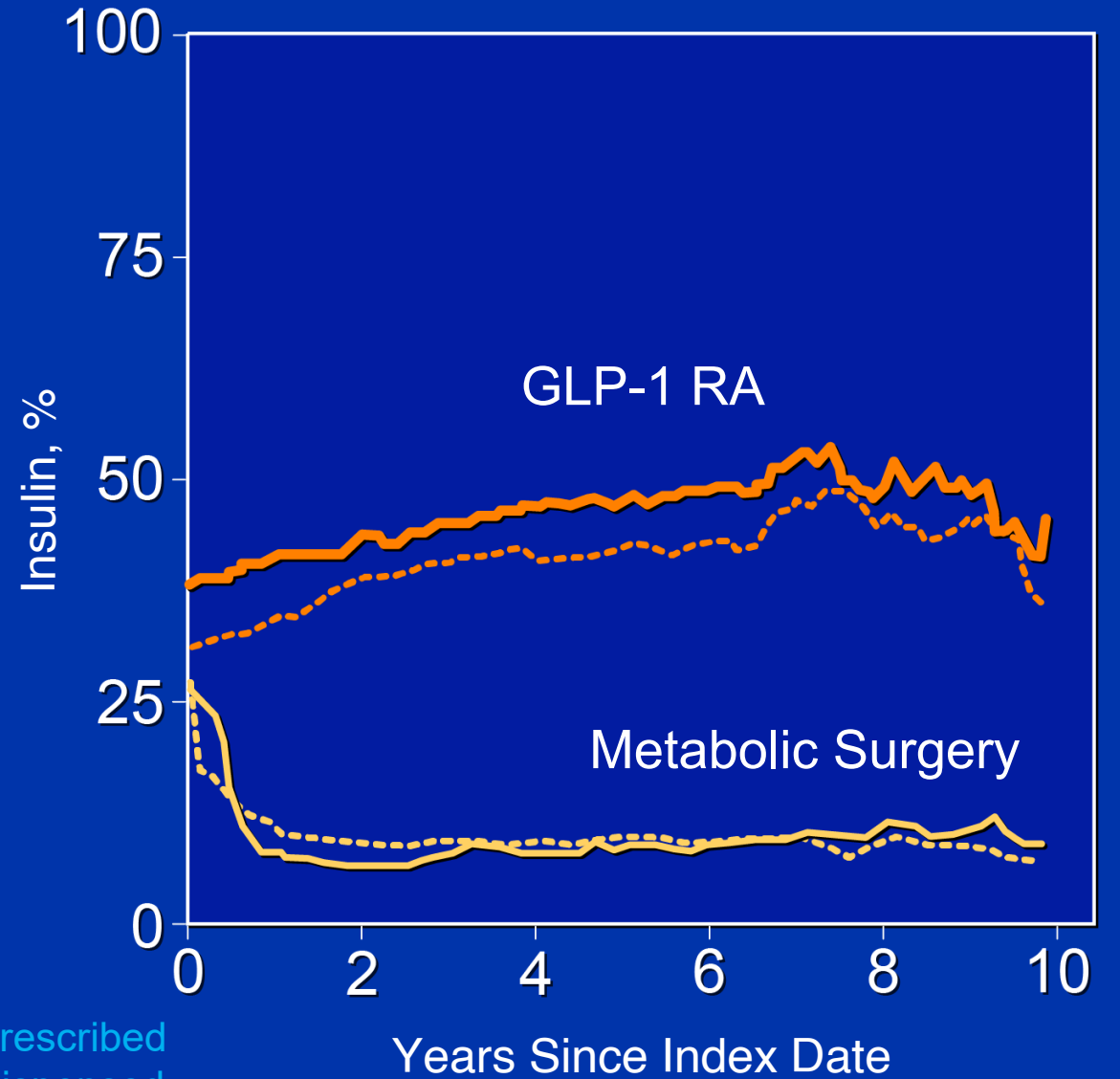
No. at Risk

2275	2046	1765	956	218	53
1657	1312	1167	879	569	275

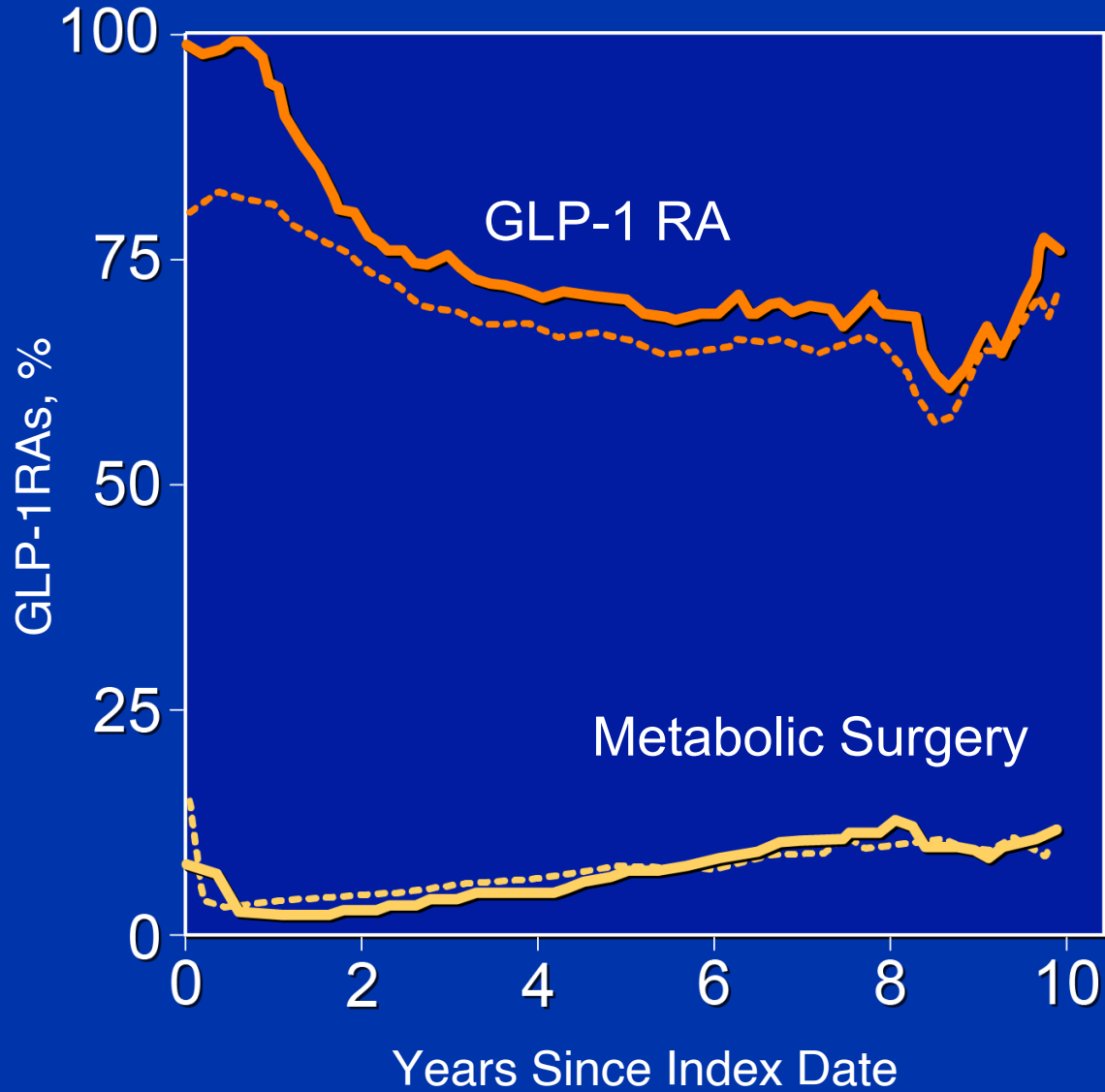
Oral Hypoglycemic Agents



Insulin



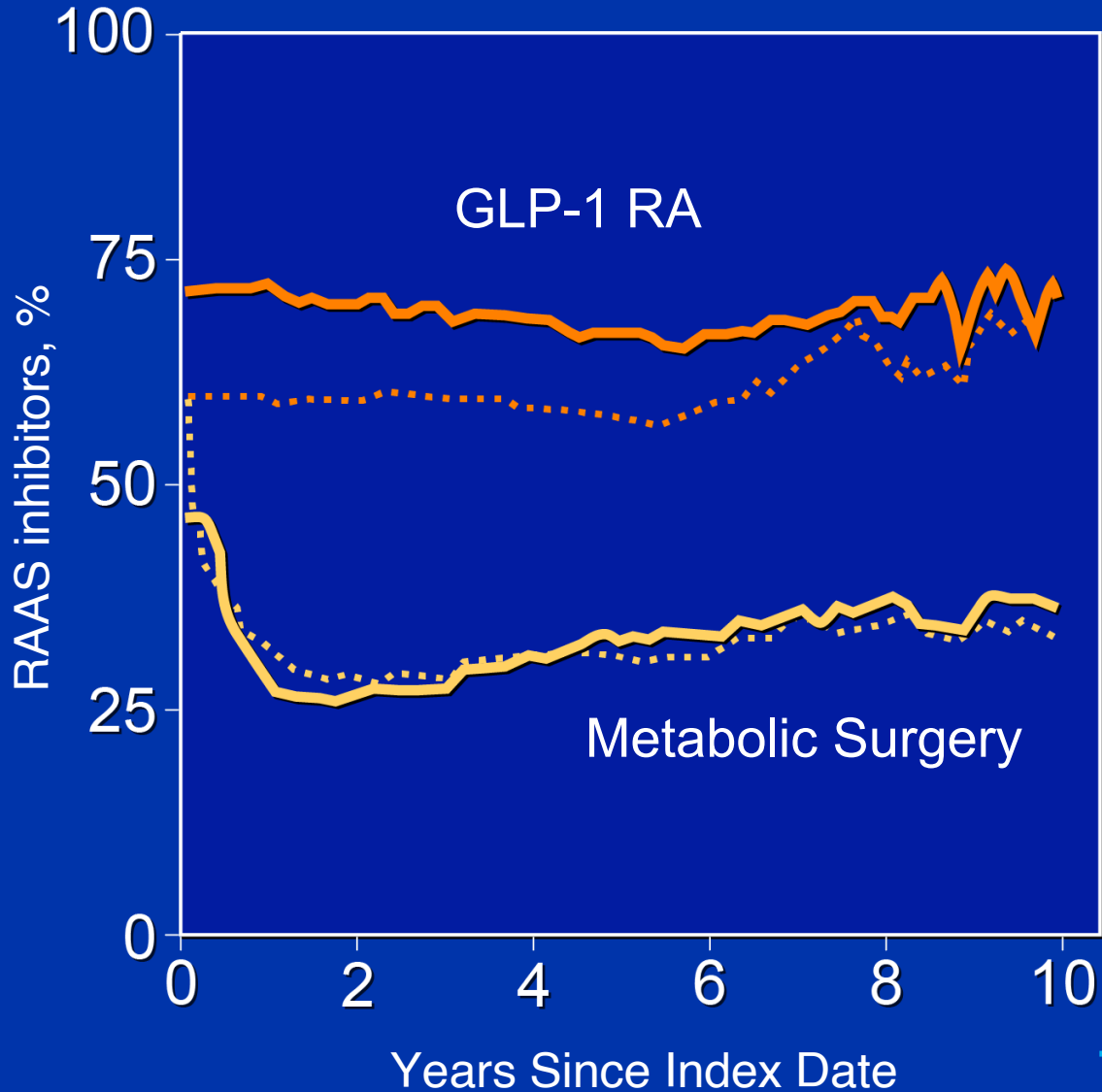
GLP-1 RAs



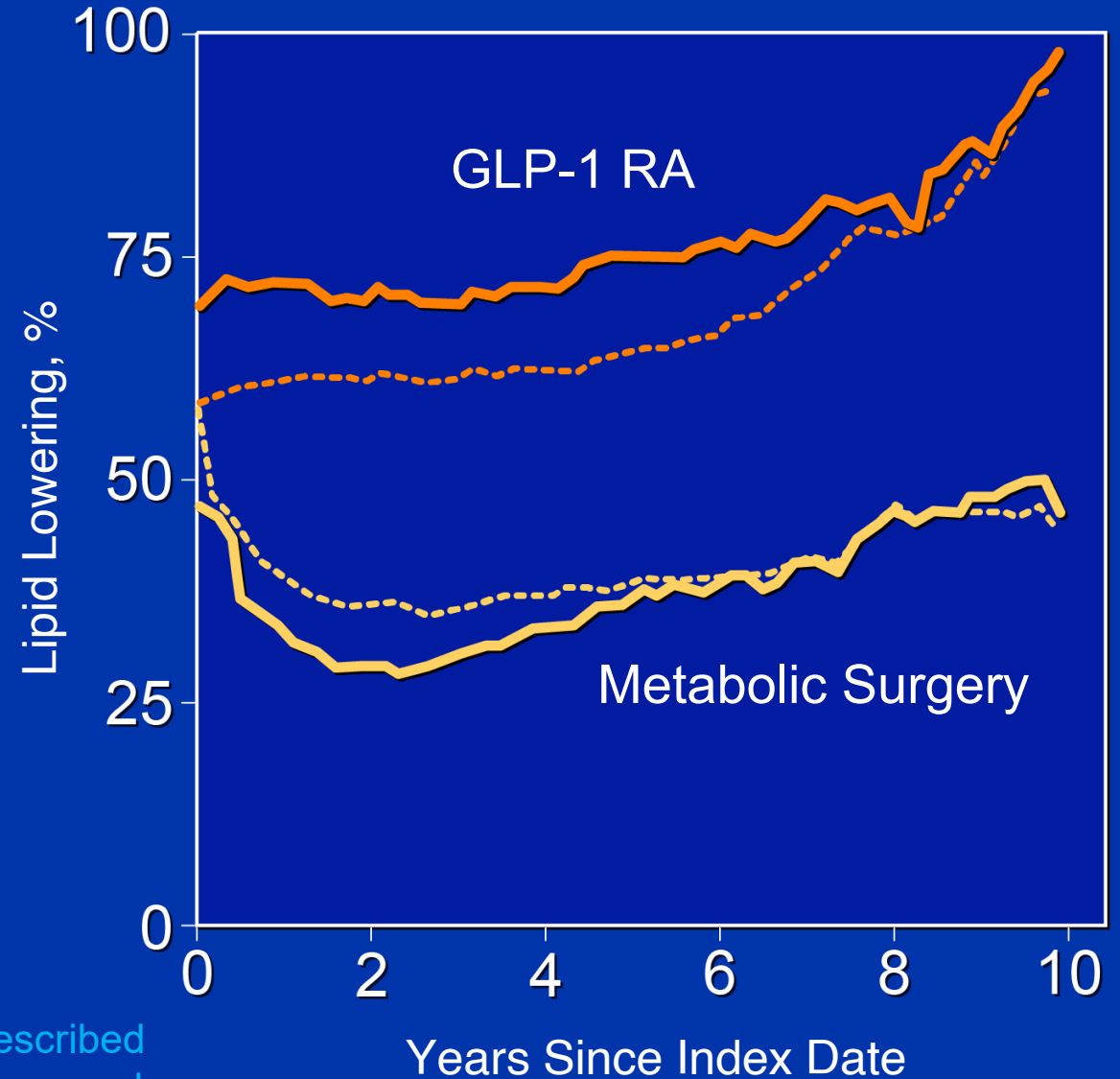
Semaglutide or Tirzepatide



RAAS Inhibitors



Lipid Lowering Drugs



Obstructive Sleep Apnea

MOSAIC

(Metabolic surgery for OSA and Incident Cardiovascular disease)



No therapy has been shown to reduce the risk of major adverse cardiovascular events (MACE) and death in patients with obstructive sleep apnea (OSA).

