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# The Future of Endobariatrics in the GLP-1 Era

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Director of Bariatric Endoscopy

# ■ Conflicts of Interest

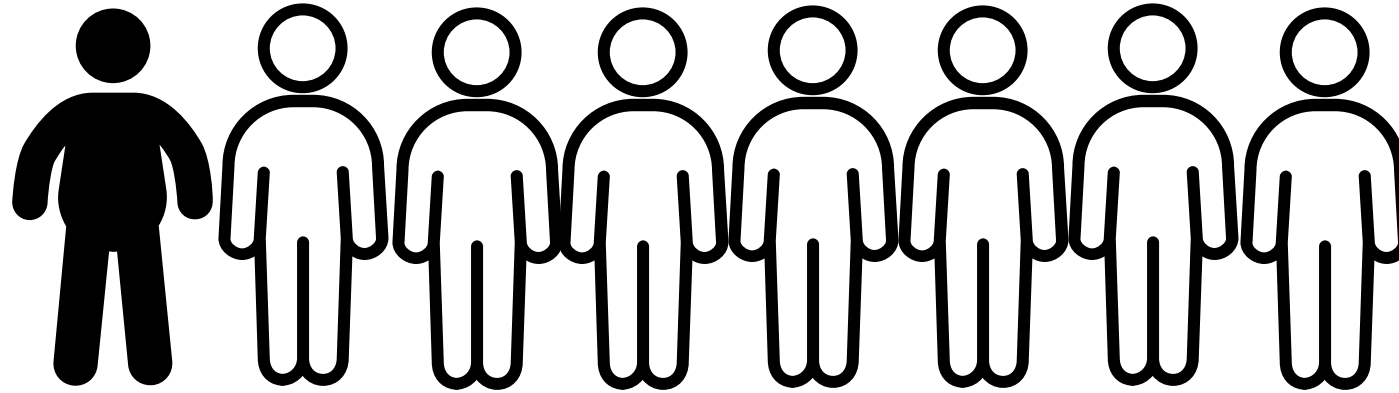
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No Conflicts of Interest

# ■ Outline

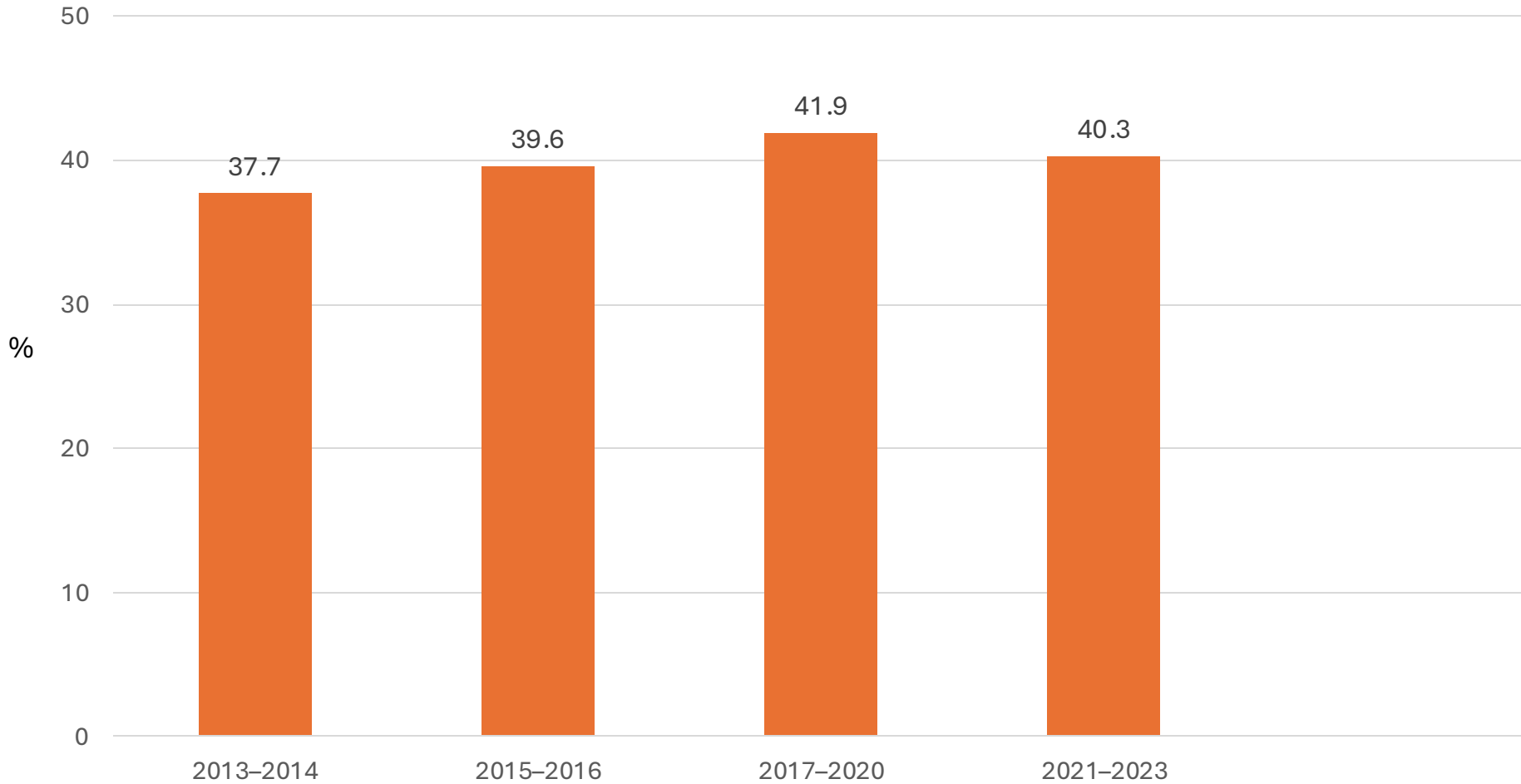
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- Obesity: Why It Matters
- Treatments for Obesity:
  - Lifestyle Interventions
  - Medications
  - Surgery
  - Endobariatrics

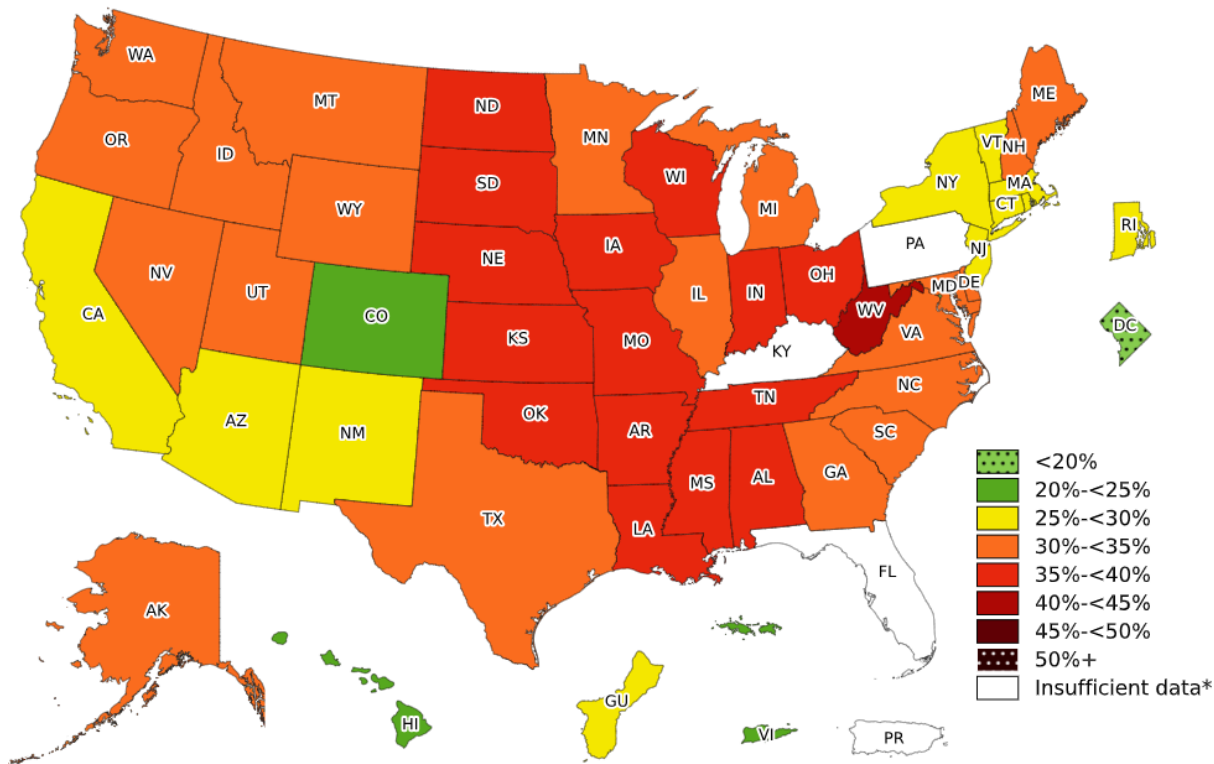


1 in 8 people in the world have obesity

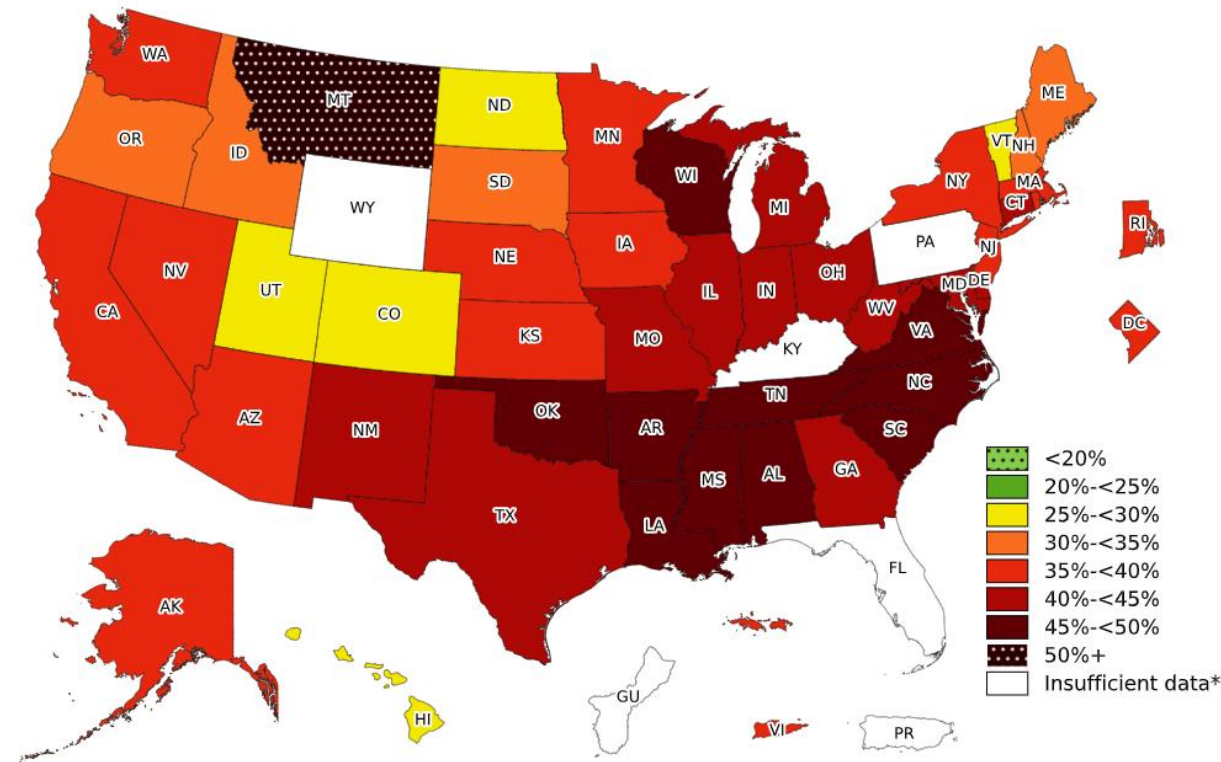
# Trends in age-adjusted obesity prevalence in adults 20 years and older, USA



# ■ Prevalence of Obesity



Prevalence of Obesity, Non-Hispanic White Adults, 2021-2023



Prevalence of Obesity, Non-Hispanic Black Adults, 2021-2023

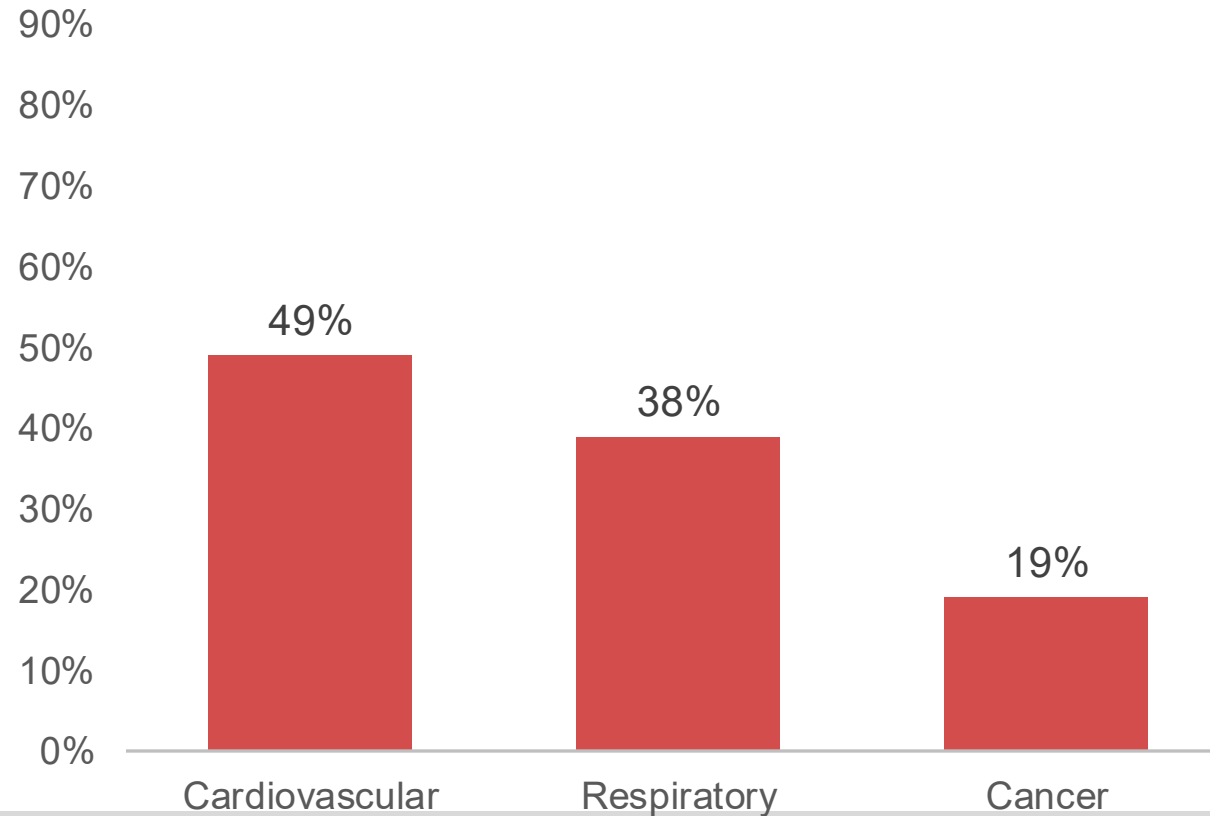


## Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents

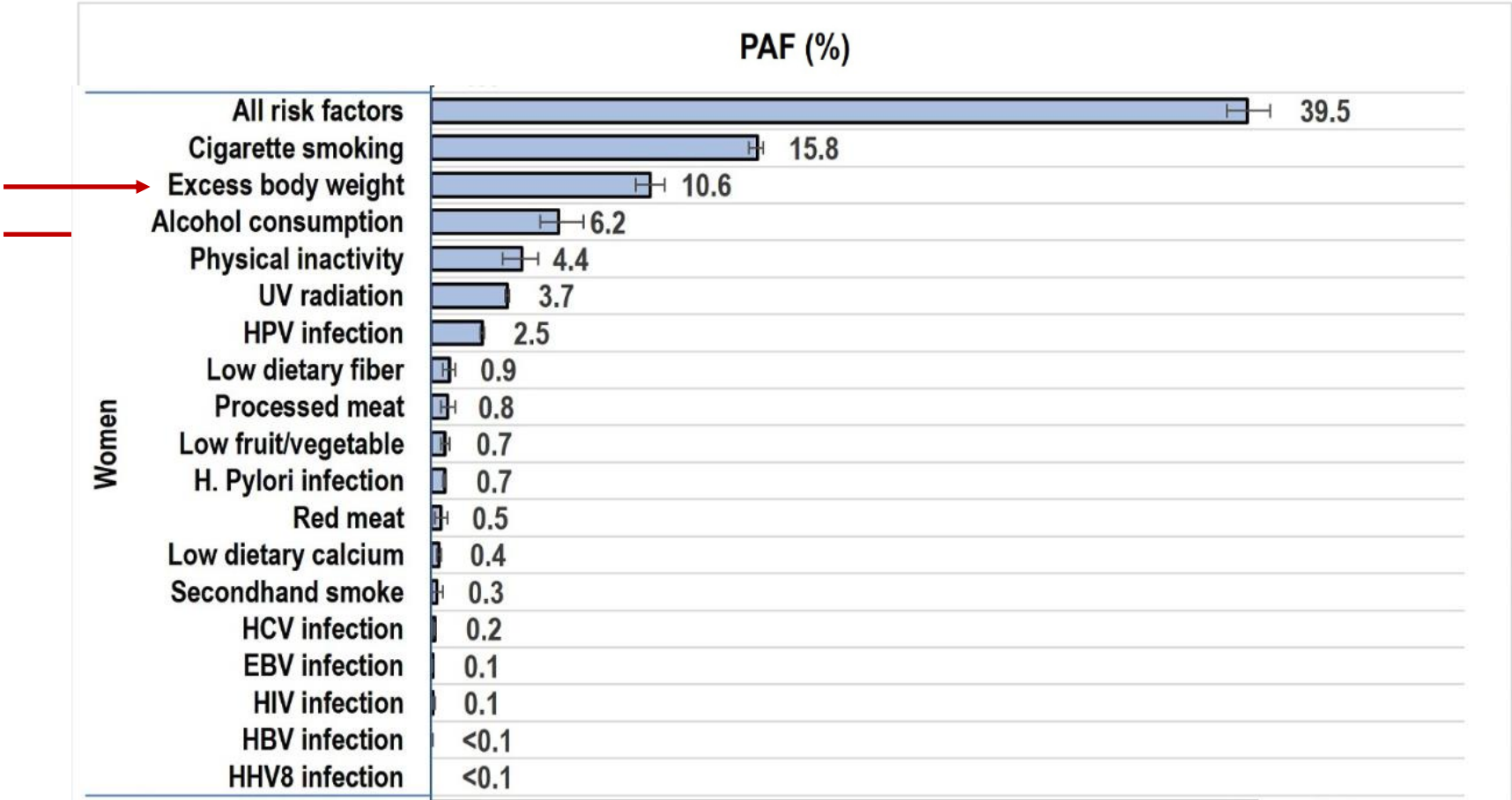


The Global BMI Mortality Collaboration\*

- 10 million patients throughout the world that participated in prospective studies
- For each 5 unit increase in BMI, i.e. from 30 to 35, the corresponding increases in risk were 49% for cardiovascular mortality, 38% for respiratory disease, and 19% for cancer mortality.



# Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States, 2019



## White Paper AGA: POWER — Practice Guide on Obesity and Weight Management, Education, and Resources

Andres Acosta,\* Sarah Streett,† Mathew D. Kroh,§ Lawrence J. Cheskin,|| Katherine H. Saunders,¶ Marina Kurian,# Marsha Schofield,\*\* Sarah E. Barlow,†† and Louis Aronne¶

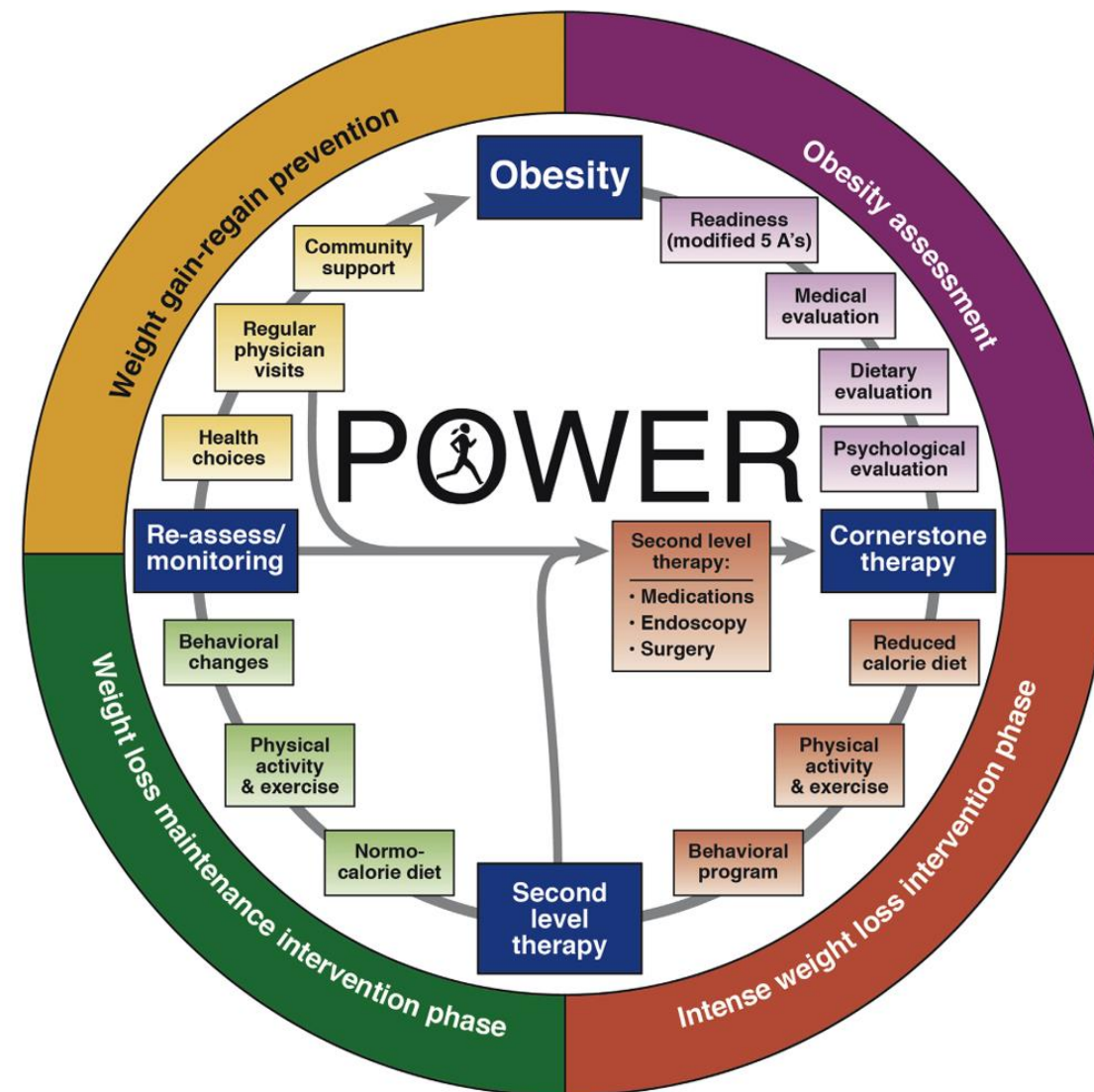


### Cornerstone Therapy

- Lifestyle Modifications with Diet and Exercise
- Best delivered by a multidisciplinary team

### Second Level Therapy

- Pharmacotherapy
- Surgery
- Endoscopy



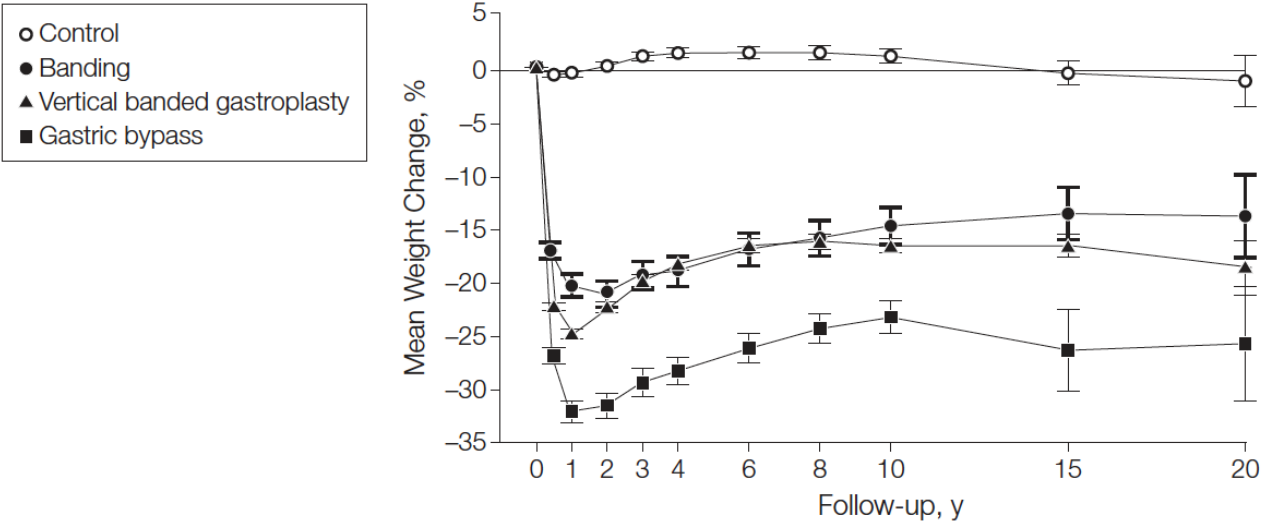
# Lifestyle Modifications & Obesity

	Diabetes Prevention Program <sup>*52</sup>	Finnish Diabetes Prevention Study <sup>53,54</sup>	Look AHEAD <sup>55</sup>	DIRECT <sup>56</sup>	WRAP <sup>57†</sup>
Participants	3234 participants with impaired glucose tolerance; 68% women, mean age 51 years; mean BMI 34 kg/m <sup>2</sup>	522 participants with impaired glucose tolerance; 67% women, mean age 55 years; mean BMI 31 kg/m <sup>2</sup>	5145 participants with type 2 diabetes; 59% women, mean age 59 years; mean BMI 36 kg/m <sup>2</sup>	298 participants with type 2 diabetes <6 years duration; 41% female, mean age 54 years; mean BMI 35 kg/m <sup>2</sup>	1269 participants; 68% women, mean age 53 years; mean BMI 34 kg/m <sup>2</sup>
Intervention	Low-calorie, low-fat diet, moderate intensity physical activity ≥150 minutes/week, 16 individual counselling sessions over 24 weeks then monthly group sessions	Low-fat diet (<30% kcal from fat and <10% from saturated fat), ≥15 g of fibre per 1000 kcal/day, moderate intensity physical activity ≥30 min/day, 7 individual sessions over 52 weeks, plus optional supervised exercise training	1200 to 1800 kcal/day (<30% from fat and >15% from protein), moderate intensity physical activity ≥175 minutes/week, one individual and three group sessions monthly for the first 6 months, followed by one individual and two group sessions per month for the next 6 months, then two individual sessions per month in years 2 through 4, then one individual session monthly for the remainder of the follow-up	Withdrawal of medications for diabetes and hypertension; 825 to 853 kcal/day total diet replacement for 3 months then structured food reintroduction and maintenance; physical activity up to 15 000 steps/day; individual sessions every 2 weeks for 20 weeks then monthly for 2 years	Given vouchers and asked to attend local WW (formerly Weight Watchers); weekly meetings and access WW web tools for 52 weeks
Goal reduction in % bodyweight	7%	≥5%	7%	≥15 kg	Not stated
Follow-up (years)	Mean 10.0 years	Median 9.0 years	Median 9.6 years	Mean 5.0 years	Mean 5.1 years
Mean weight loss % at 1 year and end of follow-up	At 1 year: 7.4 (control 0.1%); end of follow-up: 2.0% (control 1.0%)	At 1 year: 4.7% (control 0.9%); end of follow-up: 1.0% (control 0.6%)	At 1 year: 8.6% (control 0.7%); end of follow-up: 6.0% (control 3.5%)	At 1 year: 9.9% (control 1.0%); end of follow-up: 5.5% (control 4.7%)	At 1 year: 7.1% (control 3.4%); <sup>58</sup> end of follow-up: 2.8% (control 0.5%)
Glycaemic outcomes	Reduction in incidence of type 2 diabetes by 58% and 34% vs standard care at 3 and 10 years	Reduction in incidence of type 2 diabetes by 58% and 38% vs standard care at 3 and 9 years	Partial or complete type 2 diabetes remission‡ in 11.5% and 7.3% (vs 2.0% and 2.0% standard care) at 1 and 4 years	Type 2 diabetes remission§ in 46% and 7% (vs 4% and 3% standard care) at 1 and 5 years	No difference between groups in HbA <sub>1c</sub> or in progression from normoglycaemia or non-diabetic hyperglycaemia at baseline to type 2 diabetes at 5 years

# Bariatric Surgery and Long-term Cardiovascular Events

- Prospective nonrandomized matched study
- 25 public surgical departments and 480 primary health care centers in Sweden
- 2010 participants with obesity underwent bariatric surgery. Matched to 2037 obese controls who received usual care.
- Surgery group had sustained loss of more than 25% total bodyweight over 20 years

**Figure 1.** Mean Weight Change Percentages From Baseline for Controls and the 3 Surgery Groups Over 20 Years in the Swedish Obese Subjects Study



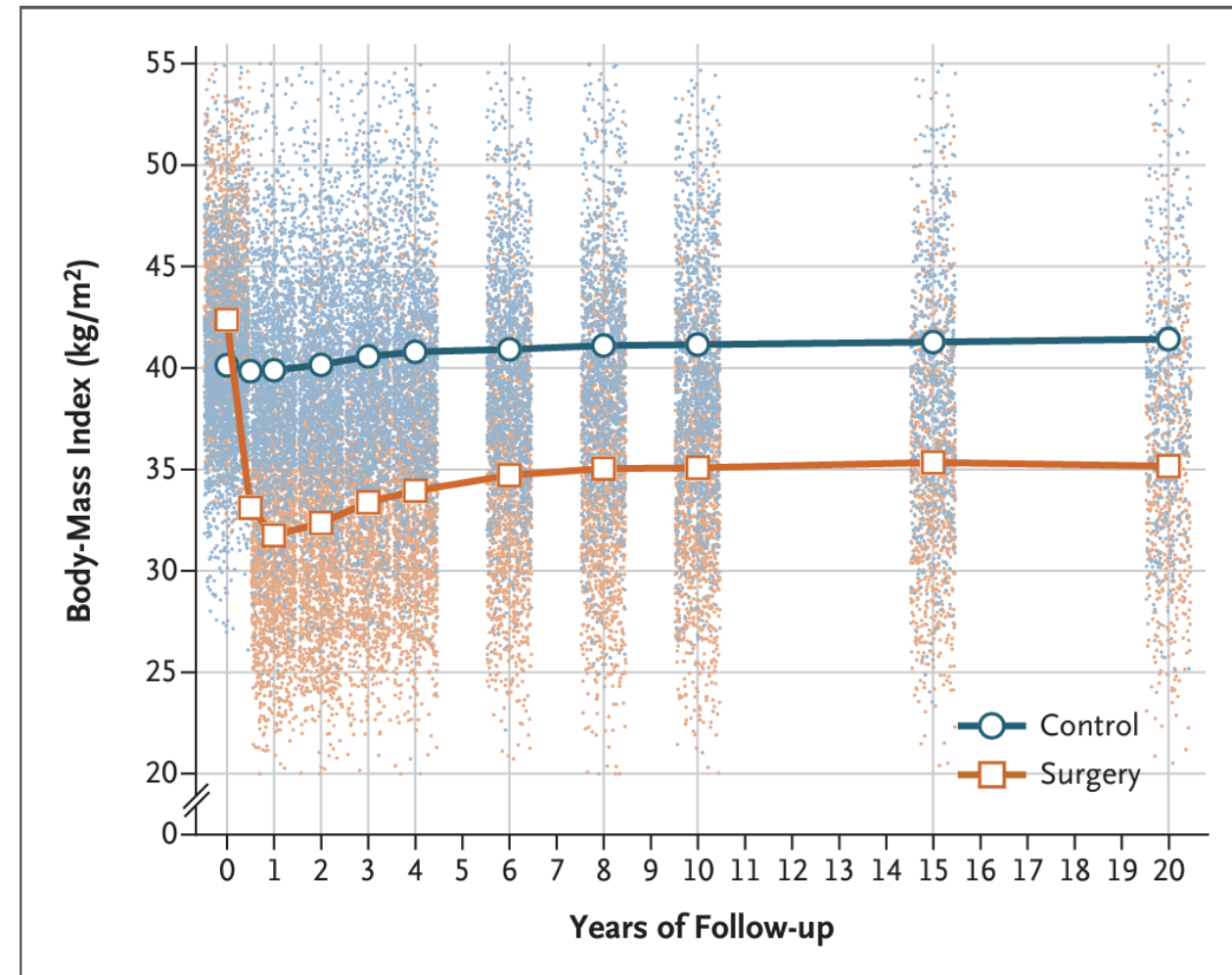
No. of patients						
Control	2037	1490	1242	1267	556	176
Banding	376	333	284	284	150	50
Vertical banded gastroplasty	1369	1086	987	1007	489	82
Gastric bypass	265	209	184	180	37	13

ORIGINAL ARTICLE

## Life Expectancy after Bariatric Surgery in the Swedish Obese Subjects Study

Lena M.S. Carlsson, M.D., Ph.D., Kajsa Sjöholm, Ph.D.,  
Peter Jacobson, M.D., Ph.D., Johanna C. Andersson-Assarsson, Ph.D.,  
Per-Arne Svensson, Ph.D., Magdalena Taube, Ph.D.,  
Björn Carlsson, M.D., Ph.D., and Markku Peltonen, Ph.D.