13,657 adult patients with moderate-to-severe OSA and obesity

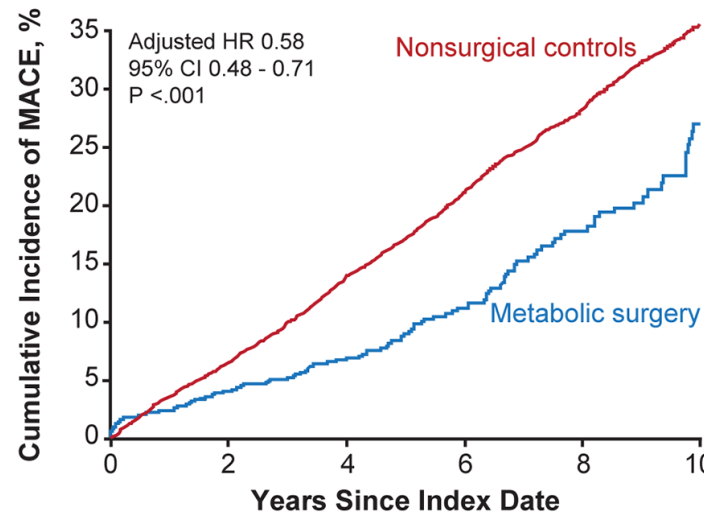
970 patients in metabolic surgery group

VS

12,687 patients in nonsurgical control group



Cumulative Incidence for MACE

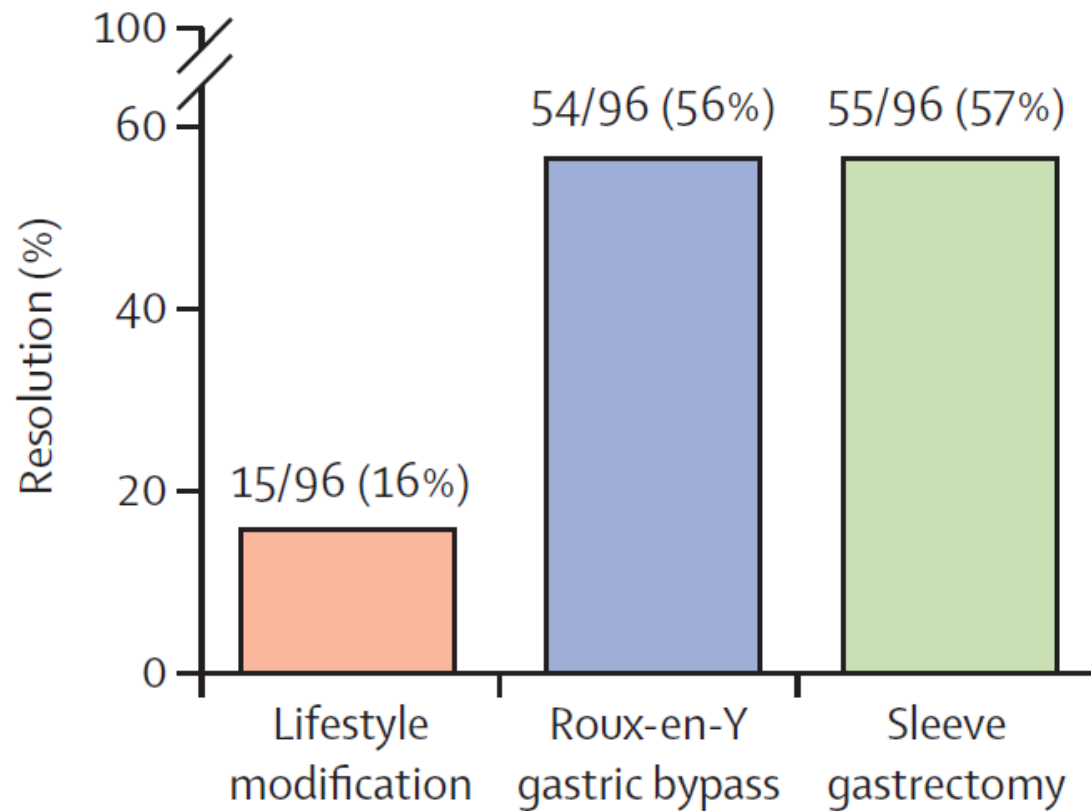


Health benefits of metabolic surgery in 10-years compared with usual care in patients with OSA:

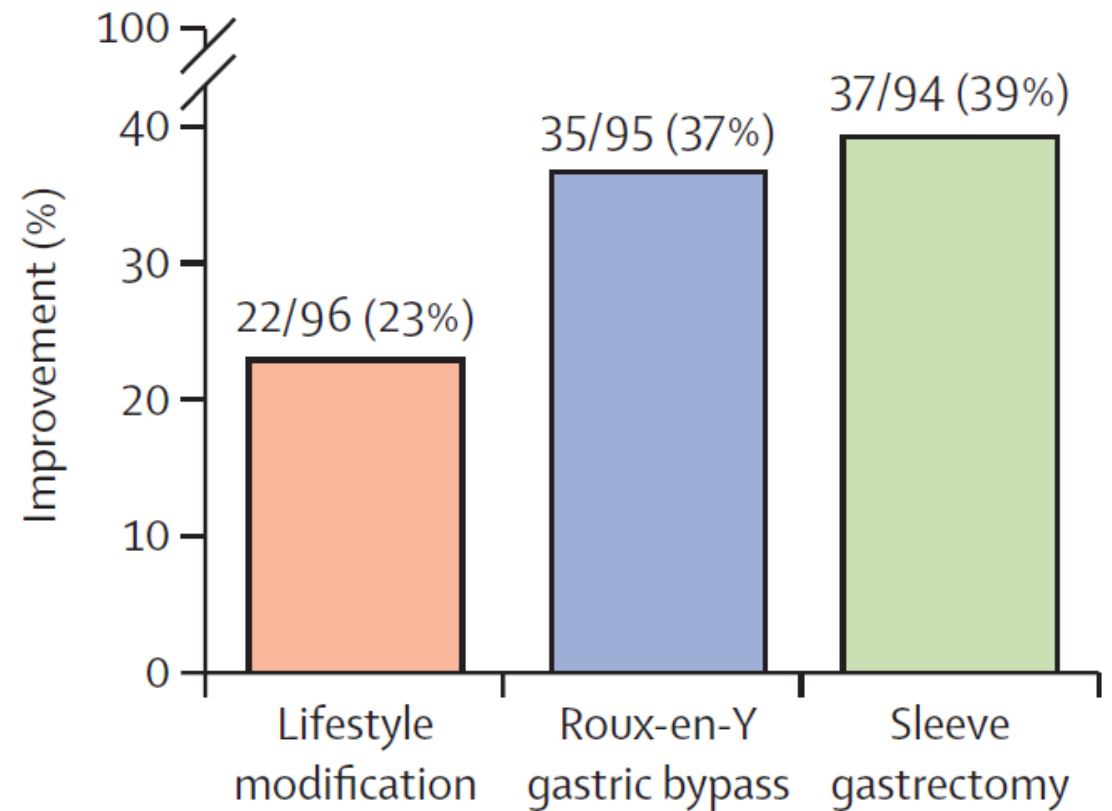
- 42% lower risk of MACE
- 37% lower risk of death
- 70% lower risk of heart failure
- 24% greater weight loss

BRAVES RCT

A NASH resolution without worsening of fibrosis (ITT population)



B Improvement of at least one stage of liver fibrosis without worsening of NASH (ITT population)