- Evaluated mortality over a three-decade long span
- Decreased risk of mortality from cardiovascular disease in the surgery group (**0.70, 95% CI 0.57-0.85**)
- Decreased risk of death from cancer in the surgery group (**0.77, 95% CI 0.61-0.96**)
- Median life expectancy in surgery group: 3 years longer than control



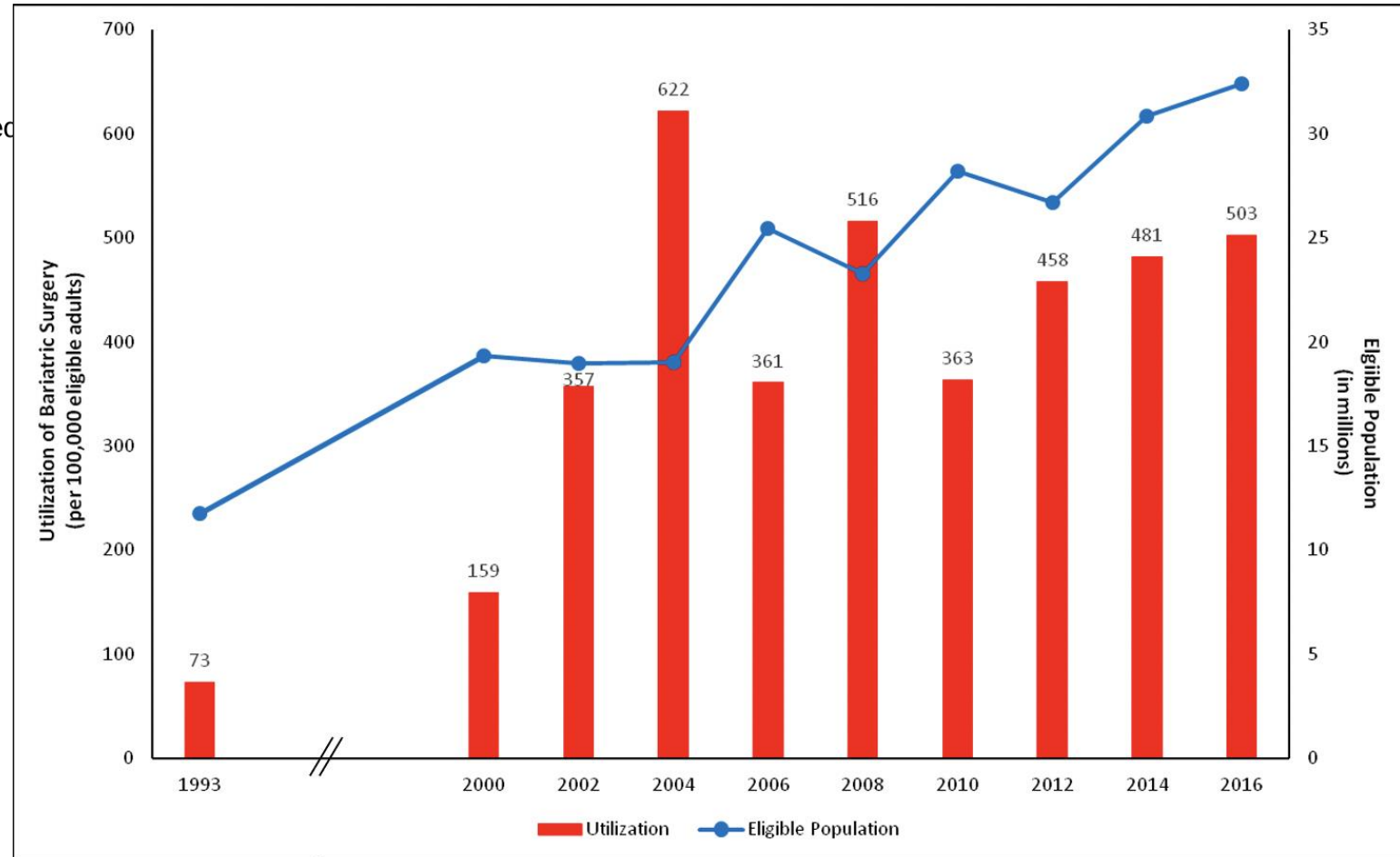
## Bariatric Surgery Trends in the U.S.: 1% is the Loneliest Number

Natalie Liu, MD\*, Luke M. Funk, MD, MPH\*,†,✉

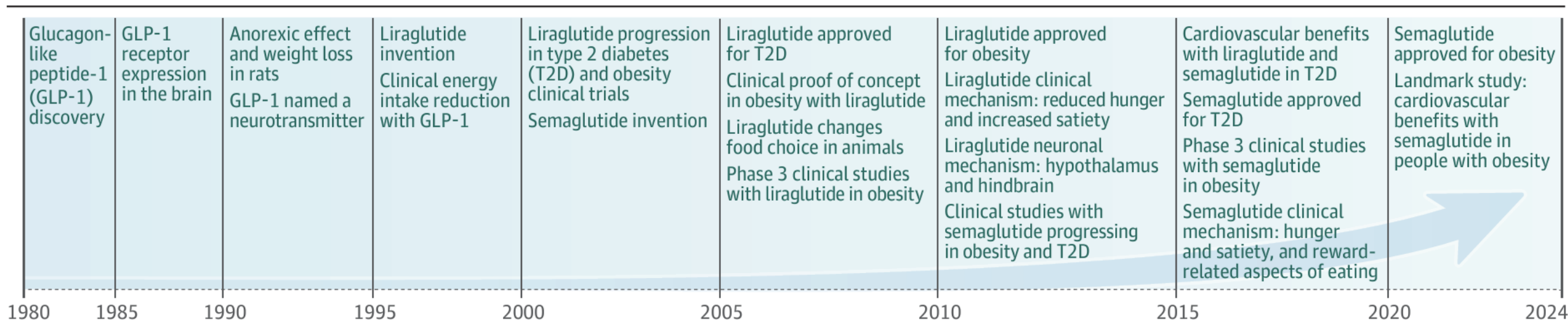
† William S. Middleton Memorial VA, Madison, Wisconsin

\* Department of Surgery, University of Wisconsin School of Medicine  
Wisconsin

- National Inpatient Sample and National Health and Nutrition Examination Survey over a 23-year period
- Improved safety profile of bariatric and metabolic surgeries over the study period with complication rates dropping from 11.7% to 1.4%
- Bariatric surgery is underutilized increasing from 0.07% to 0.5% among persons eligible for surgery based on BMI criteria



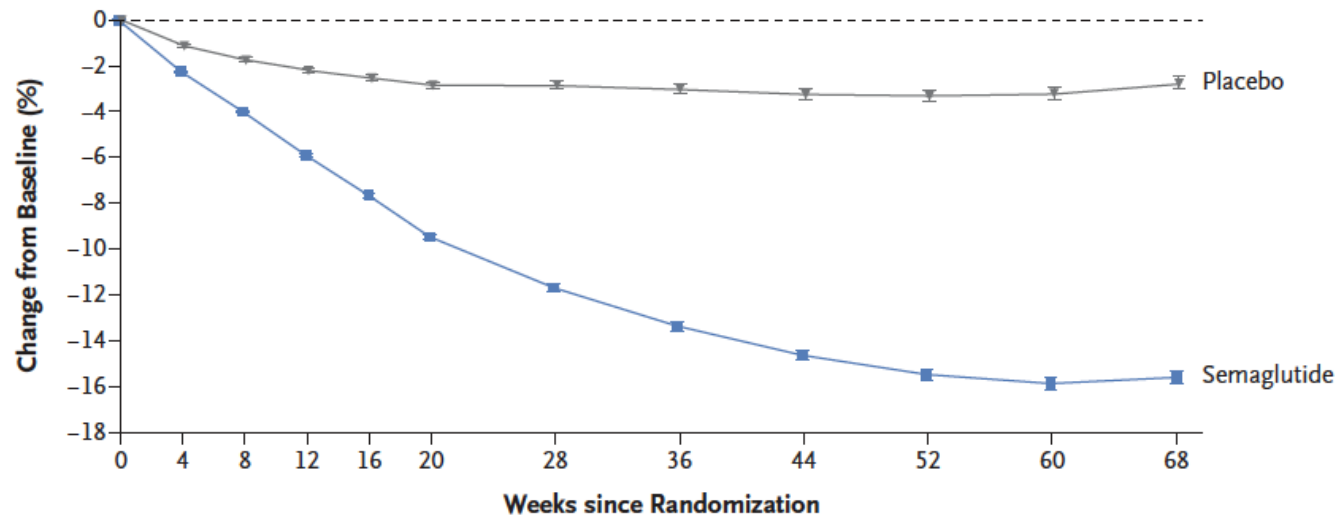
# ■ Glucagon-Like Peptide-1 (GLP-1)



## Once-Weekly Semaglutide in Adults with Overweight or Obesity

John P.H. Wilding, D.M., Rachel L. Batterham, M.B., B.S., Ph.D., Salvatore Calanna, Ph.D., Melanie Davies, M.D., Luc F. Van Gaal, M.D., Ph.D., Ildiko Lingvay, M.D., M.P.H., M.S.C.S., Barbara M. McGowan, M.D., Ph.D., Julio Rosenstock, M.D., Marie T.D. Tran, M.D., Ph.D., Thomas A. Wadden, Ph.D., Sean Wharton, M.D., Pharm.D.,

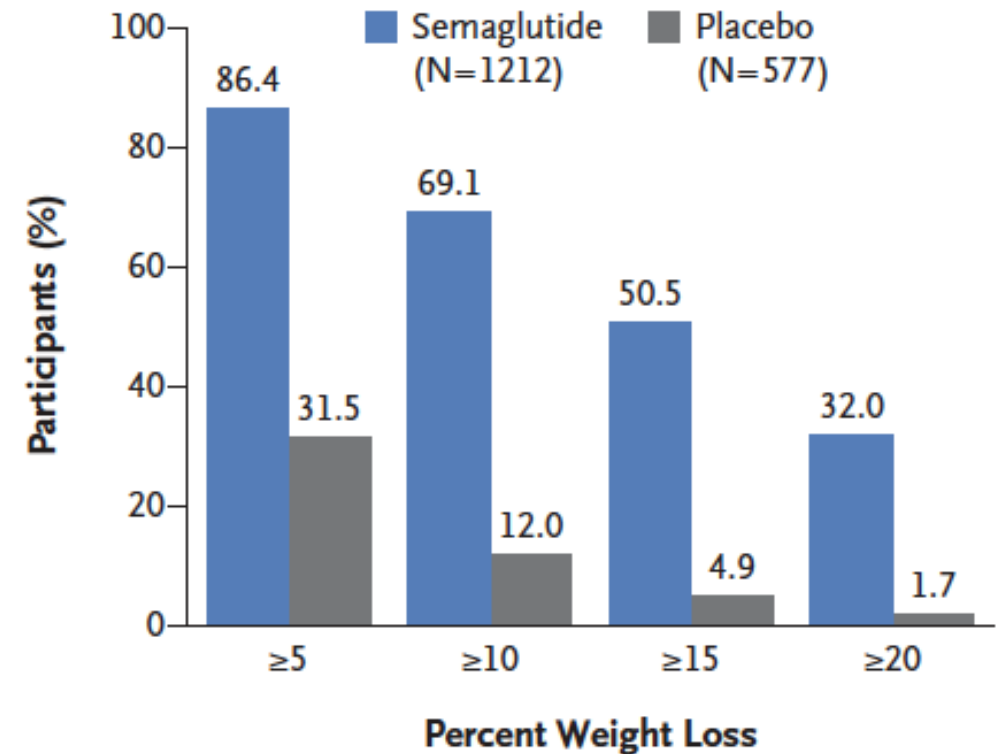
**A** Body Weight Change from Baseline by Week, Observed In-Trial Data



**No. at Risk**

Placebo	655	649	641	619	615	603	592	571	554	549	540	577
Semaglutide	1306	1290	1281	1262	1252	1248	1232	1228	1207	1203	1190	1212

**C** In-Trial Data at Wk 68



# The NEW ENGLAND JOURNAL of MEDICINE

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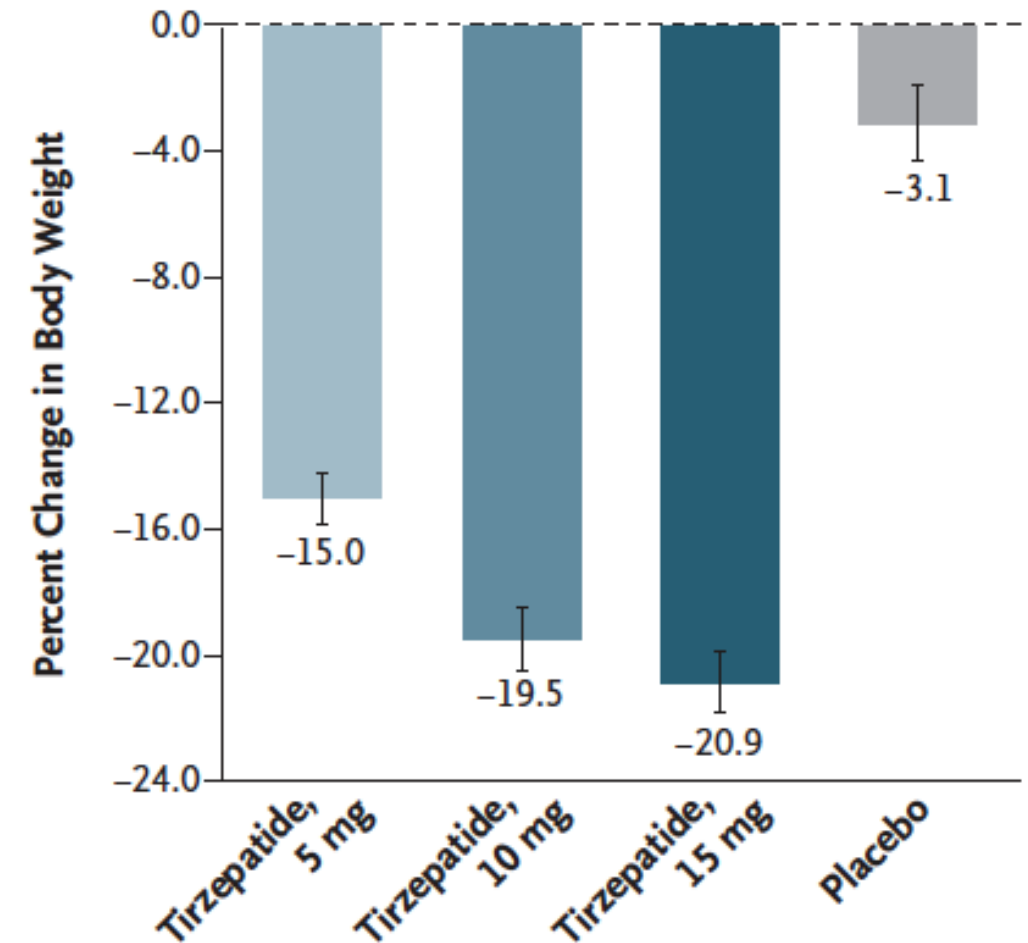
VOL. 387 NO. 3

## Tirzepatide Once Weekly for the Treatment of Obesity

Ania M. Jastreboff, M.D., Ph.D., Louis J. Aronne, M.D., Nadia N. Ahmad, M.D., M.P.H., Sean Wharton, M.D., Pharm.D., Lisa Connery, M.D., Breno Alves, M.D., Arihiro Kiyosue, M.D., Ph.D., Shuyu Zhang, M.S., Bing Liu, Ph.D., Mathijs C. Bunck, M.D., Ph.D., and Adam Stefanski, M.D., Ph.D., for the SURMOUNT-1 Investigators\*

- 2539 adults with BMI 30 or more
  - Or 27 or more with at least 1 weight-related complication, excluding diabetes
- Randomized to Tirzepatide or placebo for 72 weeks
- Mean change of weight with Tirzepatide 5, 10, and 15 mg : 15.0%, 19.5%, and 20.9%
- Adverse events (GI) were mainly during dose escalation but caused discontinuation in 4.3%, 7.1%, and 6.2% of participants receiving 5 mg, 10 mg, and 15 mg doses respectively

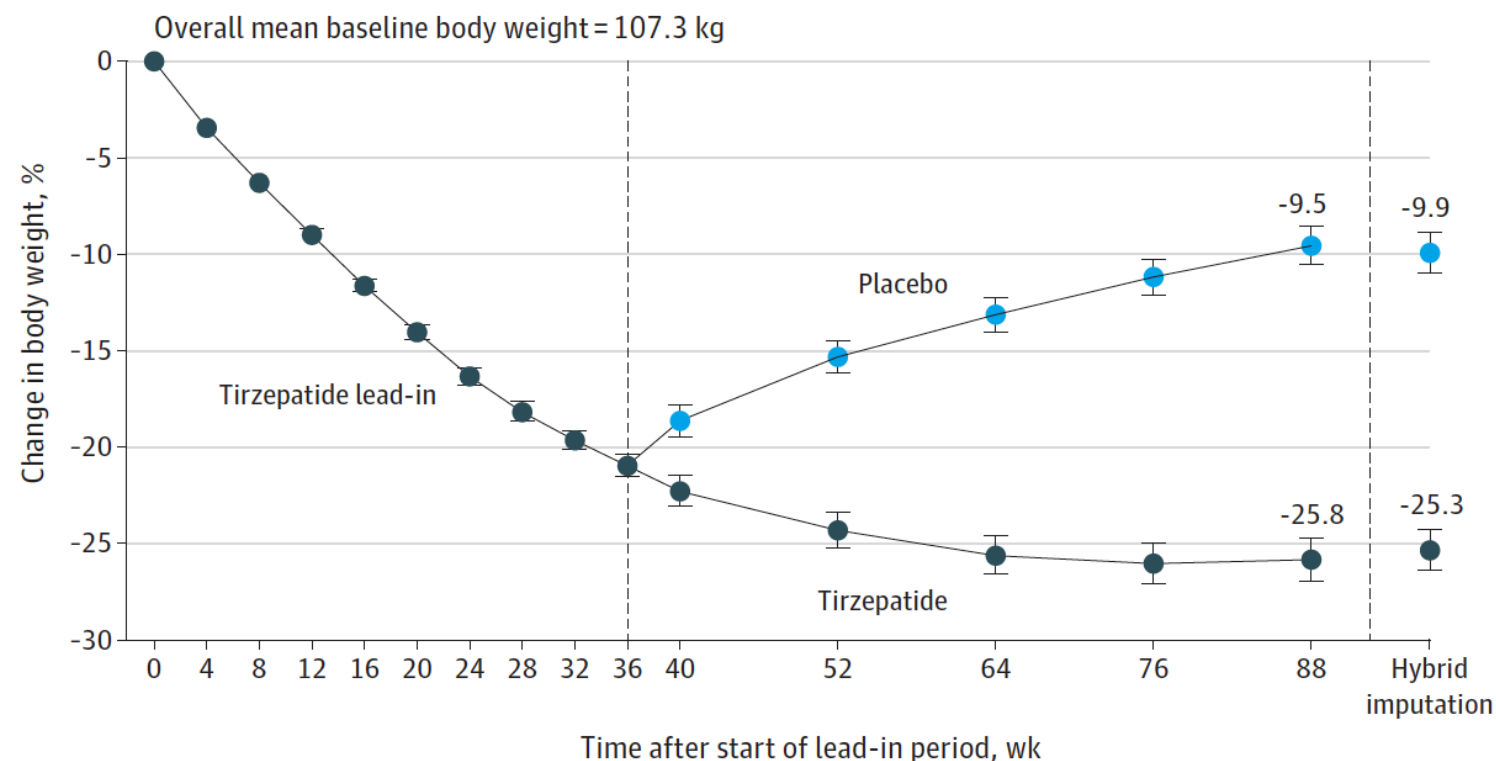
**A Overall Percent Change in Body Weight from Baseline (treatment-regimen estimand)**



# Continued Treatment With Tirzepatide for Maintenance of Weight Reduction in Adults With Obesity

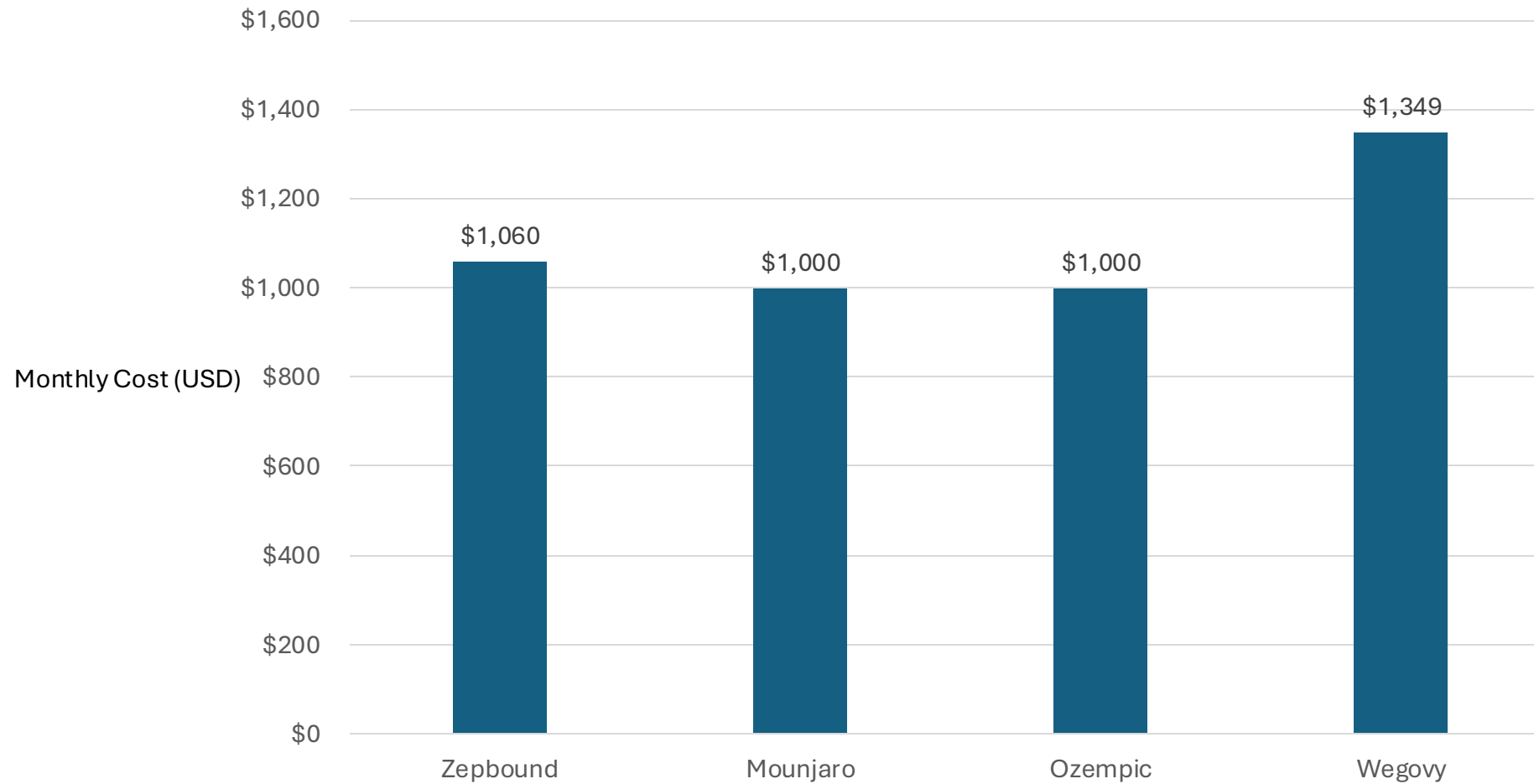
## The SURMOUNT-4 Randomized Clinical Trial

**A** Percent change in body weight (week 0-88)



- 783 patients with 36-week lead in with tirzepatide
- At 36 weeks, 670 participants randomized 1:1 to tirzepatide vs. placebo x 52 weeks (total 88 weeks)
- Mean percent change from week 36 to 88:
  - **Tirzepatide: -5.5%**
  - **Placebo: 14.0%**

# Access to GLP-1RA Medications



# ■ Endoscopic Bariatric Therapies

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## Gastric

————→ Gastric Remodeling  
Outlet Reduction  
Procedureless  
Space Occupying  
Outlet Obstruction  
Aspiration

## Small Bowel

Sleeves  
Duodenal Resurfacing  
Flow altering

# Gastric Remodeling: Endoscopic Sleeve Gastroplasty

- **What is it:**
  - Endoscopically suturing anterior and posterior aspects of the stomach together using the OverStich Device.
  - Created a tubular 'sleeve' appearing stomach to help restrict food intake
  - Outpatient procedure
- **Who Qualifies?**
  - Patients 18 years and older
  - BMI at least 27 kg/m<sup>2</sup>
  - Prior attempts at weight loss were unsuccessful
  - Do not qualify for surgery or do not want surgery
  - Bridge to surgery for patients who do not qualify due to BMI and/or comorbidities

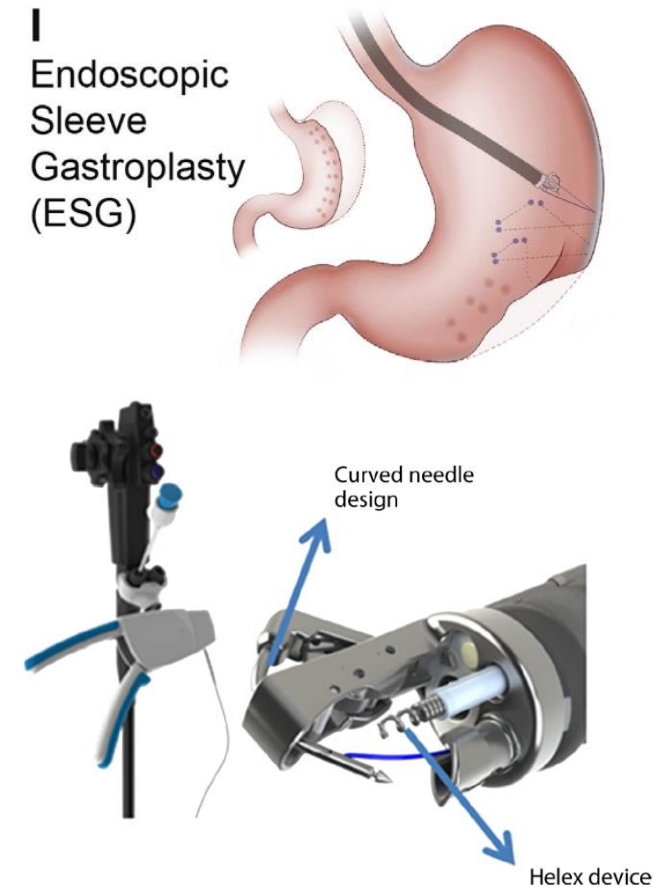
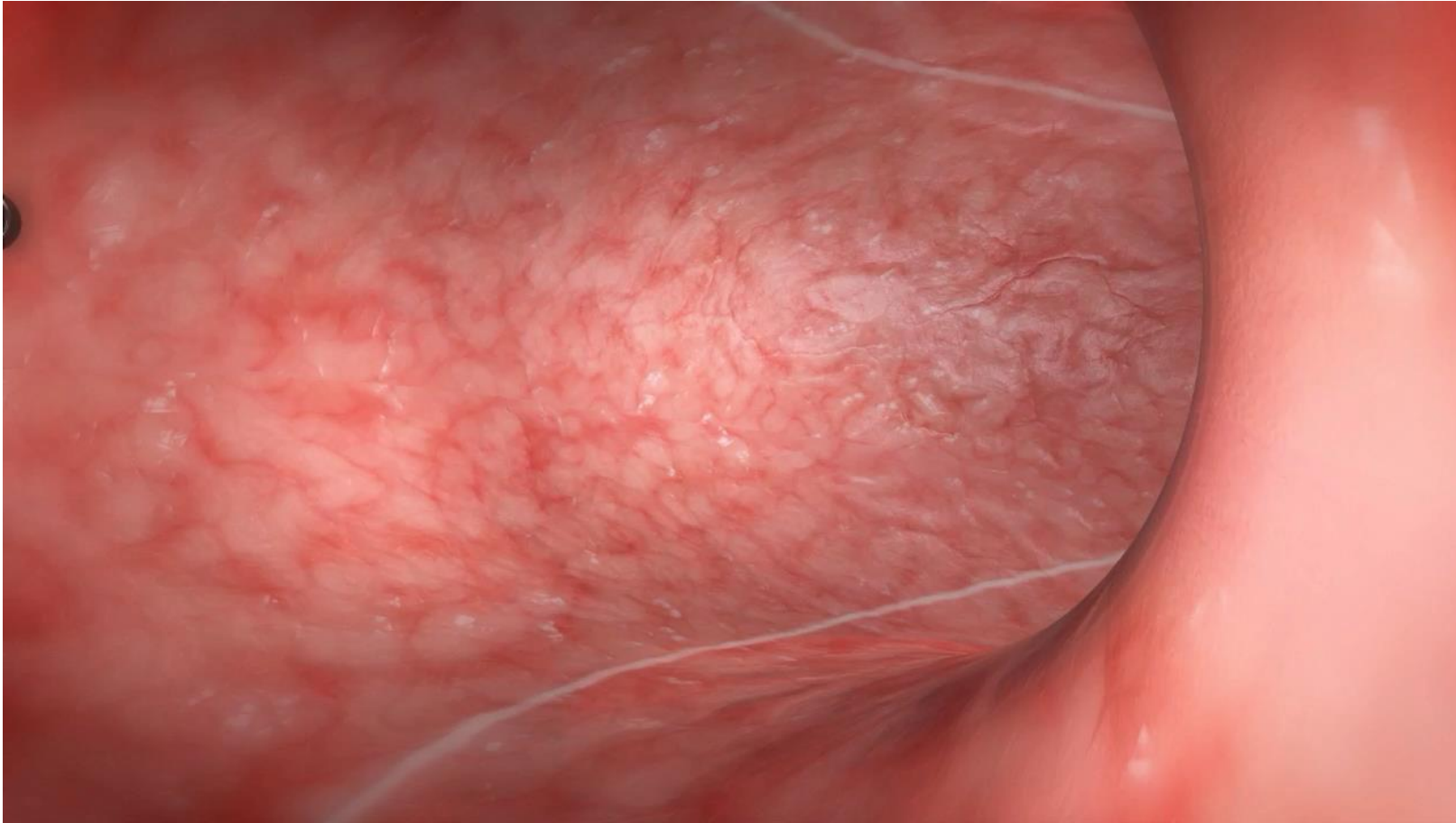
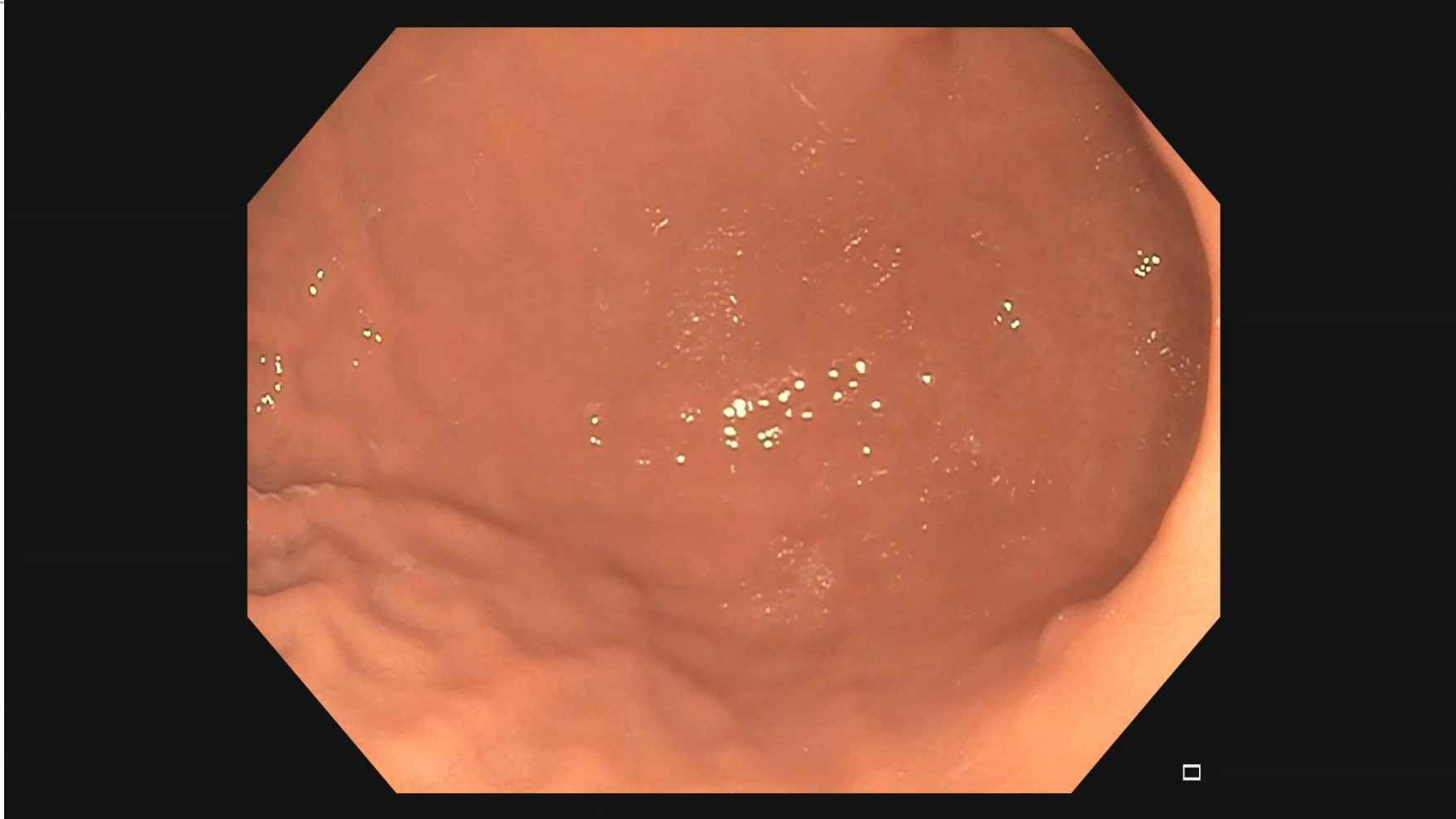


Figure 2. Endoscopic suturing system used in our study.

# ■ Gastric Remodeling: Endoscopic Sleeve Gastroplasty



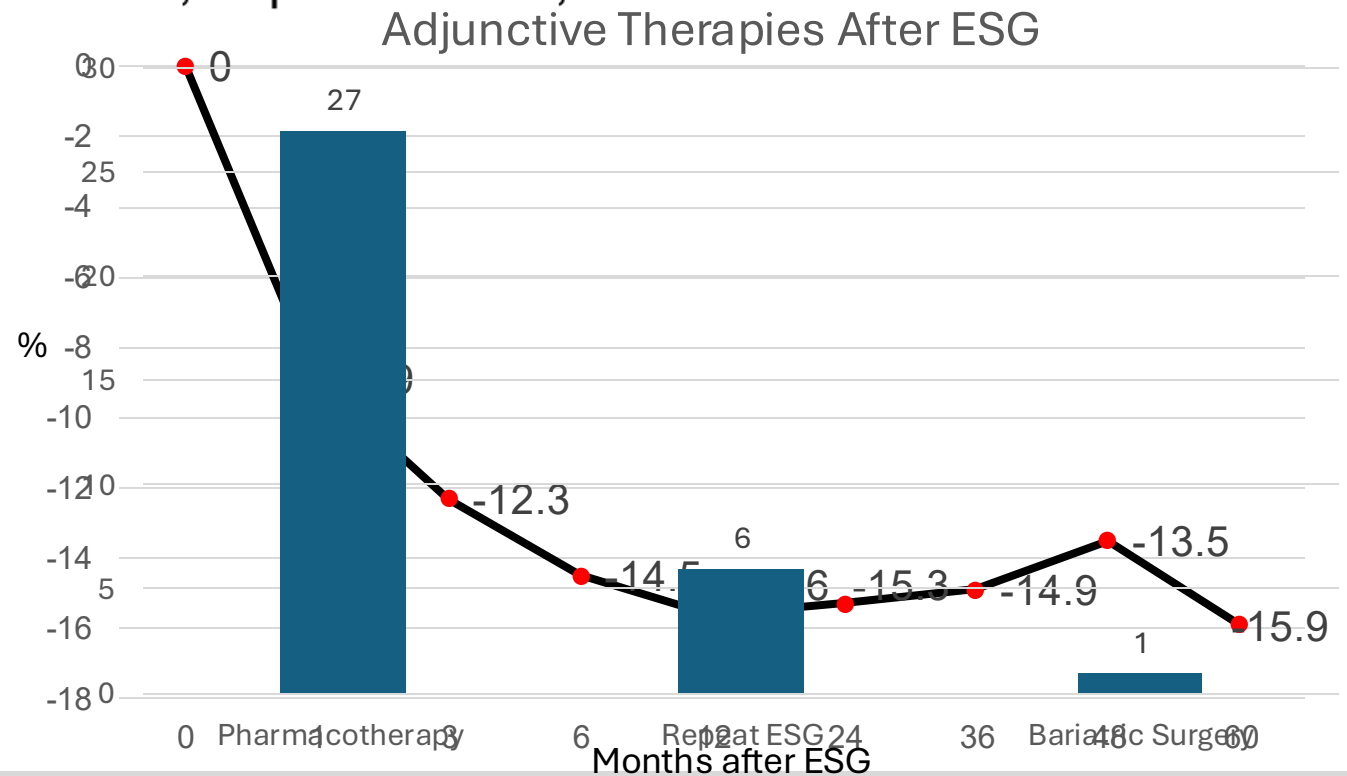
# Gastric Remodeling: Endoscopic Sleeve Gastroplasty