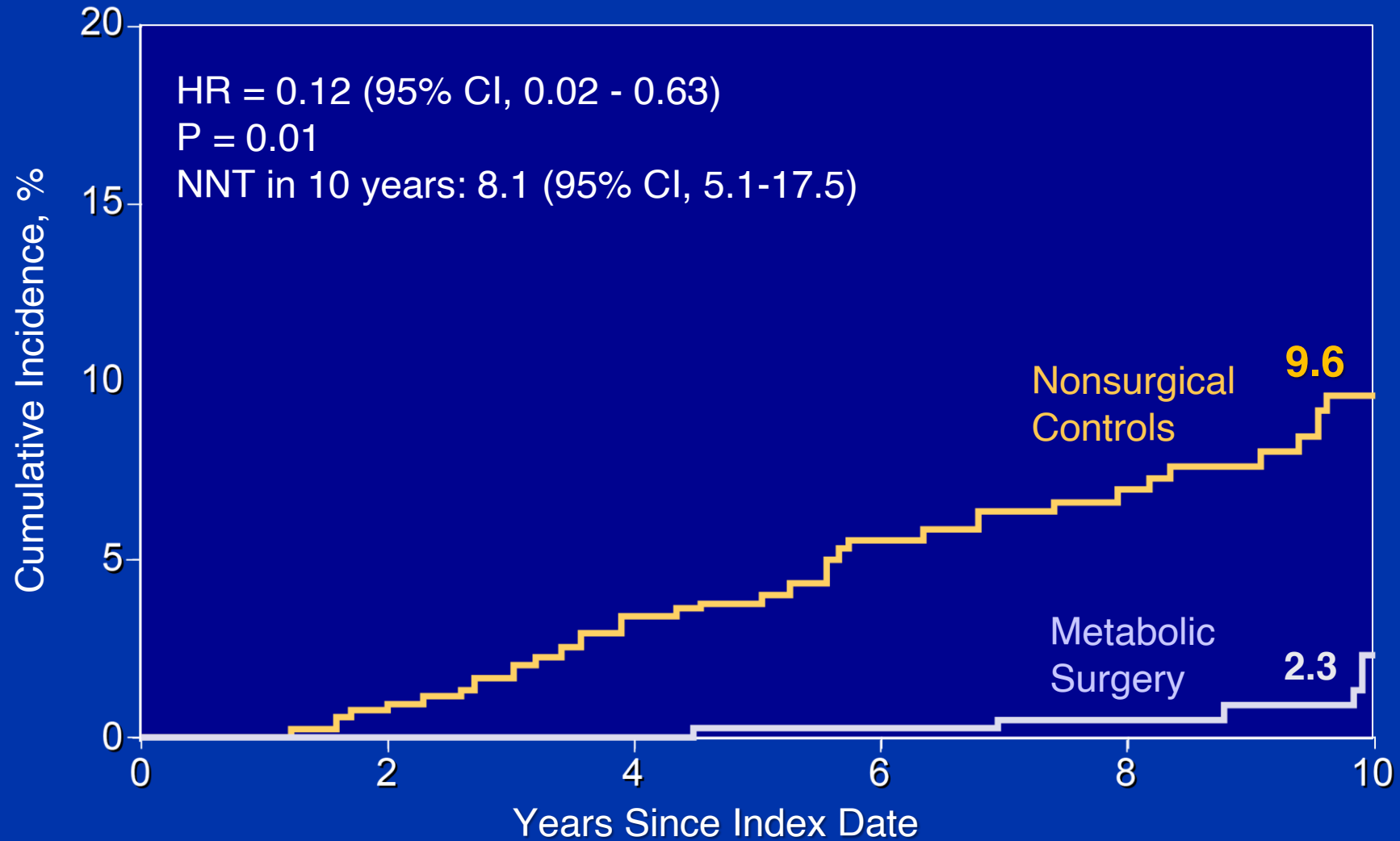
JAMA | Original Investigation

Association of Bariatric Surgery With Major Adverse Liver and Cardiovascular Outcomes in Patients With Biopsy-Proven Nonalcoholic Steatohepatitis

Ali Aminian, MD; Abbas Al-Kurd, MD; Rickesha Wilson, MD; James Bena, MS; Hana Fayazzadeh, MD; Tavankit Singh, MD; Vance L. Albaugh, MD, PhD; Faiz U. Shariff, MD; Noe A. Rodriguez, MD; Jian Jin, MS; Stacy A. Brethauer, MD, MBA; Srinivasan Dasarathy, MD; Naim Alkhouri, MD; Philip R. Schauer, MD; Arthur J. McCullough, MD; Steven E. Nissen, MD

**Surgical Procedures and Long-term Effectiveness in
NASH Disease and Obesity Risk (SPLENDOR)**

Major Adverse Liver Outcomes (MALO)



N at risk

Nonsurgical Controls	508	422	376	283	211	146
Metabolic Surgery	650	525	463	381	252	153

JAMA | **Original Investigation**

Association of Bariatric Surgery With Cancer Risk and Mortality in Adults With Obesity

Ali Aminian, MD; Rickesha Wilson, MD; Abbas Al-Kurd, MD; Chao Tu, MS; Alex Milinovich, BA; Matthew Kroh, MD; Raul J. Rosenthal, MD; Stacy A. Brethauer, MD; Philip R. Schauer, MD; Michael W. Kattan, PhD; Justin C. Brown, PhD; Nathan A. Berger, MD; Jame Abraham, MD; Steven E. Nissen, MD

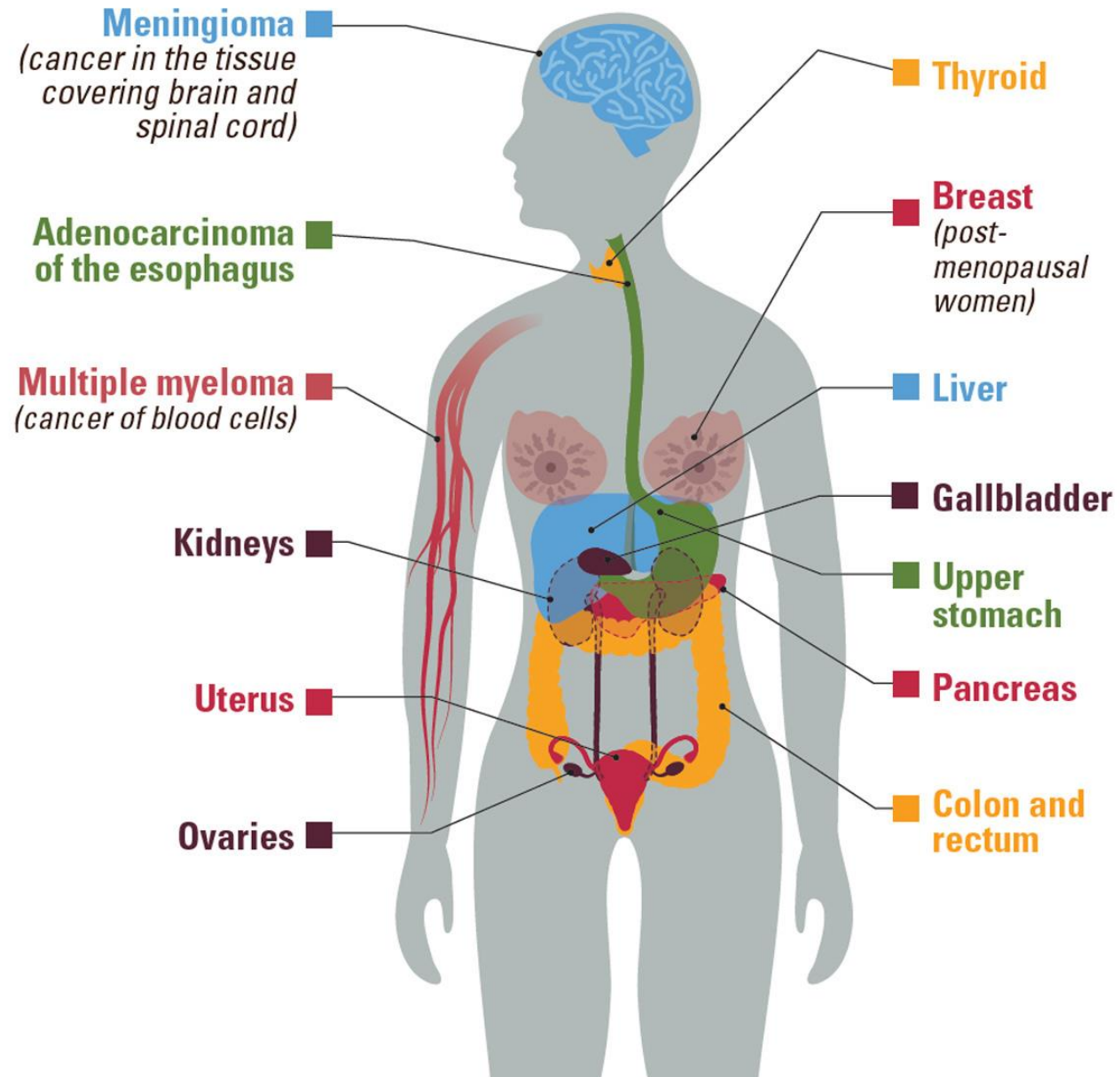
Surgical **P**rocedures and **L**ong-term **E**ffectiveness in
Neoplastic **D**isease **I**ncidence and **D**eath (**SPLENDID**)



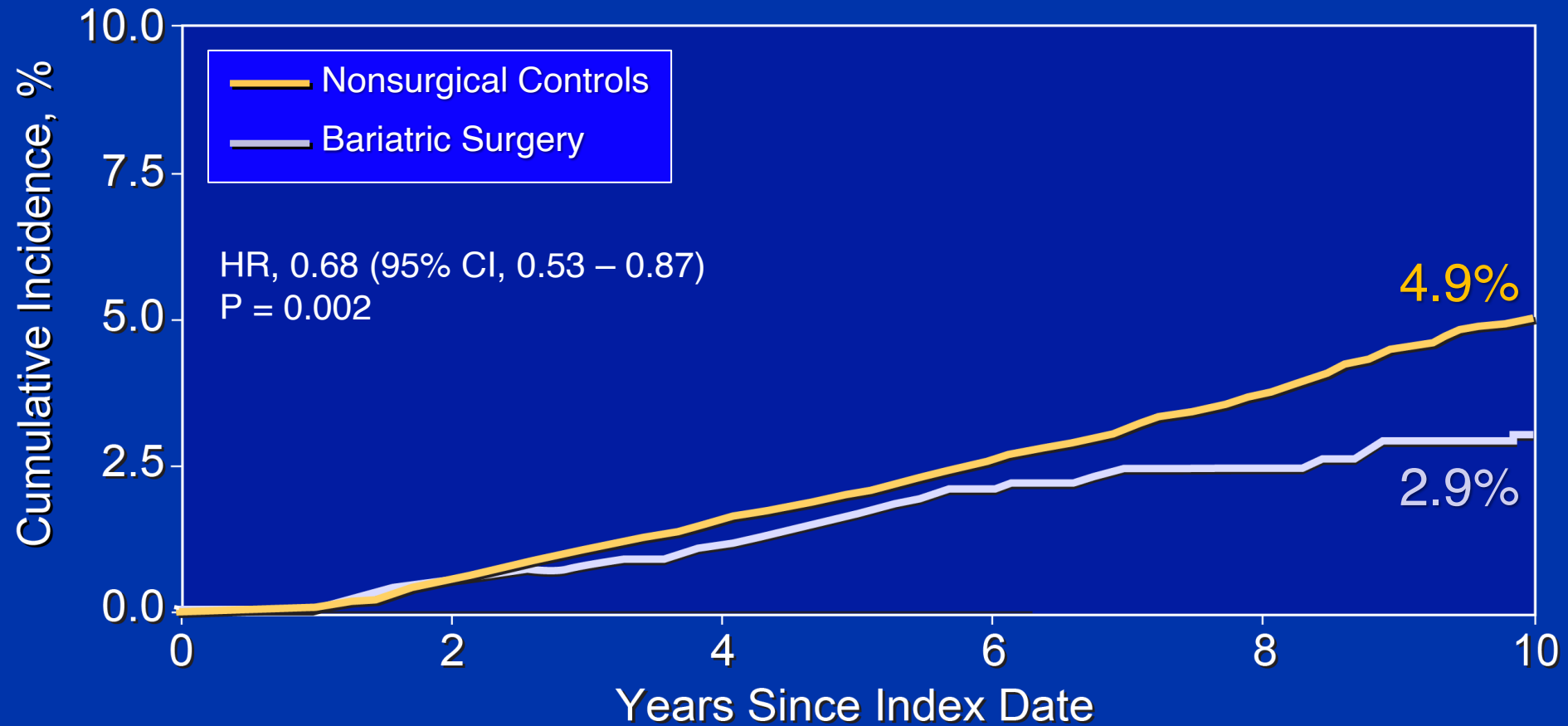
Cleveland Clinic
Bariatric and Metabolic Institute



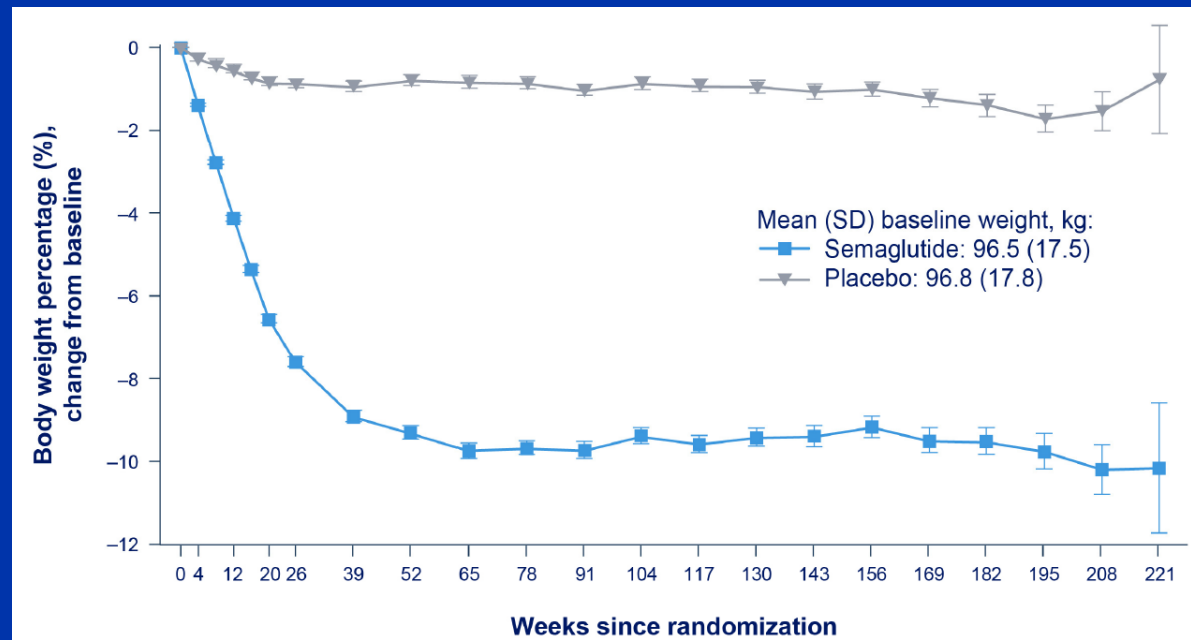
13 cancers are associated with overweight and obesity