# Five-Year Outcomes of Endoscopic Sleeve Gastroplasty for the Treatment of Obesity

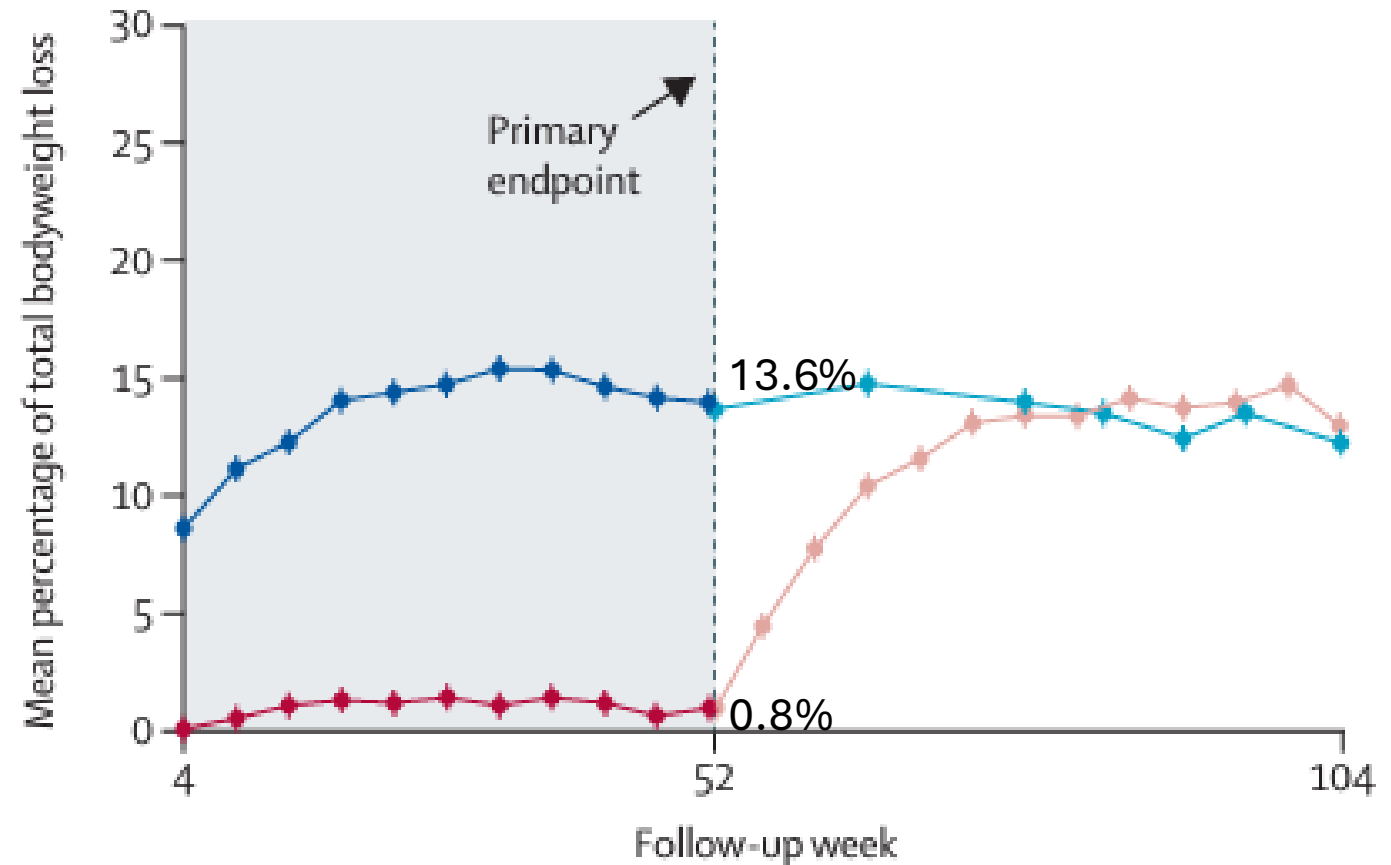
Reem Z. Sharaiha,<sup>\*</sup> Kaveh Hajifathalian,<sup>\*</sup> Rekha Kumar,<sup>‡</sup> Katherine Saunders,<sup>‡</sup> Amit Mehta,<sup>\*</sup> Bryan Ang,<sup>§</sup> Daniel Skaf,<sup>§</sup> Shawn Shah,<sup>\*</sup> Andrea Herr,<sup>\*</sup> Leon Igel,<sup>‡</sup> Qais Dawod,<sup>\*</sup> Enad Dawod,<sup>§</sup> Kartik Sampath,<sup>\*</sup> David Carr-Locke,<sup>\*</sup> Robert Brown,<sup>\*</sup> David Cohen,<sup>\*</sup> Andrew J. Dannenberg,<sup>||</sup> Srihari Mahadev,<sup>\*</sup> Alpana Shukla,<sup>‡</sup> and Louis J. Aronne<sup>‡</sup>

- August 2013 to August 2019
- 216 patients mean BMI 39 kg/m<sup>2</sup>
- At 5 years, TBWL was 15.9% (n=68)
- Adverse Events:
  - Mild AE : 32%
  - Moderate AE: 1.3%

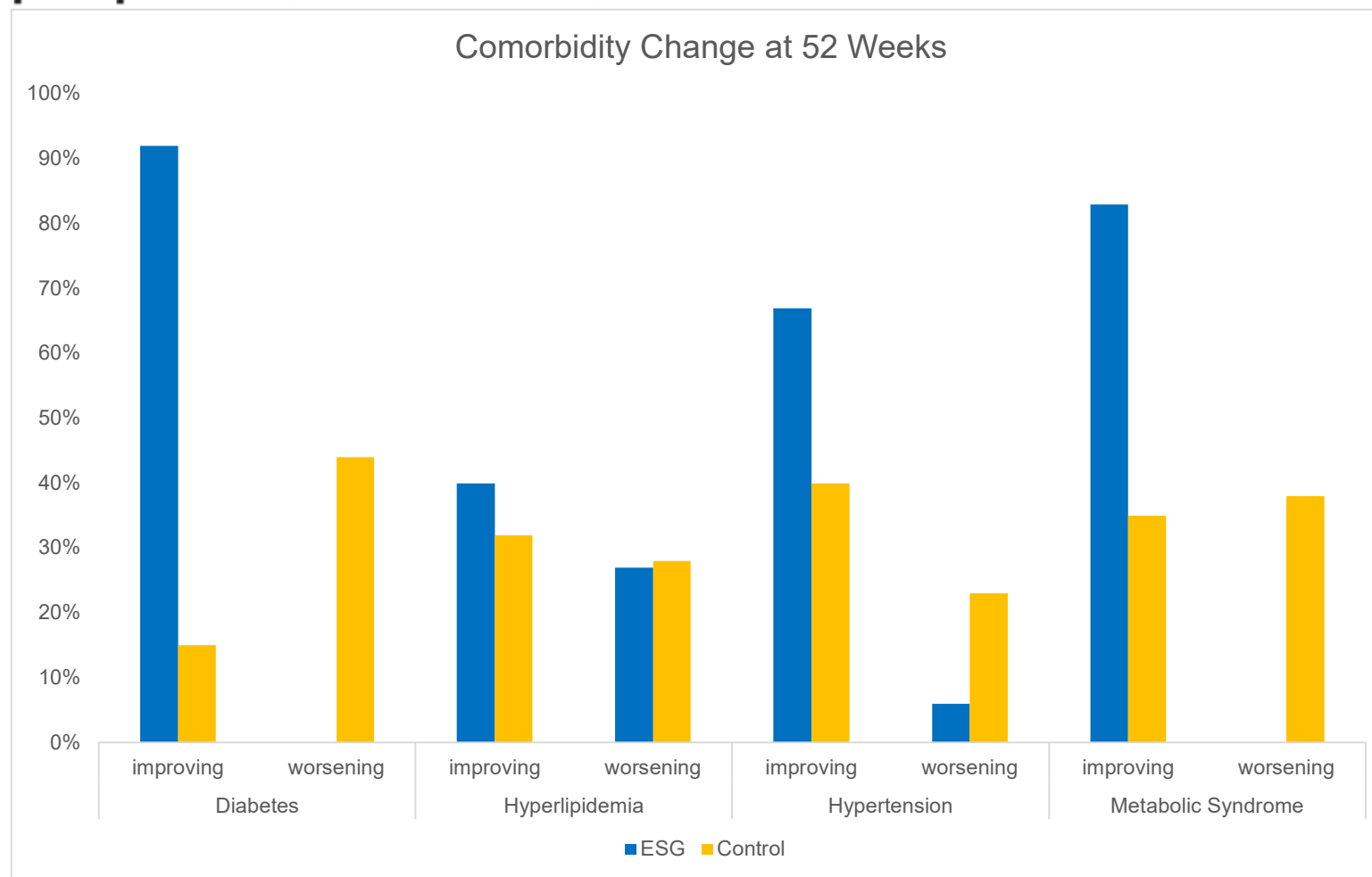


# Endoscopic sleeve gastroplasty for treatment of class 1 and 2 obesity (MERIT): a prospective, multicentre, randomised trial

- MERIT trial : first randomized controlled trial on ESG
- US Centers, 21-65 years of age with class 1 or 2 obesity
- ESG with lifestyle modifications (n=68) vs. lifestyle modifications only (n=89)
- Allowed for potential retightening or crossover to ESG at 52 weeks



# Endoscopic sleeve gastroplasty for treatment of class 1 and 2 obesity (MERIT): a prospective, multicentre, randomised trial

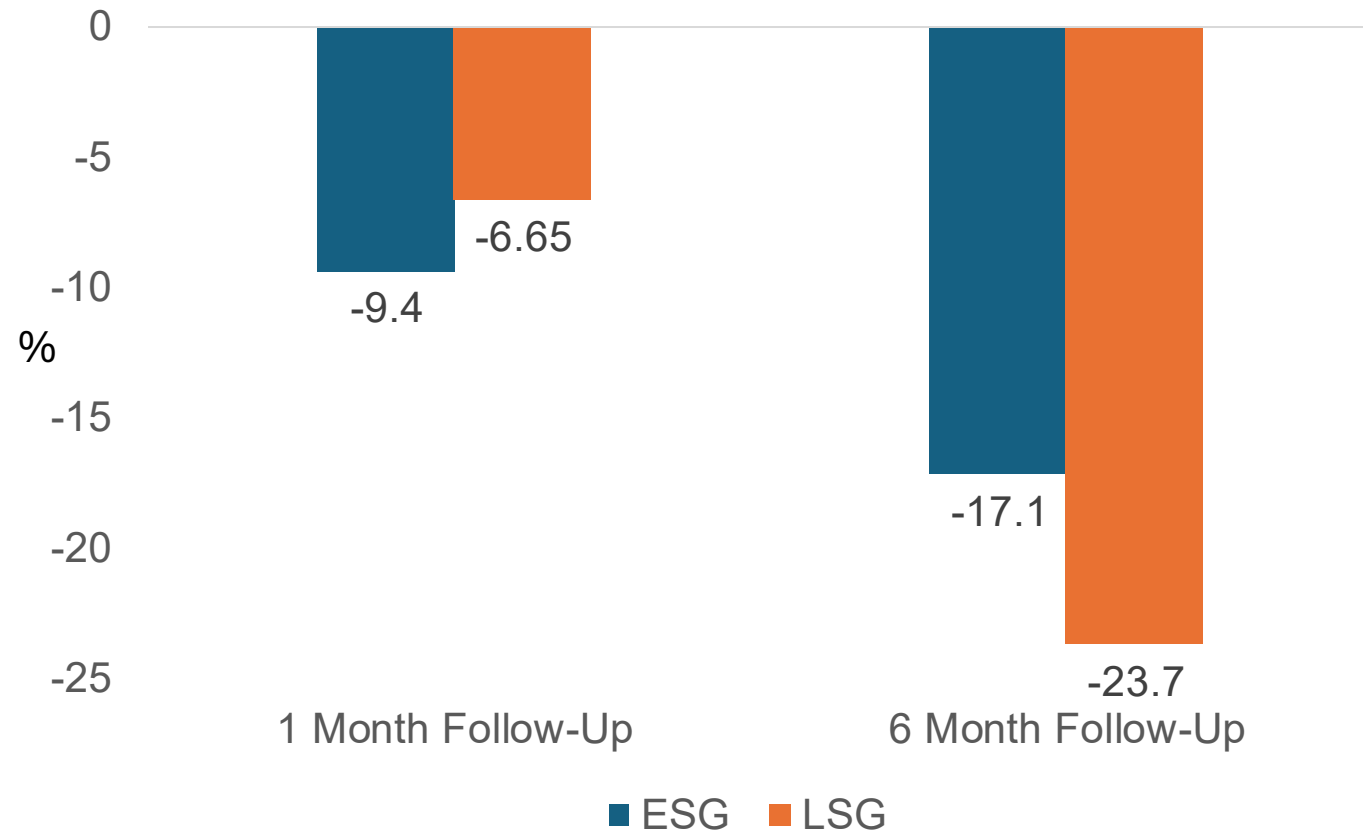


# Endoscopic sleeve gastroplasty versus laparoscopic sleeve gastrectomy: a case-matched study

Lea Fayad, MD,<sup>1</sup> Atif Adam, MD, MPH, PhD,<sup>2</sup> Michael Schweitzer, MD,<sup>3</sup>  
Lawrence J. Cheskin, MD, FACP, FTOS,<sup>4</sup> Tokunbo Ajayi, MD,<sup>5</sup> Margo Dunlap, BSN,<sup>1</sup>  
Dilhana S. Badurdeen, MD,<sup>1</sup> Christine Hill, BA, BS,<sup>4</sup> Neethi Paranj, MD,<sup>1</sup> Sepehr Lalezari, MD,<sup>3</sup>  
Anthony N. Kalloo, MD,<sup>1</sup> Mouen A. Khashab, MD,<sup>1</sup> Vivek Kumbhari, MD<sup>1</sup>

Baltimore, Maryland, USA

- Retrospective study matched for age, sex, and BMI
- 52 ESG patients matched to 83 LSG patients
- At 6-months, LSG patients with greater TBWL as compared to ESG group
- New onset GERD lower in ESG group (1.9%) as compared to LSG group (14.5%)



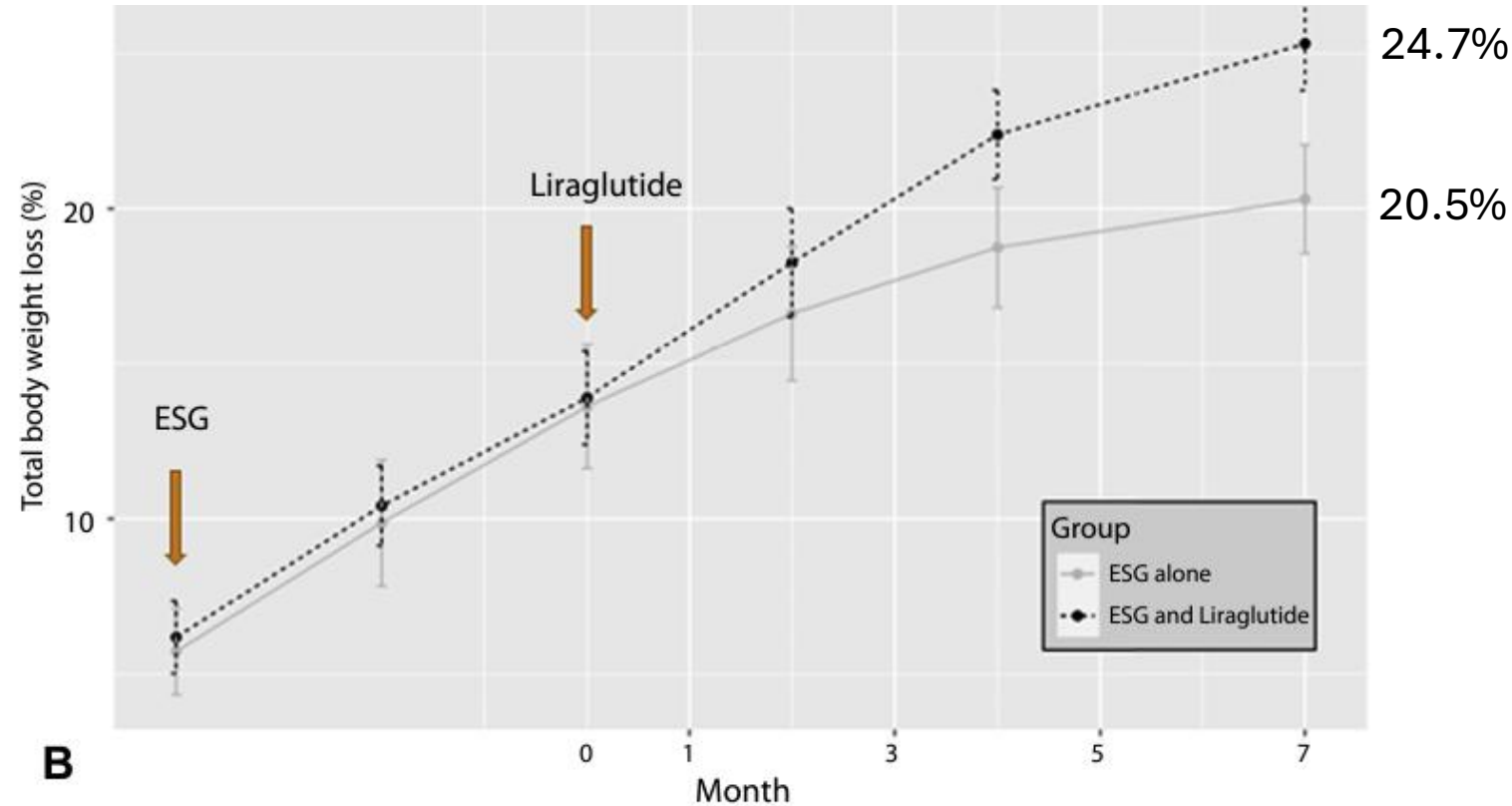
# Endoscopic sleeve gastroplasty plus liraglutide versus endoscopic sleeve gastroplasty alone for weight loss

CME



Dilhana Badurdeen, MD,<sup>1</sup> Anna Carolina Hoff, MD,<sup>2</sup> Abdellah Hedjoudje, MD, MSc,<sup>1</sup> Atif Adam, PhD, MD,<sup>1</sup> Mohamad I. Itani, MD,<sup>1</sup> Jad Farha, MD,<sup>1</sup> Shahem Abbarh, MBBS,<sup>1</sup> Anthony N. Kalloo, MD,<sup>1</sup> Mouen A. Khashab, MD,<sup>1</sup> Vikesh K. Singh, MD, MSc,<sup>1</sup> Andrea Oberbach, MD, PhD, MPH,<sup>1</sup> Manoel Galvao Neto, MD,<sup>3</sup> Sergio Barrichello, MD,<sup>4</sup> Vivek Kumbhari, MD, PhD<sup>1</sup>

- Retrospective study at 3 outpatient centers
- Liraglutide offered to all patients 5 months after ESG
- ESG-L patients matched 1:1 to ESG only patients



# Cost-effectiveness of endoscopic, surgical and pharmacological obesity therapies: a microsimulation and threshold analyses

Monica Saumoy,<sup>1</sup> Devika Gandhi,<sup>2</sup> Seth Buller,<sup>3</sup> Shae Patel,<sup>3</sup> Yecheskel Schneider,<sup>4</sup> Gregory Cote,<sup>5</sup> Michael L Kochman,<sup>6,7</sup> Nikhil R Thiruvengadam ,<sup>2</sup> Reem Z Sharaiha <sup>8</sup>

Key Takeaways:

- Class I obesity: ESG
- Class II/III obesity: SG
- Semaglutide not cost-effective
- Cost of semaglutide to be cost-effective (annual):
  - Class I: \$5149
  - Class II: \$5847
  - Class III: \$7462