Obesity - Associated Cancers



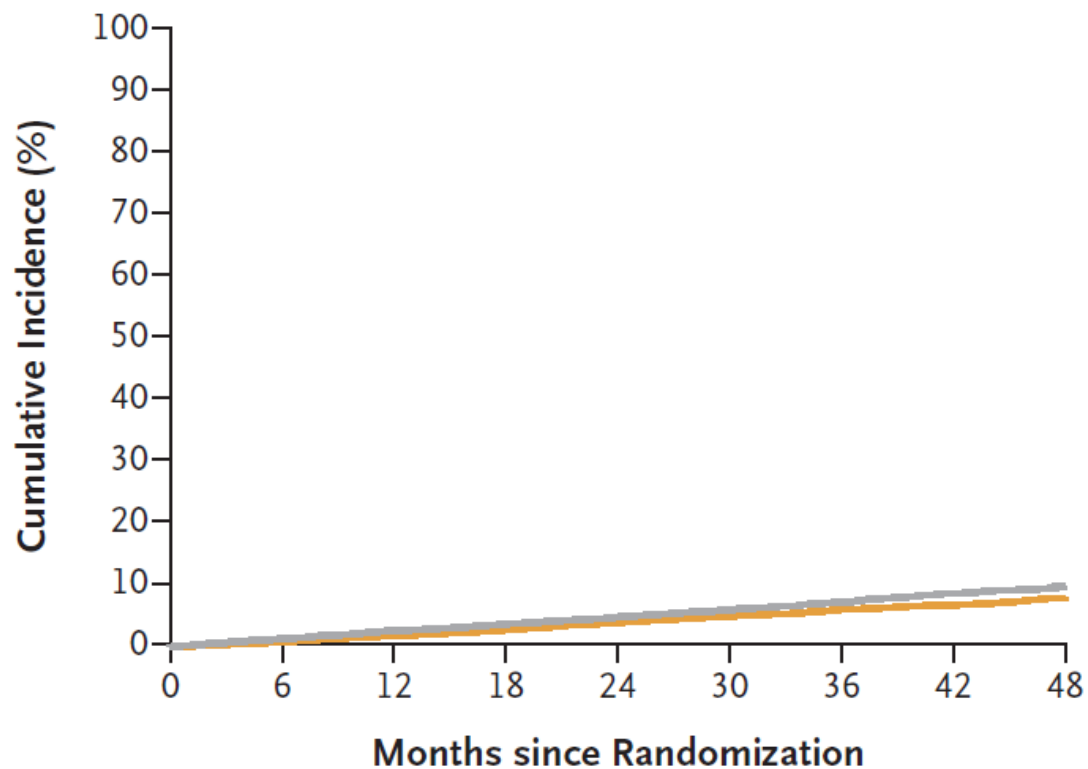
SELECT



9 Kg (%) Difference

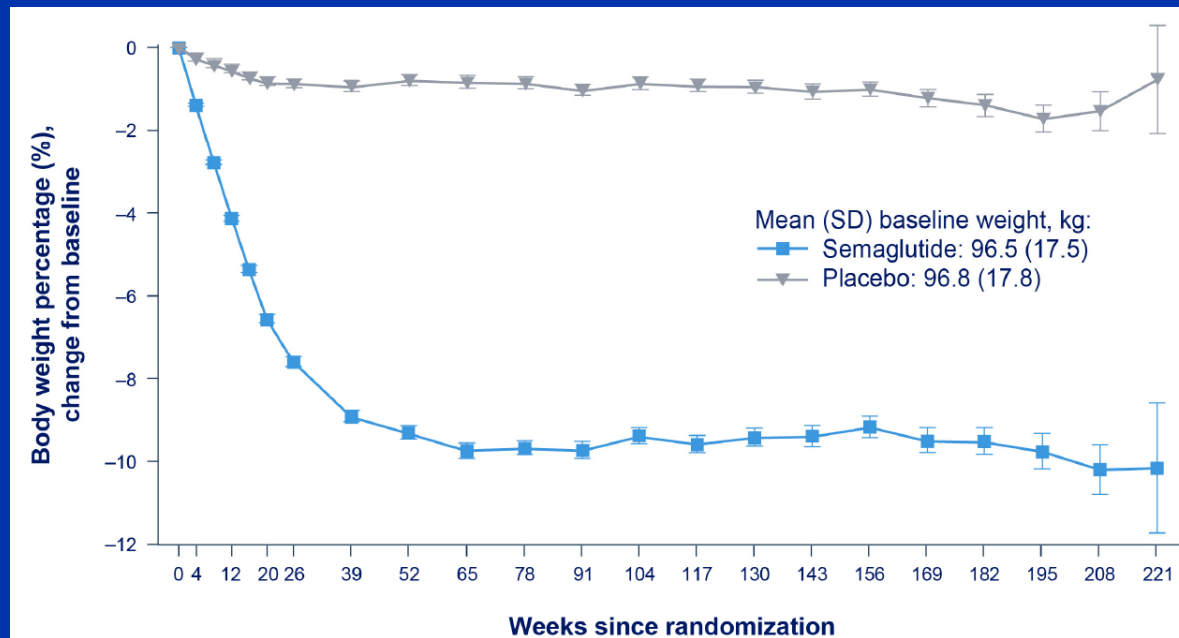
SELECT

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

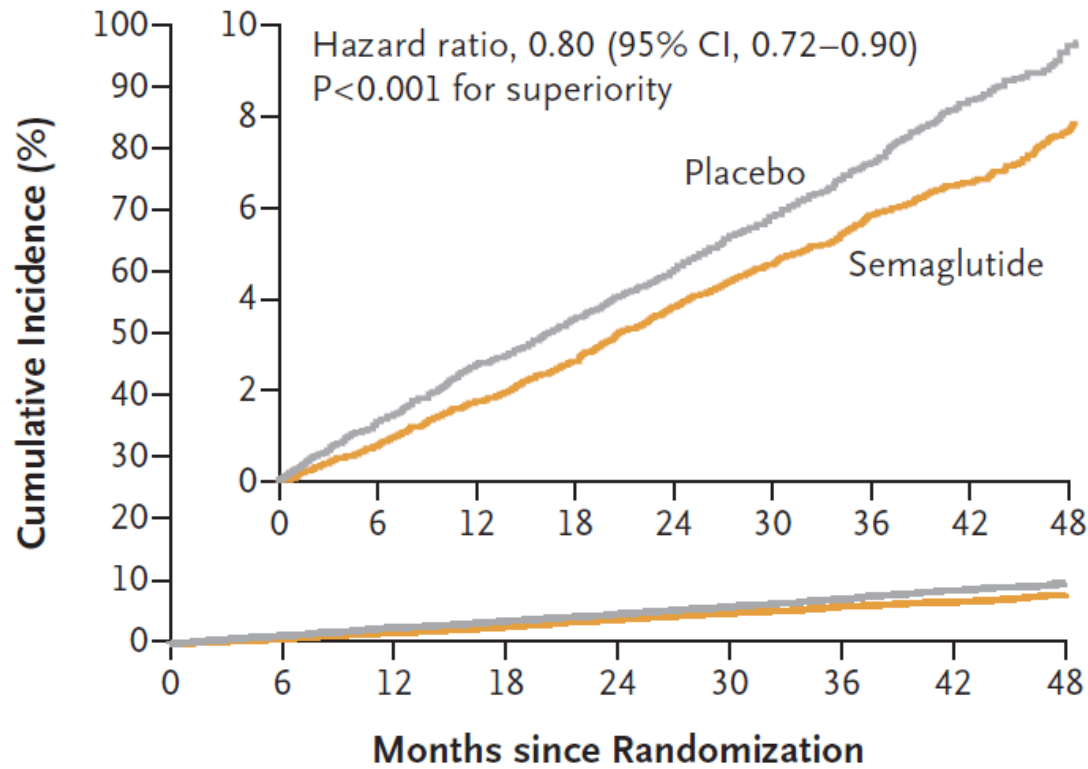


9 Kg (%) Difference



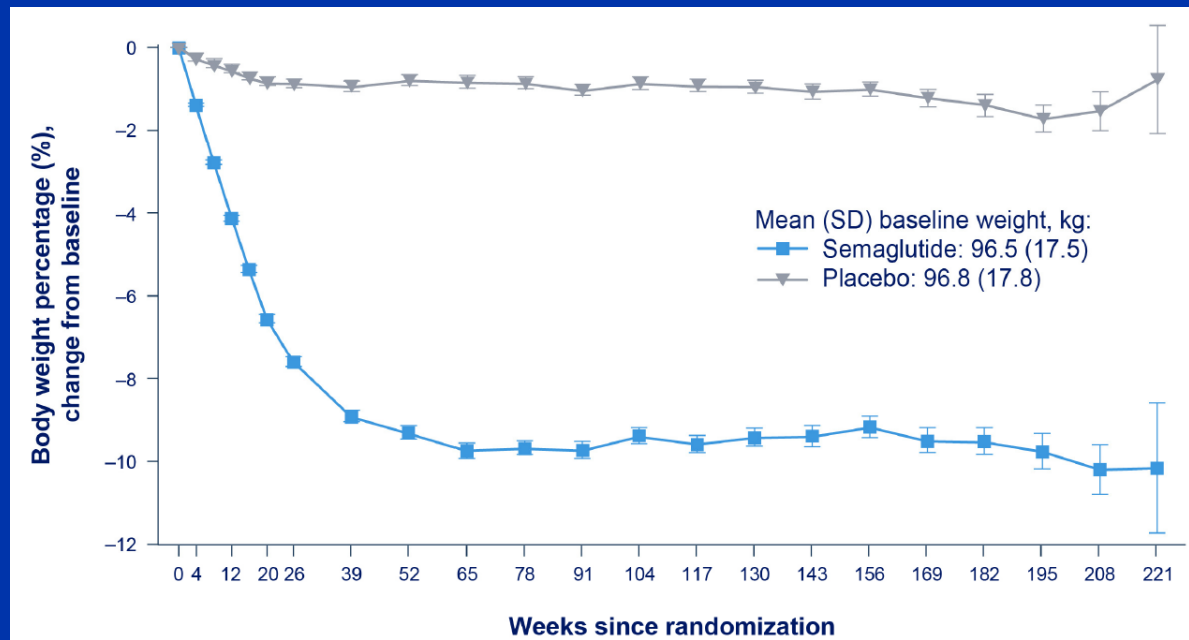
SELECT

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



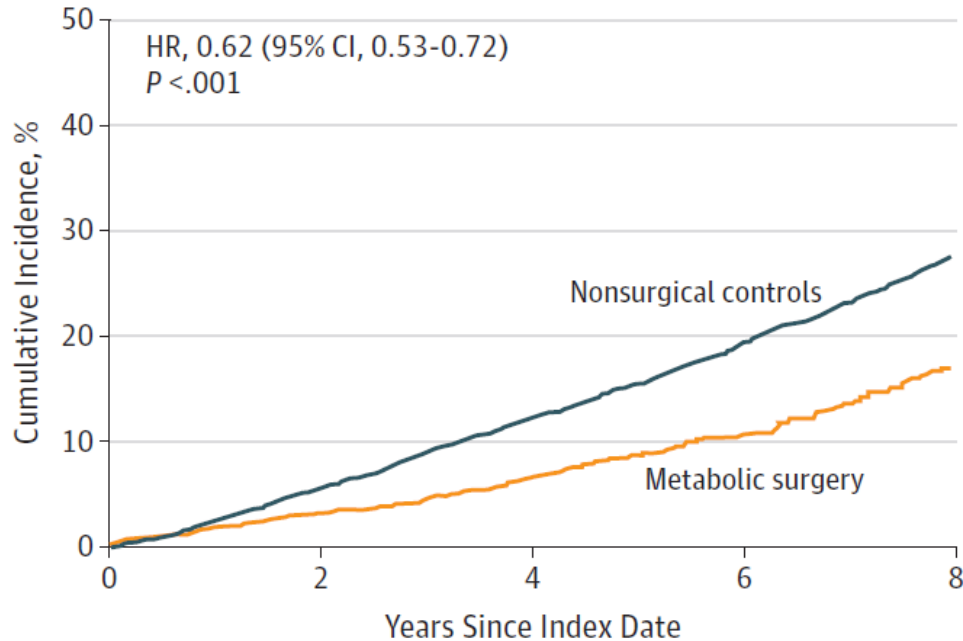
9 Kg (%) Difference



MACE: Metabolic Surgery vs SELECT

Look at the GAP!