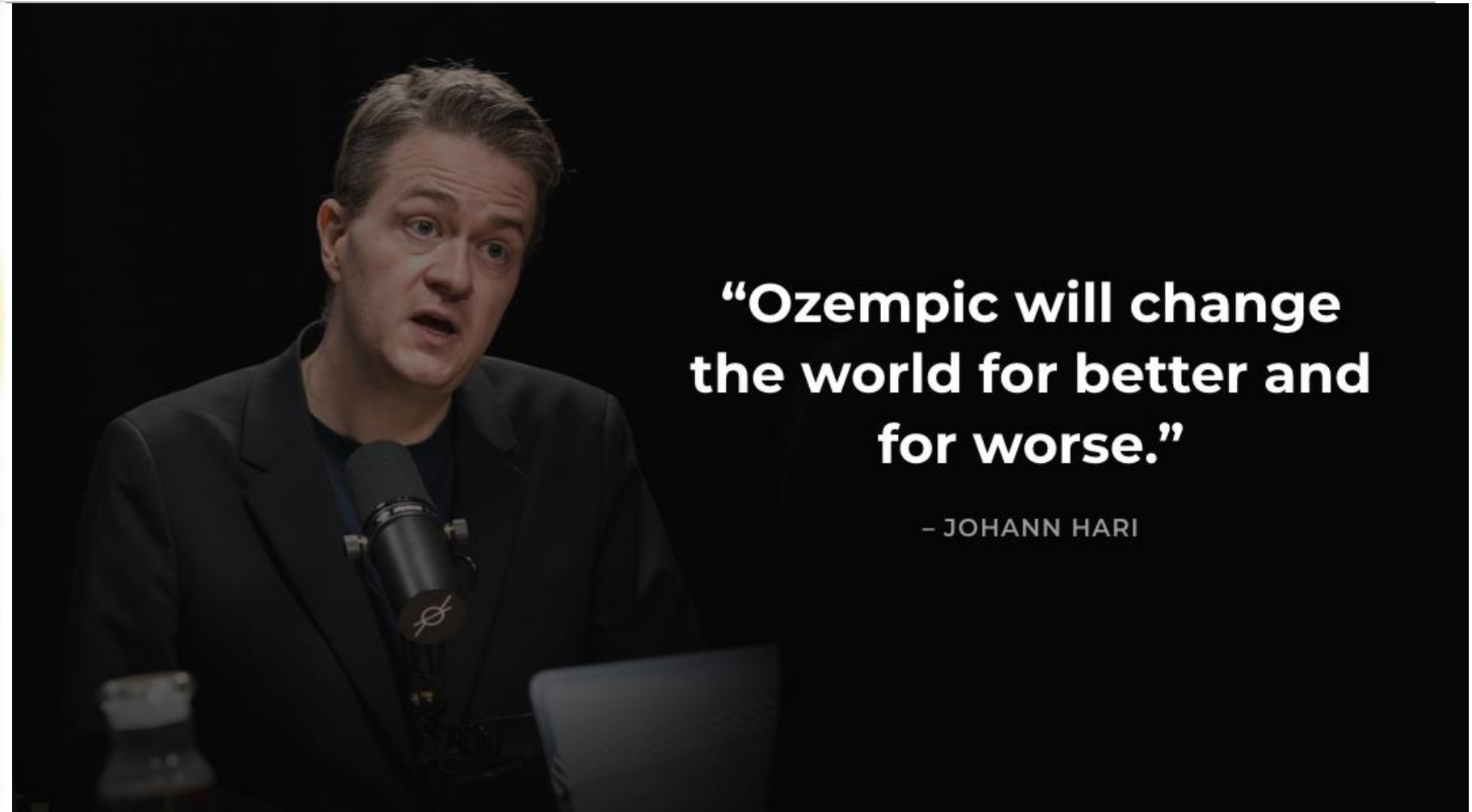
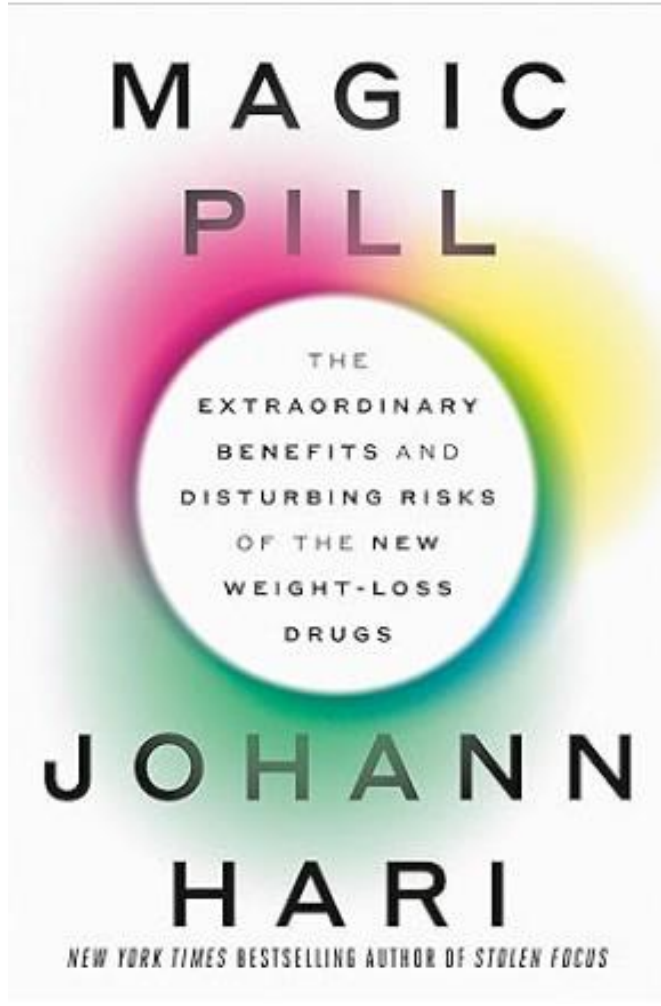
Table 2 Detailed analysis of outcomes and cost-effectiveness of weight management strategies							
Strategy*	Cost (2021 US\$)	Incr cost	Life-years lost due to obesity	Life-years gained†	Utility (QALY)	Incr utility	Incremental cost/QALY (ICER)
Patients with class I obesity (BMI 33)							
LI	124 195	--	0.858	--	15.634	--	
ESG	126 732	2537	0.501	0.358	16.252	0.618	4105
SG	139 971	13 239	0.468	0.391	16.372	0.120	110 325
Semaglutide	370 776	230 805	0.670	0.188	16.119	−0.253	Strong dominance‡
Patients with class II obesity (BMI 37)							
LI	142 606	--	1.560	--	14.828	--	
ESG	149 932	7326	0.967	0.592	15.474	0.642	Extended dominance§
SG	150 818	8212	0.555	1.005	16.224	1.396	5883
Semaglutide	389 008	238 190	1.082	0.477	15.414	−0.81	Strong dominance‡
Patients with class III obesity (BMI 44)							
LI	177 449	--	2.610	--	13.765	--	
ESG	183 355	5856	1.805	0.805	14.478	0.713	Extended dominance§
SG	188 844	11 395	1.198	1.412	15.222	1.457	7821
Semaglutide	409 571	220 727	1.976	0.634	14.427	−0.795	Strong dominance‡

# Insurance Coverage for ESG

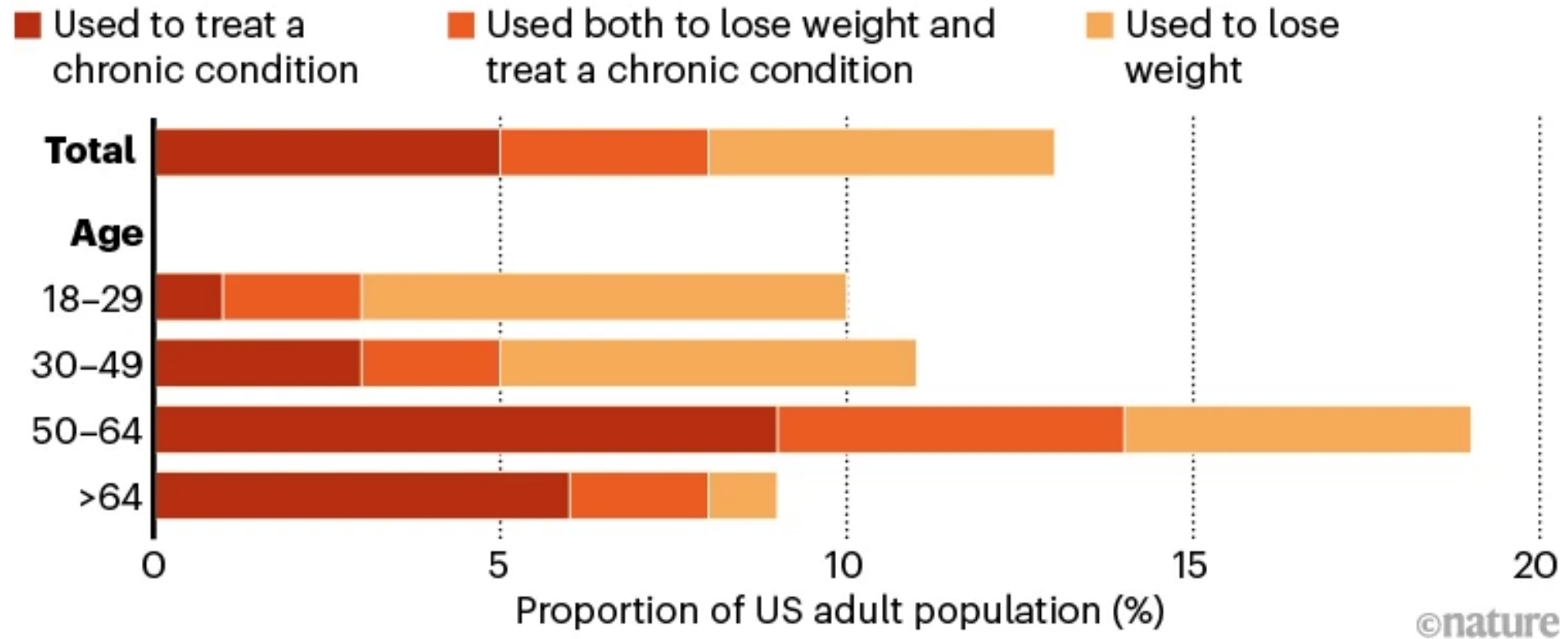
**Table 1.** Frequency of coverage for primary and secondary bariatric therapy and documented requirements for covering revisional therapy among the top 25 insurers

	Covered	Not covered	
Primary Therapy			
ESG, n (%)	0 (0)	25 (100)	0.001
IGB, n (%)	0 (0)	25 (100)	0.001
Revisional Therapy			
Revision of sleeve gastrectomy, n (%)	7 (28)	18 (72)	0.001
Transoral outlet reduction, n (%)	7 (28)	18 (72)	0.001
Surgical revision, n (%)	20 (80)	5 (20)	0.05

# ■ Does ESG have a future?

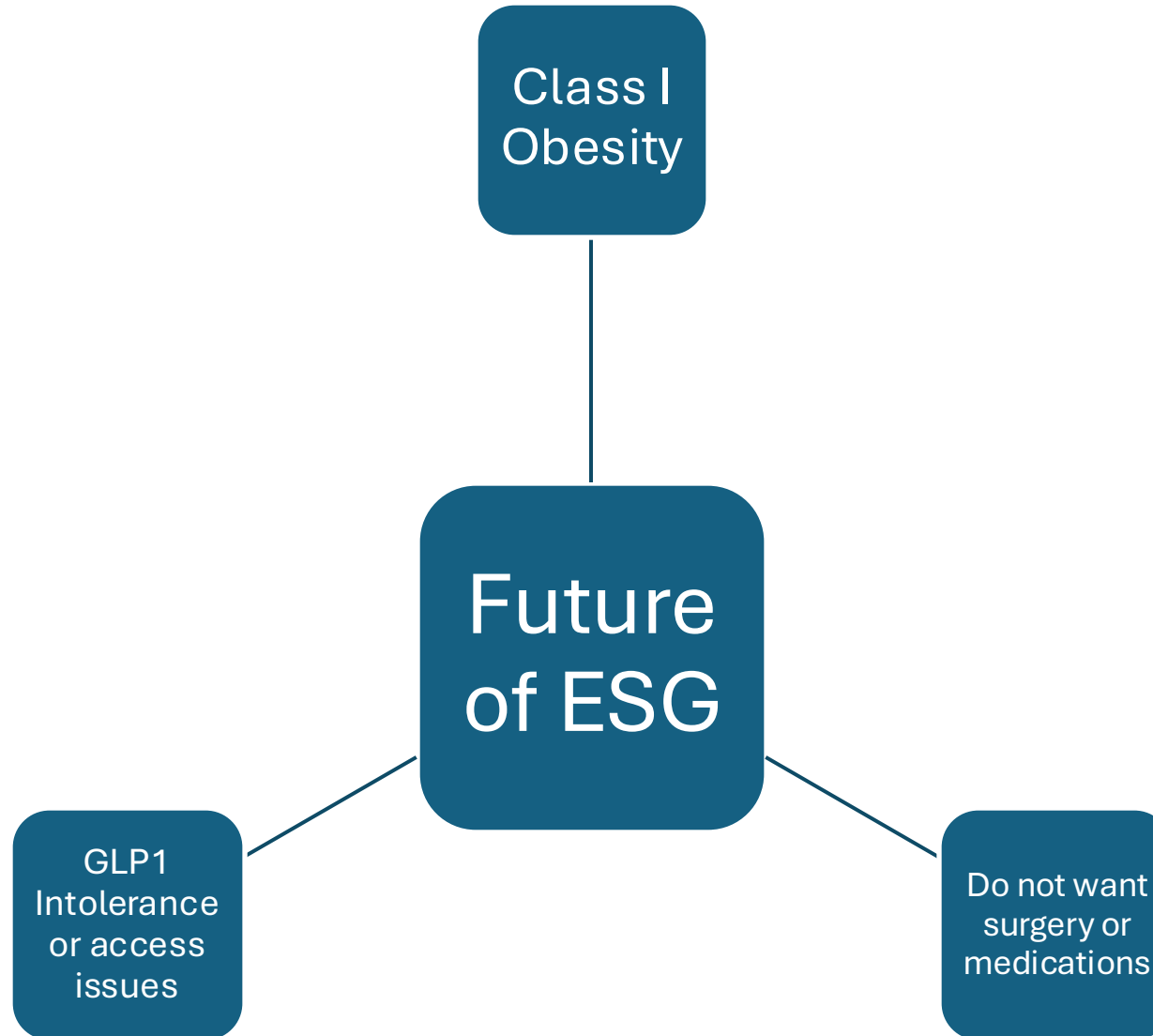


# Does ESG have a future?



# Does ESG have a future?

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# ■ Endoscopic Bariatric Therapies

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## Gastric

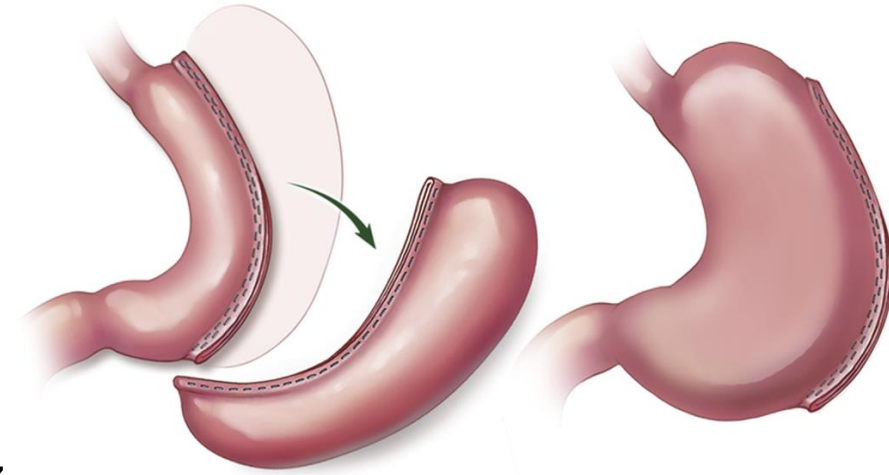
→ Gastric Remodeling  
Outlet Reduction  
Procedureless  
Space Occupying  
Outlet Obstruction  
Aspiration

## Small Bowel

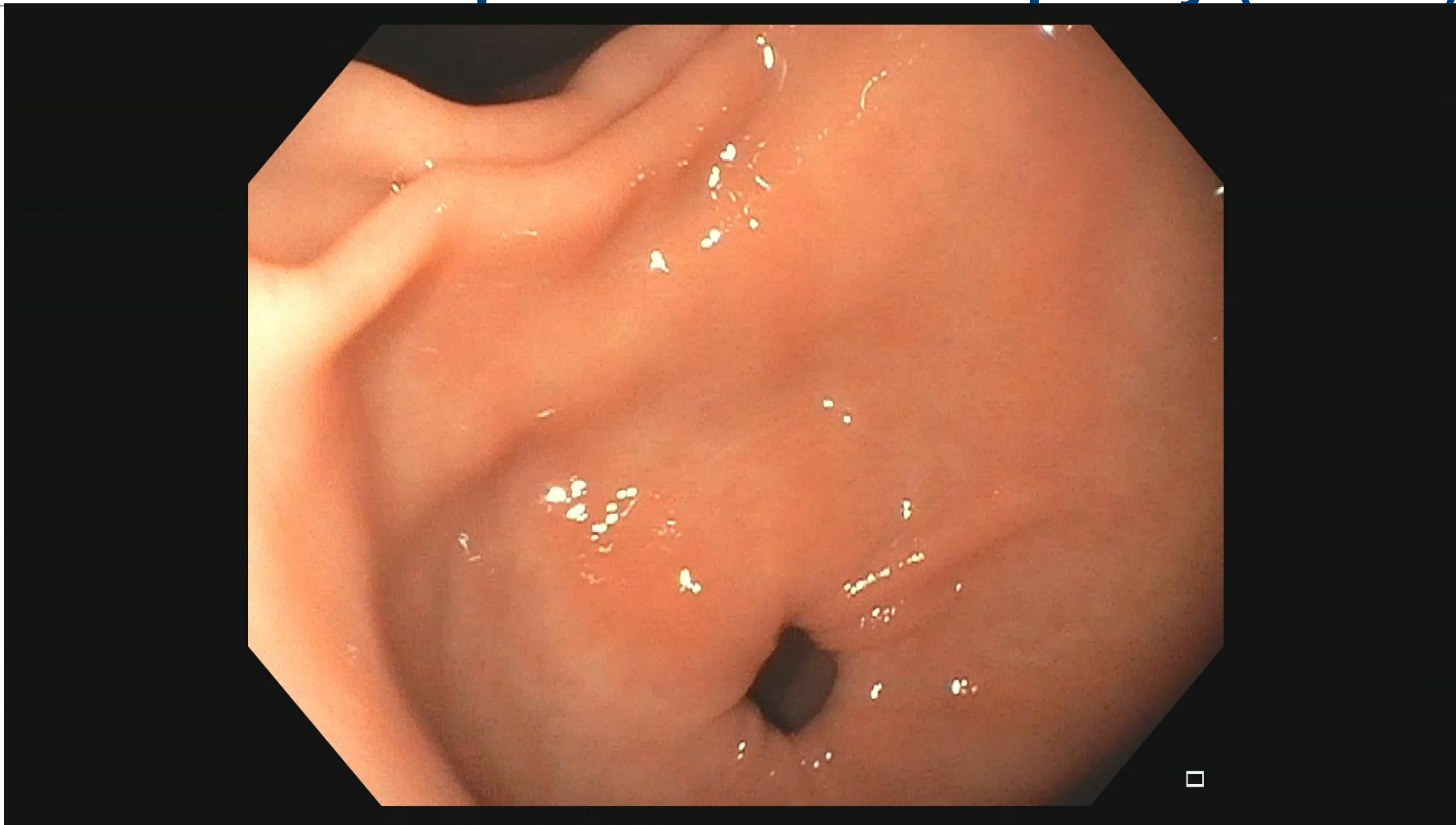
Sleeves  
Duodenal Resurfacing  
Flow altering