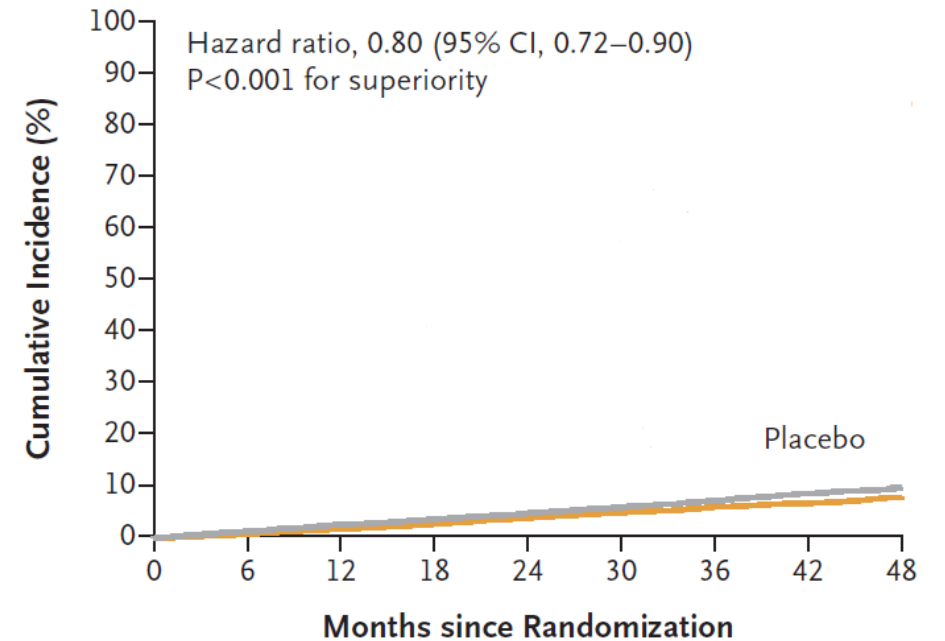
Metabolic Surgery



No. at risk	0	2	4	6	8
Nonsurgical controls	11 435	8645	5543	2826	1130
Metabolic surgery	2287	1438	991	610	336

JAMA 2019

Semaglutide (SELECT)



No. at Risk	0	6	12	18	24	30	36	42	48
Placebo	8801	8652	8487	8326	8164	7101	5660	4015	1672
Semaglutide	8803	8695	8561	8427	8254	7229	5777	4126	1734

NEJM 2023

MACE: Metabolic Surgery vs SELECT

Intervention	Relative risk reduction	Absolute risk reduction	Number needed to treat to prevent 1 MACE	Cost in 2025 to prevent 1 MACE
Semaglutide	20%			
Metabolic Surgery	40-50%			

MACE: Metabolic Surgery vs SELECT

Intervention	Relative risk reduction	Absolute risk reduction	Number needed to treat to prevent 1 MACE	Cost in 2025 to prevent 1 MACE
Semaglutide	20%	1.5%		
Metabolic Surgery	40-50%	~10%		

MACE: Metabolic Surgery vs SELECT

Intervention	Relative risk reduction	Absolute risk reduction	Number needed to treat to prevent 1 MACE	Cost in 2025 to prevent 1 MACE
Semaglutide	20%	1.5%	66	
Metabolic Surgery	40-50%	~10%	10-15	

MACE: Metabolic Surgery vs SELECT

Intervention	Relative risk reduction	Absolute risk reduction	Number needed to treat to prevent 1 MACE	Cost in 2025 to prevent 1 MACE
Semaglutide	20%	1.5%	66	\$ 3,000,000
Metabolic Surgery	40-50%	~10%	10-15	\$ 300,000

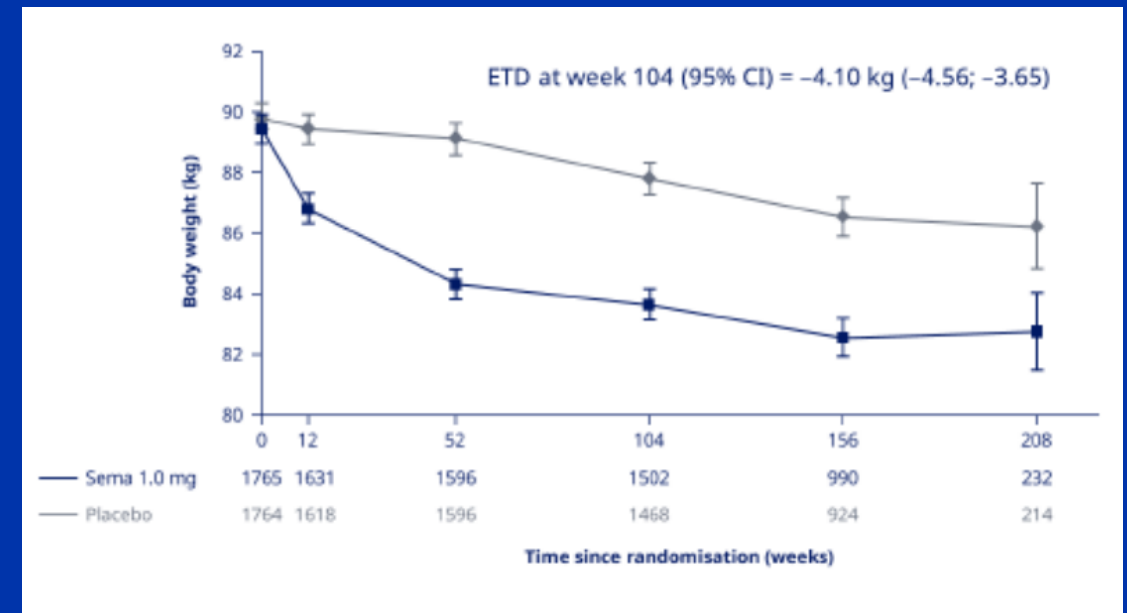
MACE: Metabolic Surgery vs SELECT

Intervention	Relative risk reduction	Absolute risk reduction	Number needed to treat to prevent 1 MACE	Cost in 2025 to prevent 1 MACE
Semaglutide	20%	1.5%	66	\$ 3,000,000
Metabolic Surgery	40-50%	~10%	10-15	\$ 300,000

If you have \$3,000,000, would you prefer to save 1 life or 10 lives?

FLOW Trial in CKD

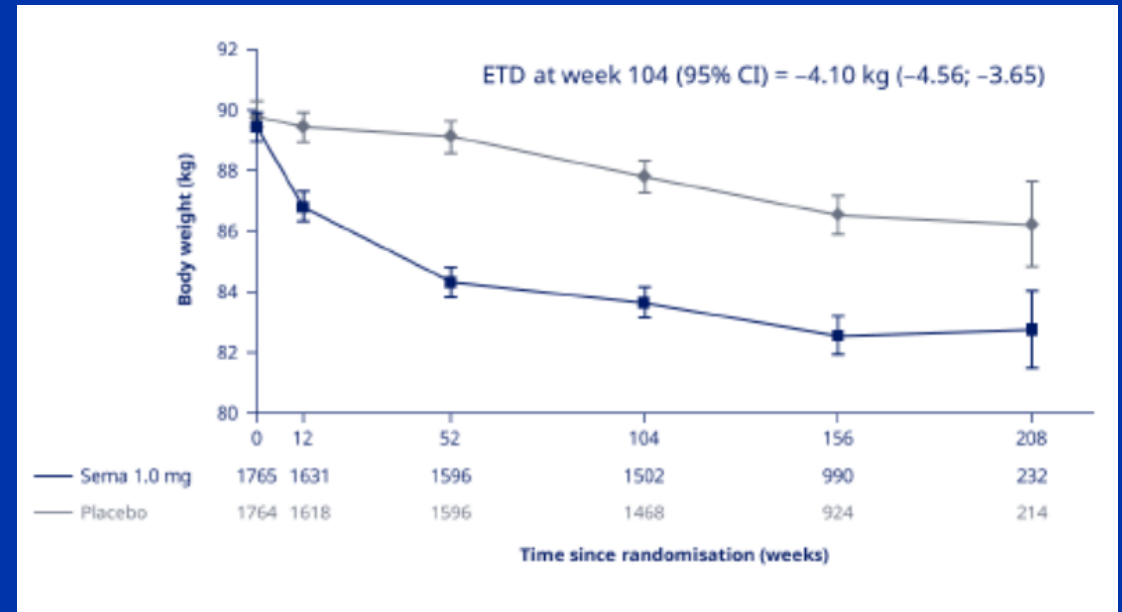
- T2DM, GFR 25-75
- Semaglutide (1 mg weekly)



4 Kg Difference

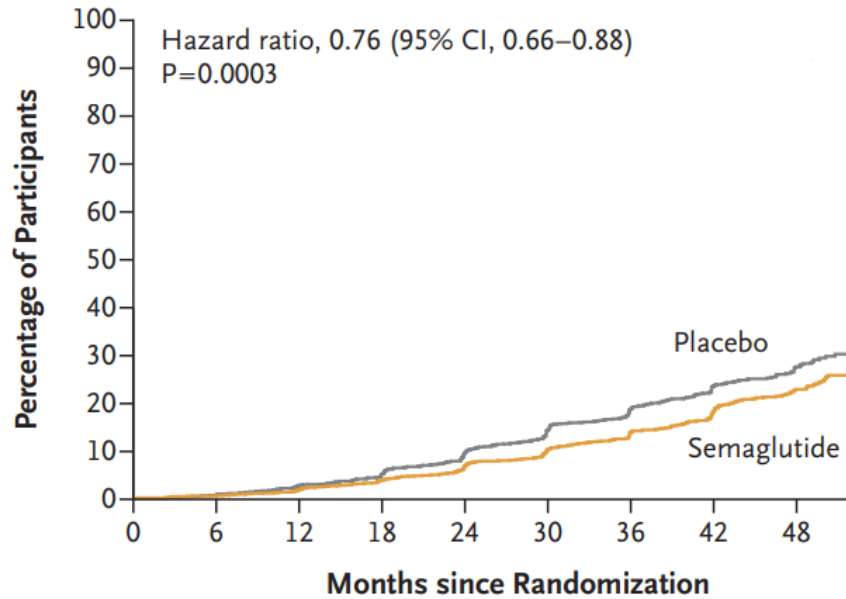
FLOW Trial in CKD

- T2DM, GFR 25-75
- Semaglutide (1 mg weekly)



4 Kg Difference

First Major Kidney Disease Event



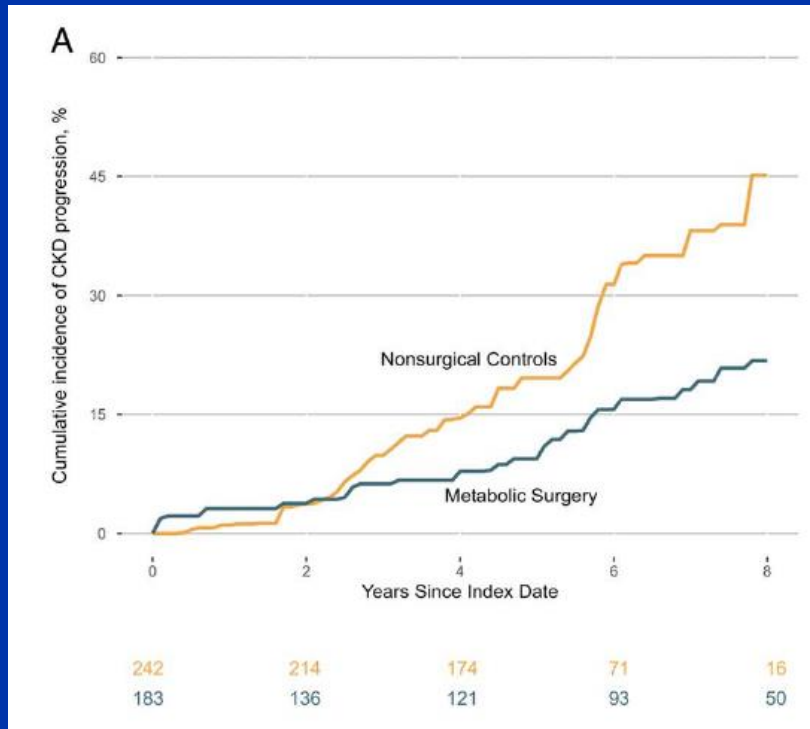
No. at Risk

Placebo	1766	1736	1682	1605	1516	1408	1048	660	354
Semaglutide	1767	1738	1693	1640	1572	1489	1131	742	392



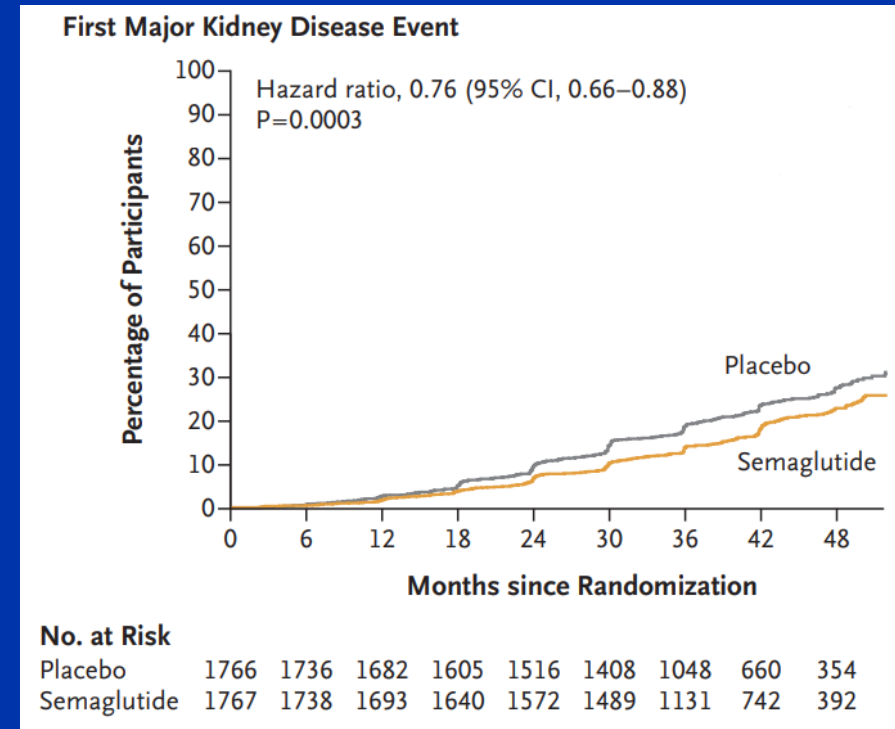
Adverse Kidney Outcomes: Metabolic Surgery vs FLOW Look at the GAP!

Metabolic Surgery



Ann Surg 2024

Semaglutide (FLOW)



NEJM 2024

Metabolic Surgery vs FLOW

Intervention	Relative risk reduction			
Semaglutide	24%			
Metabolic Surgery	60%			

Metabolic Surgery vs FLOW

Intervention	Relative risk reduction	Absolute risk reduction		
Semaglutide	24%	5%		
Metabolic Surgery	60%	18%		

Metabolic Surgery vs FLOW

Intervention	Relative risk reduction	Absolute risk reduction	Number needed to treat to protect 1 kidney	
Semaglutide	24%	5%	20	
Metabolic Surgery	60%	18%	6	

Metabolic Surgery vs FLOW

Intervention	Relative risk reduction	Absolute risk reduction	Number needed to treat to protect 1 kidney	Cost in 2025 to protect 1 kidney
Semaglutide	24%	5%	20	\$ 750,000
Metabolic Surgery	60%	18%	6	\$ 150,000

Metabolic Surgery vs FLOW

Intervention	Relative risk reduction	Absolute risk reduction	Number needed to treat to protect 1 kidney	Cost in 2025 to protect 1 kidney
Semaglutide	24%	5%	20	\$ 750,000
Metabolic Surgery	60%	18%	6	\$ 150,000

If you had \$750,000,
would you rather save 1 kidney or 5 kidneys?

Final Thoughts

- Surgical community welcomes the introduction of effective AOMs.
- Losing large amount of weight (**by metabolic surgery**, etc) can prevent and/or reverse health consequences of obesity including CV risk.
- Metabolic surgery is **durable** with **large magnitude of effects**.
- **Dose-response gradient** between weight loss & outcomes.
- Patients (and providers) must have the choice to choose between all evidence-based therapies including AOM, MBS, or combination therapy.