# ■ Revisional Endoscopic Sleeve Gastroplasty (r-ESG)

- **What is it:**
  - Reduction of a dilated laparoscopic sleeve gastrectomy using the approach used for an ESG
  - Aims to reduce the volume of the dilated gastric sleeve and shorten its length.
- **Who Qualifies?**
  - Weight recurrence or inadequate weight loss after laparoscopic sleeve gastrectomy with a BMI of at least 27 kg/m<sup>2</sup>
  - High risk for surgical revision to Roux-en-Y gastric bypass or do not want to pursue surgery



## ■ Revisional Endoscopic Sleeve Gastroplasty (r-ESG): Video

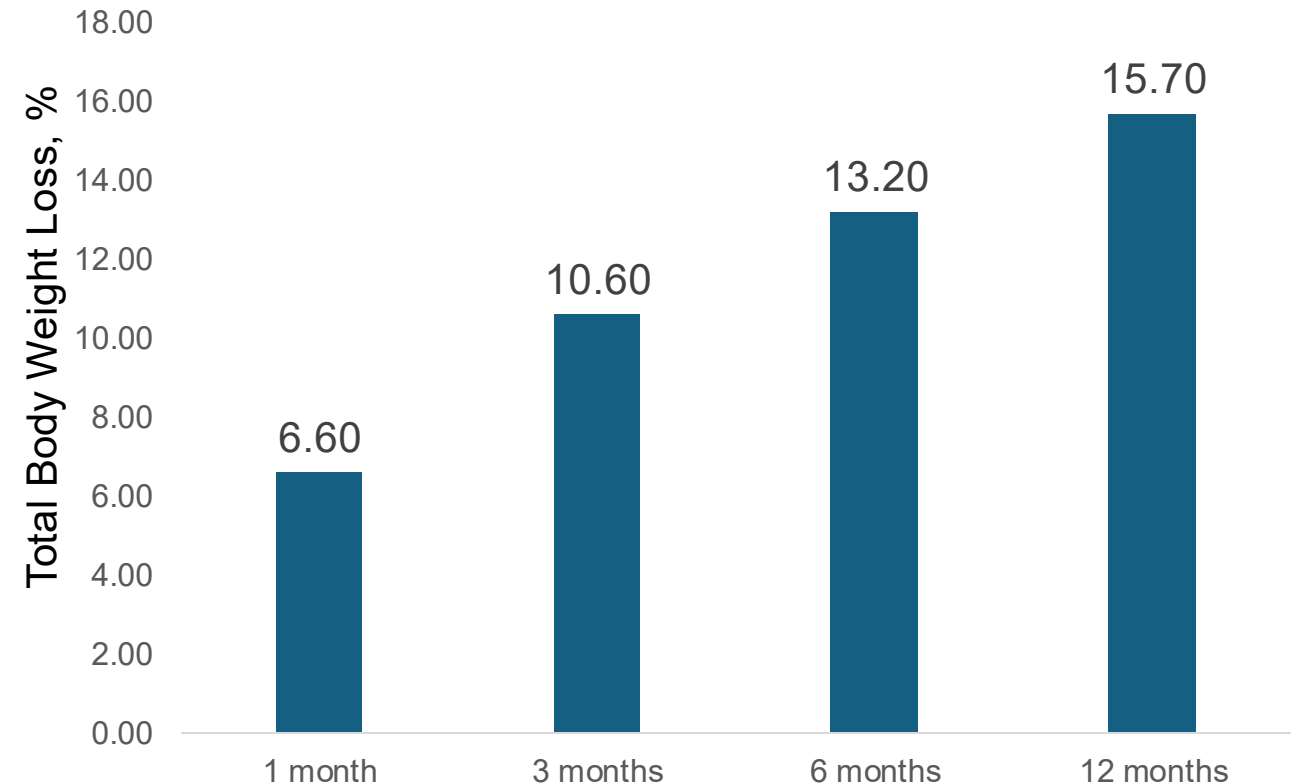


# Revisional endoscopic sleeve gastroplasty of laparoscopic sleeve gastrectomy: an international, multicenter study



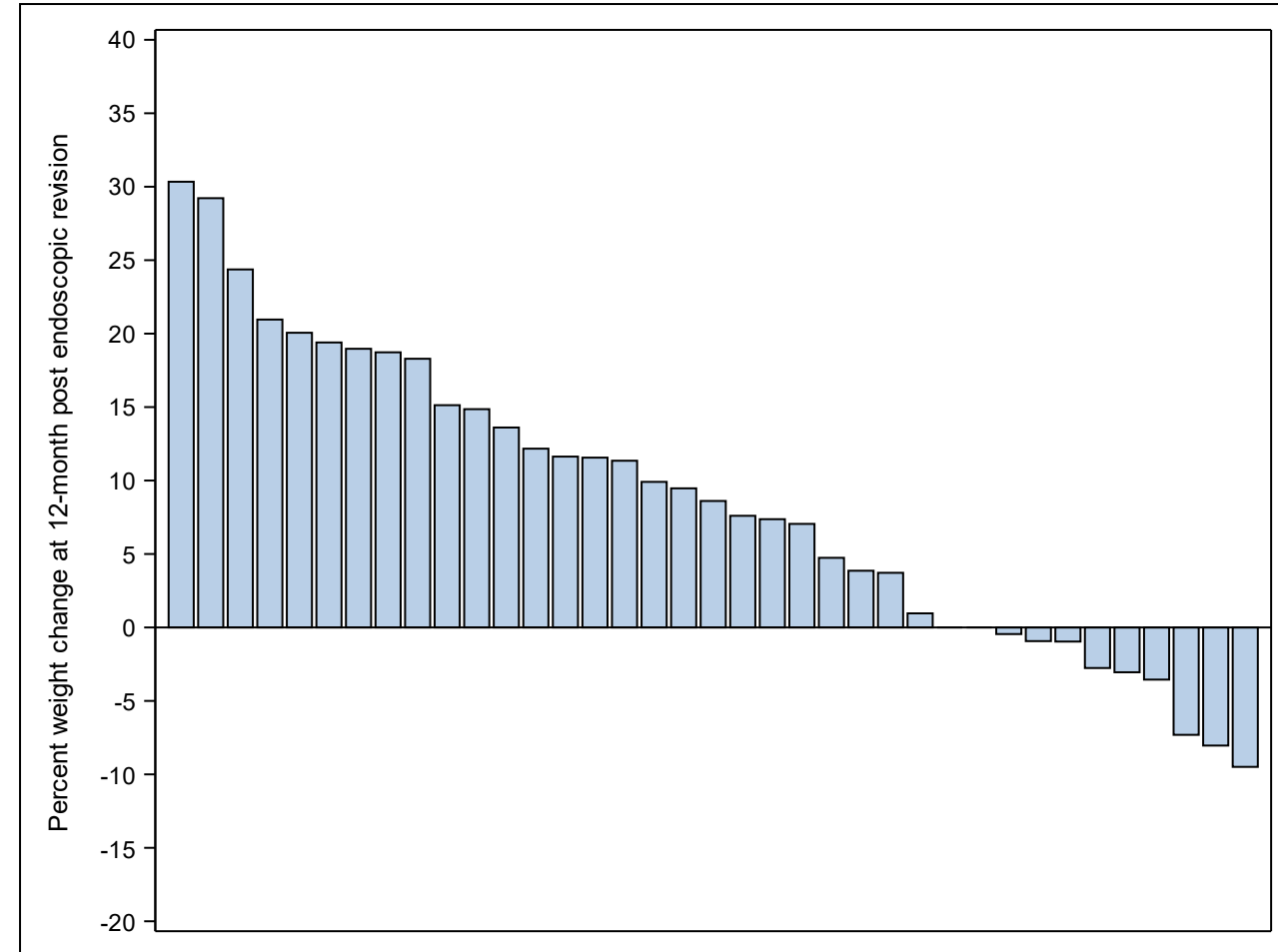
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- Multicenter study with 82 adults who underwent r-ESG for weight recurrence after LSG
- 27.9 kg weight recurrence and mean weight of 128.2 kg
- TBWL at 1, 3, 6, and 12 months
- 13/82 (15.9%) patients started on anti-obesity medications after r-ESG to augment weight loss

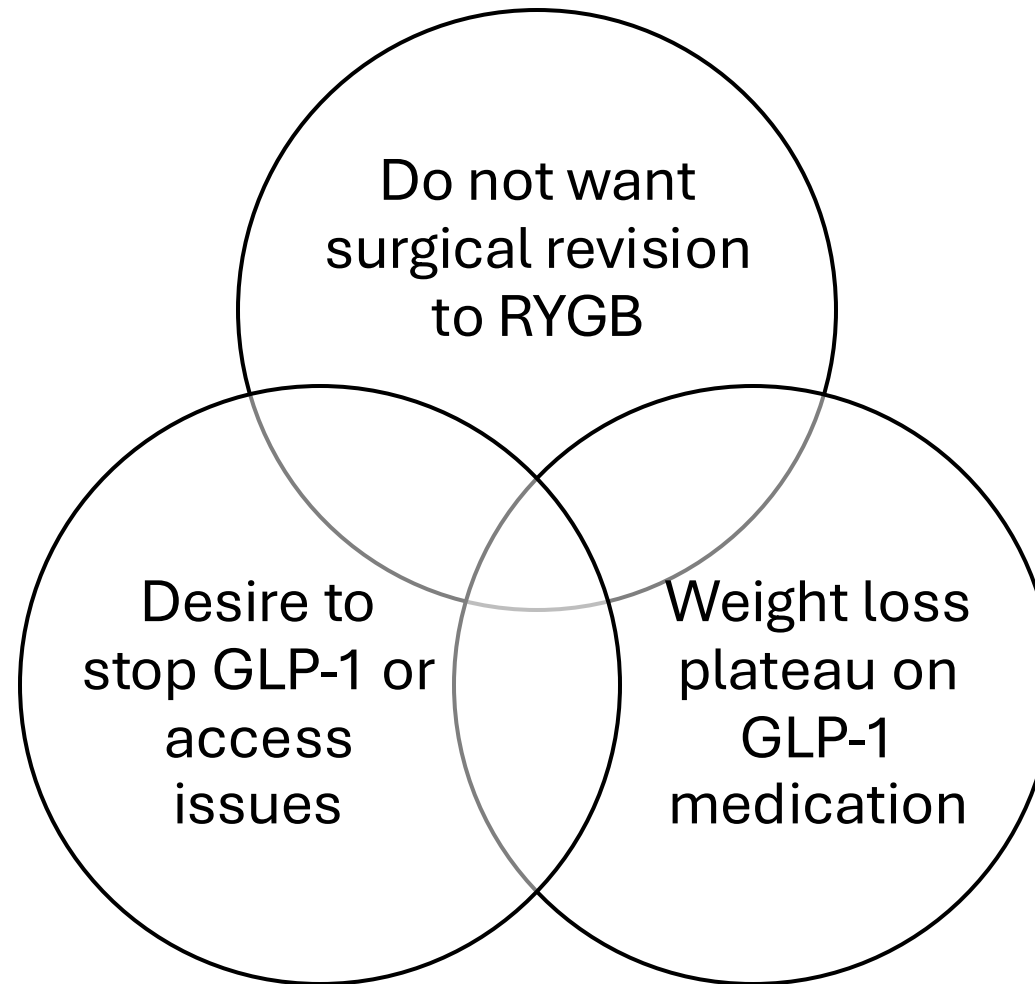


# UTSW r-ESG experience

- 55 patients who underwent r-ESG from December 2020 to November 2023
- TBWL at 12-months was 8.6% (n= 37) , 10.7% at 18-months (n= 31), 12.6% at 24 months
- Other Key Points:
  - 65% of persons were on GLP-1s at time of procedure.



## R-ESG in the GLP-1 Era: Who Benefits?



# ■ Endoscopic Bariatric Therapies

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## Gastric

→ Gastric Remodeling  
Outlet Reduction  
Procedureless  
Space Occupying  
Outlet Obstruction  
Aspiration

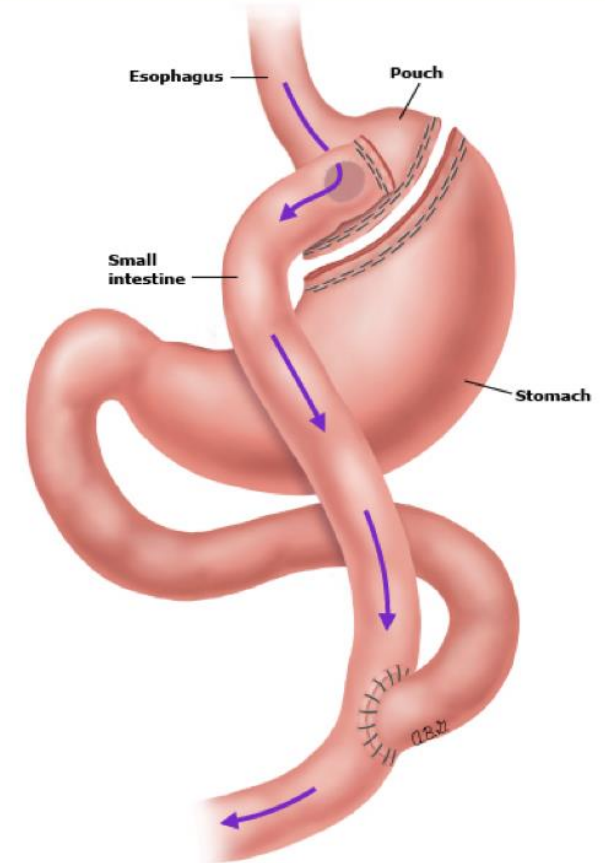
## Small Bowel

Sleeves  
Duodenal Resurfacing  
Flow altering

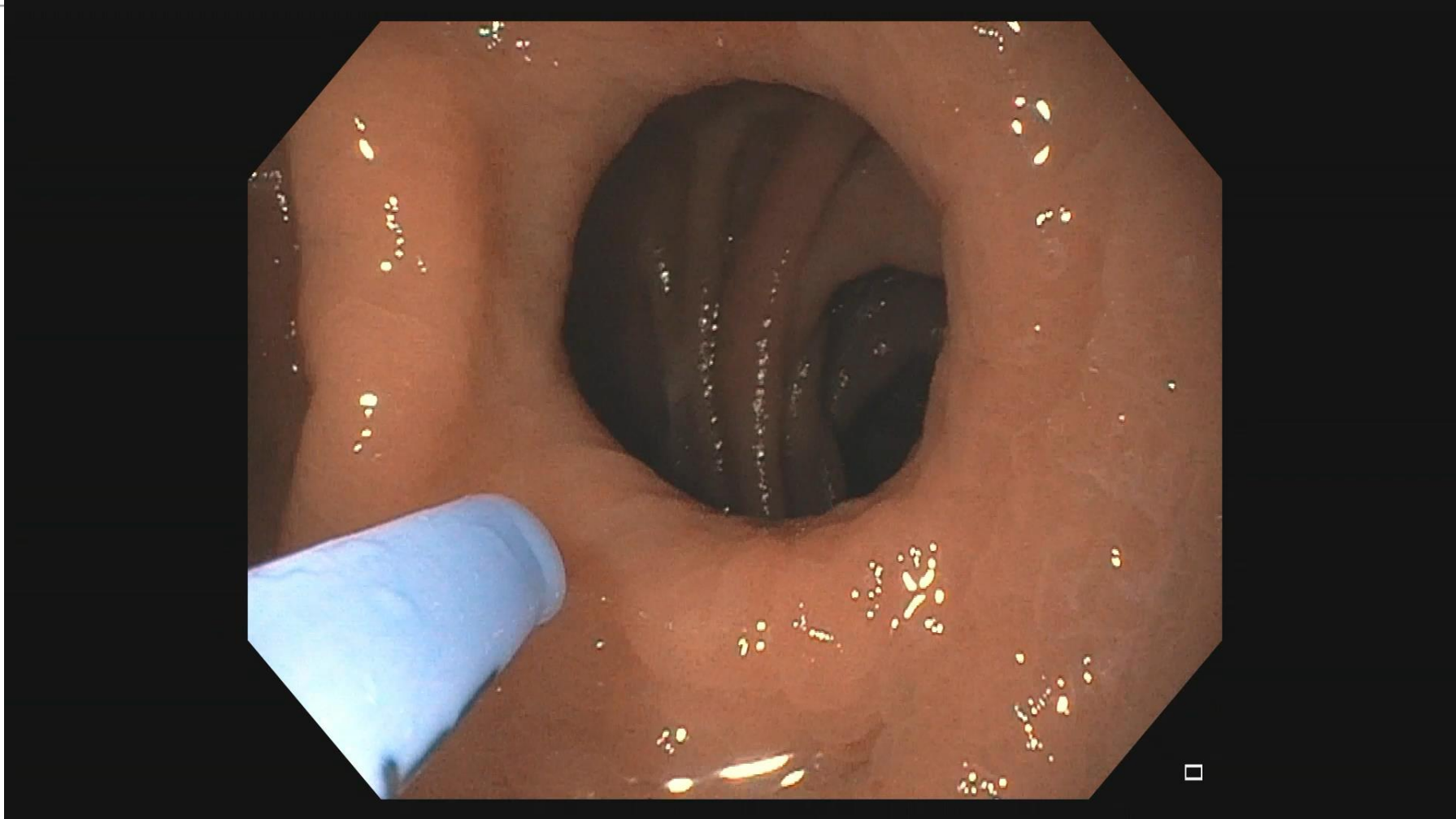
# ■ Transoral Gastric Outlet Reduction (TORE)

- **What is it:**
  - Transoral outlet reduction (TORe) uses APC and the OverStich Device to reduce the size of the GJ anastomosis.
- **Who Qualifies?**
  - Weight recurrence or inadequate weight loss after Roux-en-Y gastric bypass with BMI of at least 27 kg/m<sup>2</sup>
  - Dumping syndrome and/or reactive hypoglycemia after Roux-en-Y gastric bypass
  - Dilated gastrojejunal anastomosis

Roux-en-Y gastric bypass



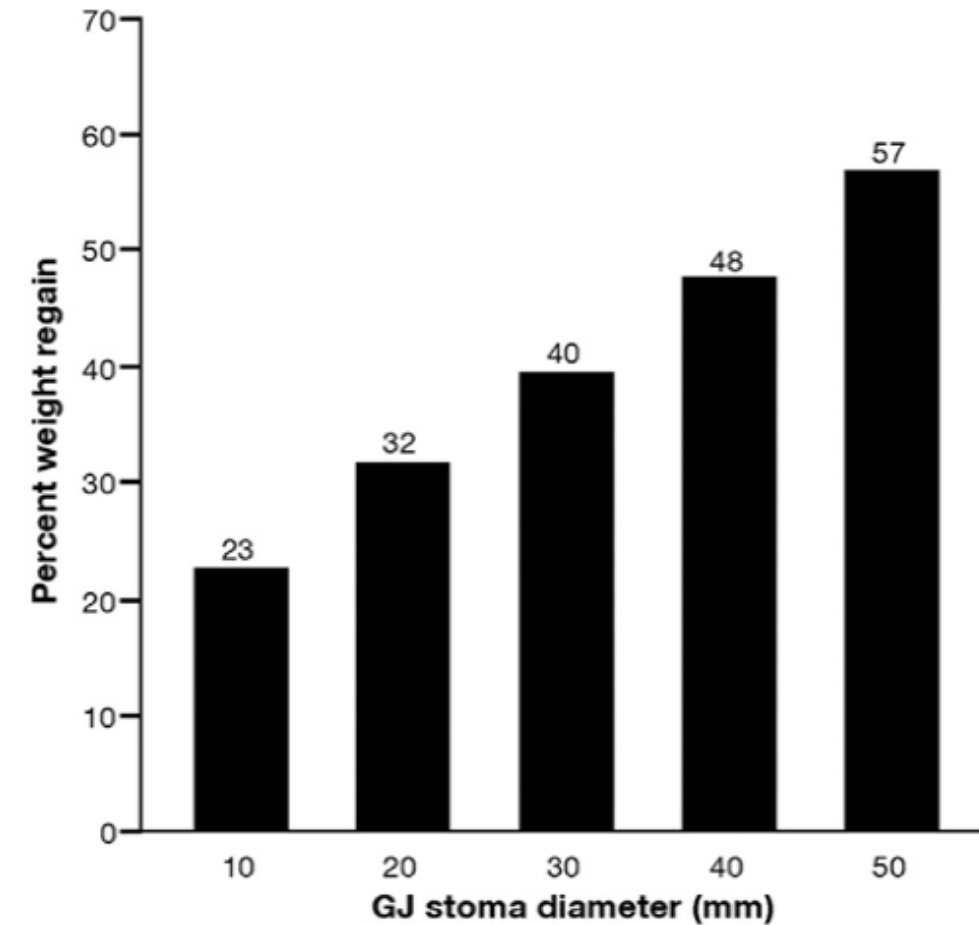
## ■ Transoral Gastric Outlet Reduction (TORE): Video



# Gastrojejunal Stoma Diameter Predicts Weight Regain After Roux-en-Y Gastric Bypass

BARHAM K. ABU DAYYEH,<sup>\*,‡</sup> DAVID B. LAUTZ,<sup>§</sup> and CHRISTOPHER C. THOMPSON<sup>‡,||</sup>

- 165 patients with weight recurrence after gastric bypass
- At 5 years after RYGB, each 10-mm increase in the GJ stoma diameter was associated with an 8% increase in the percentage of maximal weight loss after RYGB that was regained



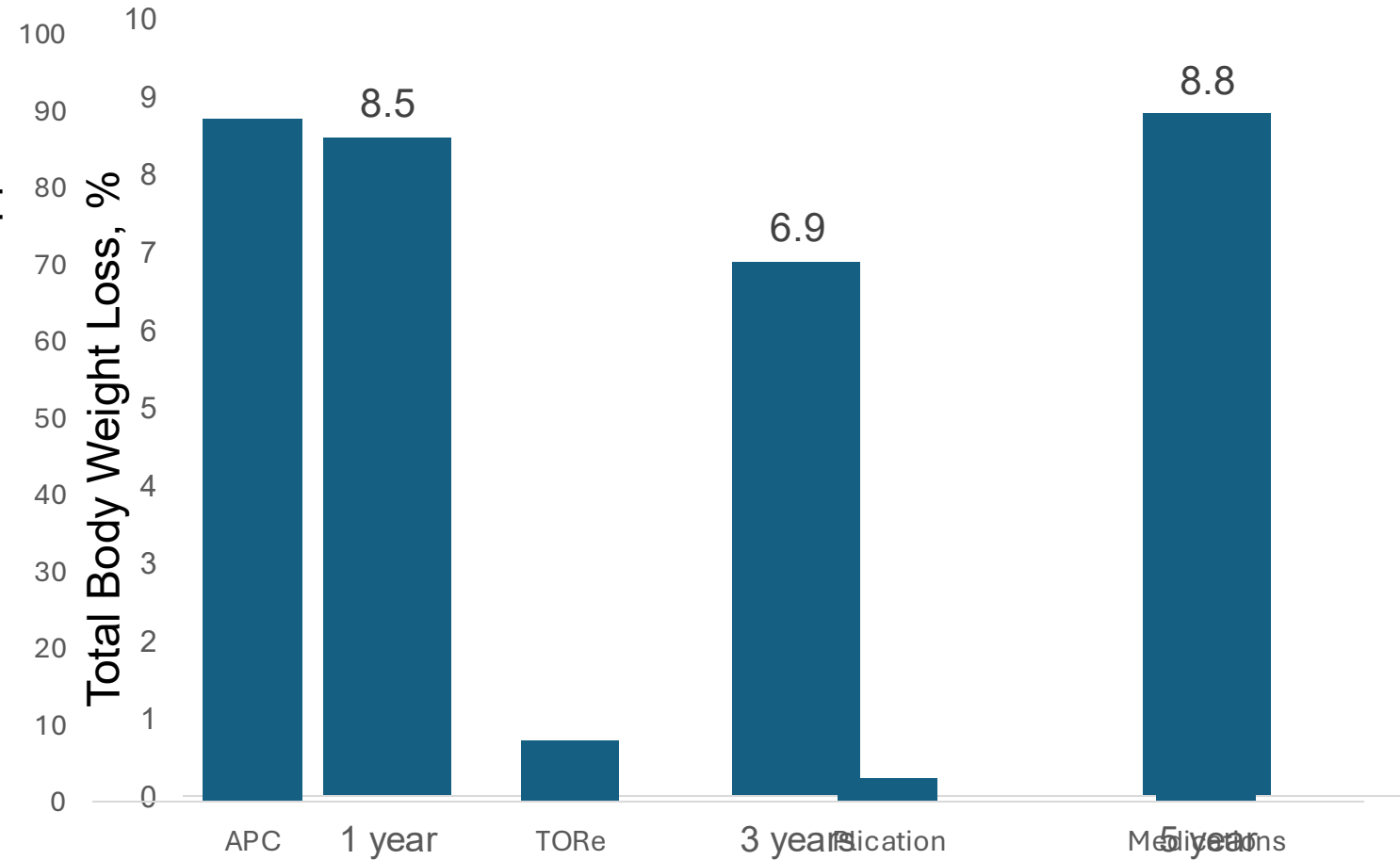
# Five-year outcomes of transoral outlet reduction for the treatment of weight regain after Roux-en-Y gastric bypass CME

Pichamol Jirapinyo, MD, MPH,<sup>1</sup> Nitin Kumar, MD,<sup>2</sup> Mohd Amer AlSamman, MD,<sup>3</sup>  
Christopher C. Thompson, MD, MSc<sup>1</sup>

Boston, Massachusetts; Effingham, Illinois; Providence, Rhode Island, USA

- 331 patients underwent 342 TORe procedures for weight recurrence or inadequate weight loss after gastric bypass
- >50% of patients underwent pouch reinforcement sutures
- 39.3% (n=130) underwent additional therapy after TORe

Additional Adjunctive Therapies after TORe

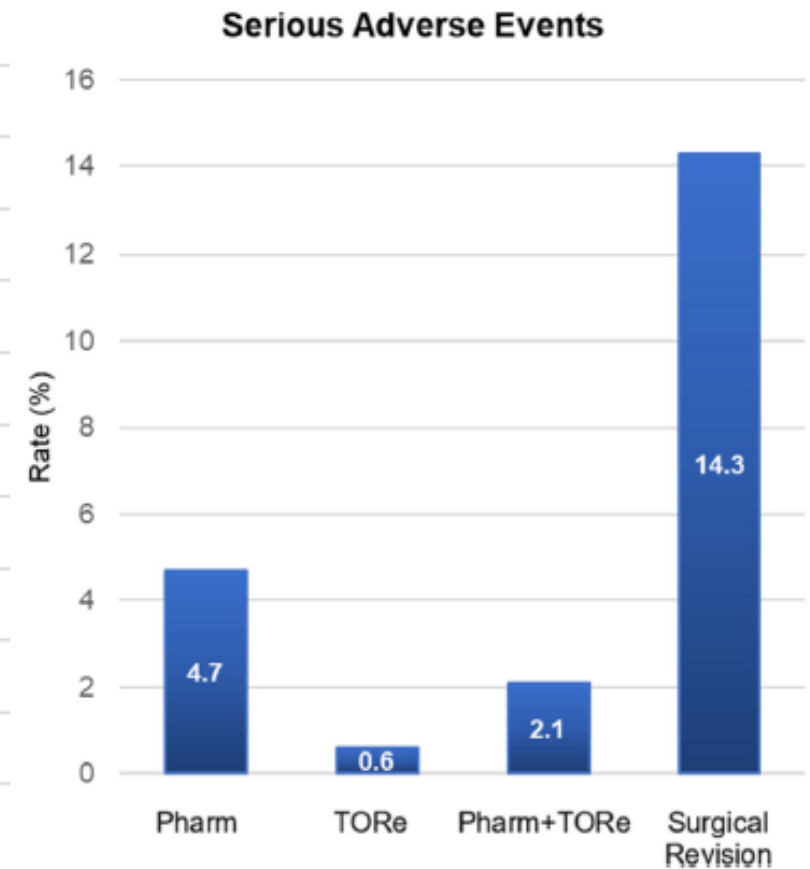
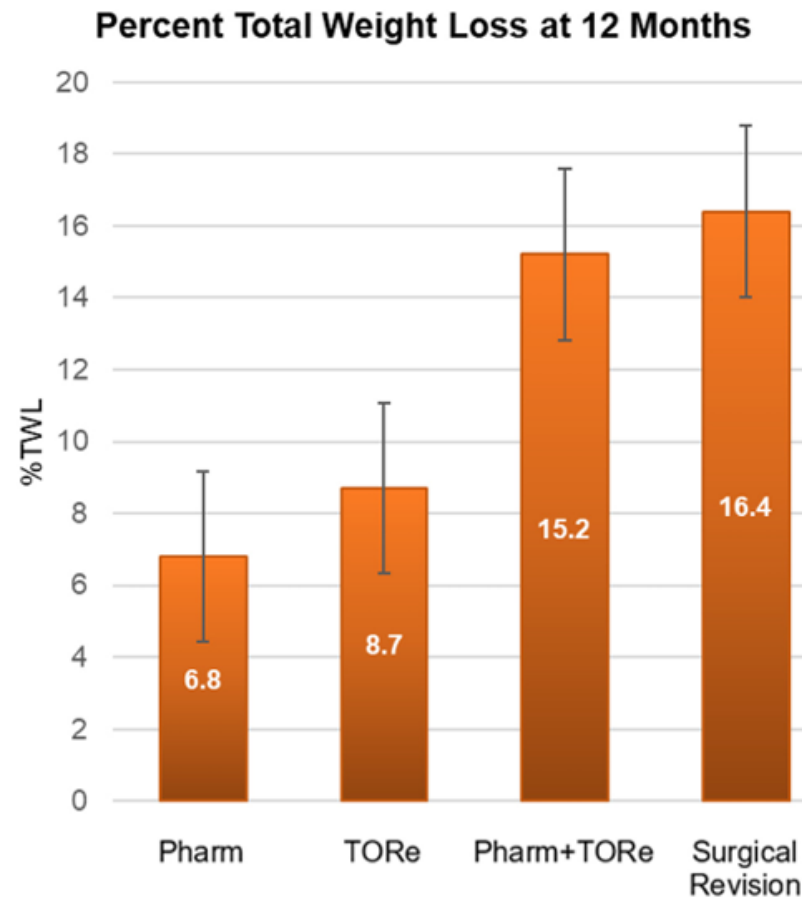


# Combining transoral outlet reduction with pharmacotherapy yields similar 1-year efficacy with improved safety compared with surgical revision for weight regain after Roux-en-Y gastric bypass (with videos) 📺

Pichamol Jirapinyo, MD, MPH,<sup>1,2</sup> Christopher C. Thompson, MD, MSc<sup>1,2</sup>

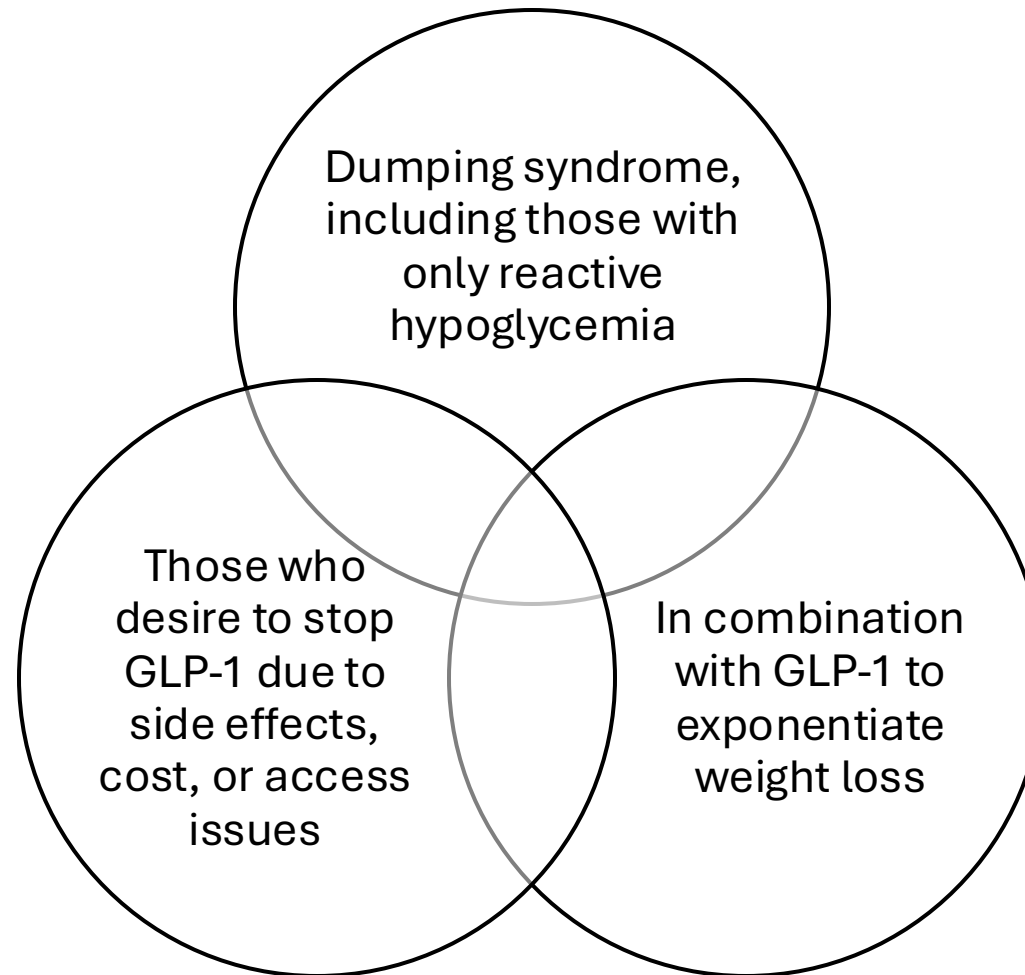
Boston, Massachusetts, USA

- 145 patients with RYGB who underwent combination therapy with anti-obesity medications
- 12-month percent total weight loss
  - Pharm + TORe > TORe alone
- Similar weight loss to surgical revision with less serious adverse events



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# TORe in the GLP-1 Era: Who Benefits?



# Summary

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- Options for overweight and obesity have expanded beyond just surgical options to include powerful medications (GLP-1 receptor agonists) and minimally invasive endoscopic options
- GLP-1 receptor agonists are one of the first medications that are highly effective for both weight and risk reduction; however, stopping them leads to weight recurrence
- Endoscopic bariatric therapies include primary (ESG) and revisional therapies (r-ESG and TORe)
- ESG is an effective option for weight reduction for class I obesity, especially given the current pricing of GLP-1 medications
- Revisional therapies, including r-ESG and TORe, are minimally invasive options to help treat weight recurrence and dumping symptoms
- Insurance coverage for primary endoscopic therapy is a major issue for ESG

# Do Endoscopic Bariatric Therapies have a future in the GLP-1 Era?

- Endobariatric procedures have an adjunctive role among those patients who either do not want surgery or medications
- Multi-modality treatment with endobariatrics + medications may be necessary for a subset of patients with obesity
- However, as more medications come onto the market, and in the future as GLP-1s become off-patent, the future of these procedures is in question
- To remain an option for patients, insurance coverage for these procedures will be essential

