In A World of Semaglutide Shortages…Endobariatrics To The Rescue!

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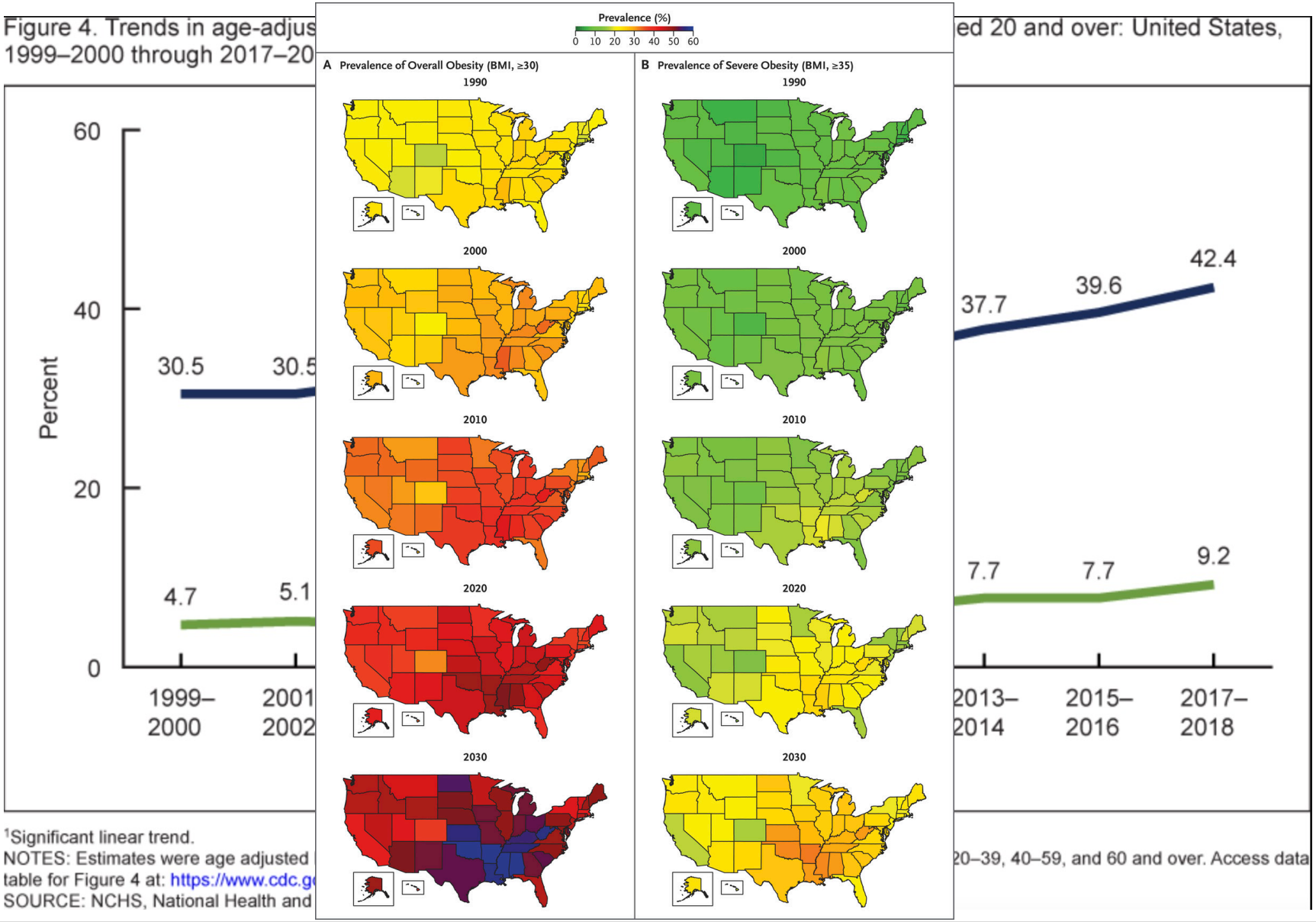
Conflicts of Interest

No Conflicts of Interest

Outline

1. Background on Obesity & Bariatric Surgery
2. Endoscopic Therapies for Obesity
3. Revision After Bariatric Surgery



https://www.cdc.gov/nchs/products/databriefs/db360.htm
ZJ Ward et al. N Engl J Med 2019;381:2440-2450.

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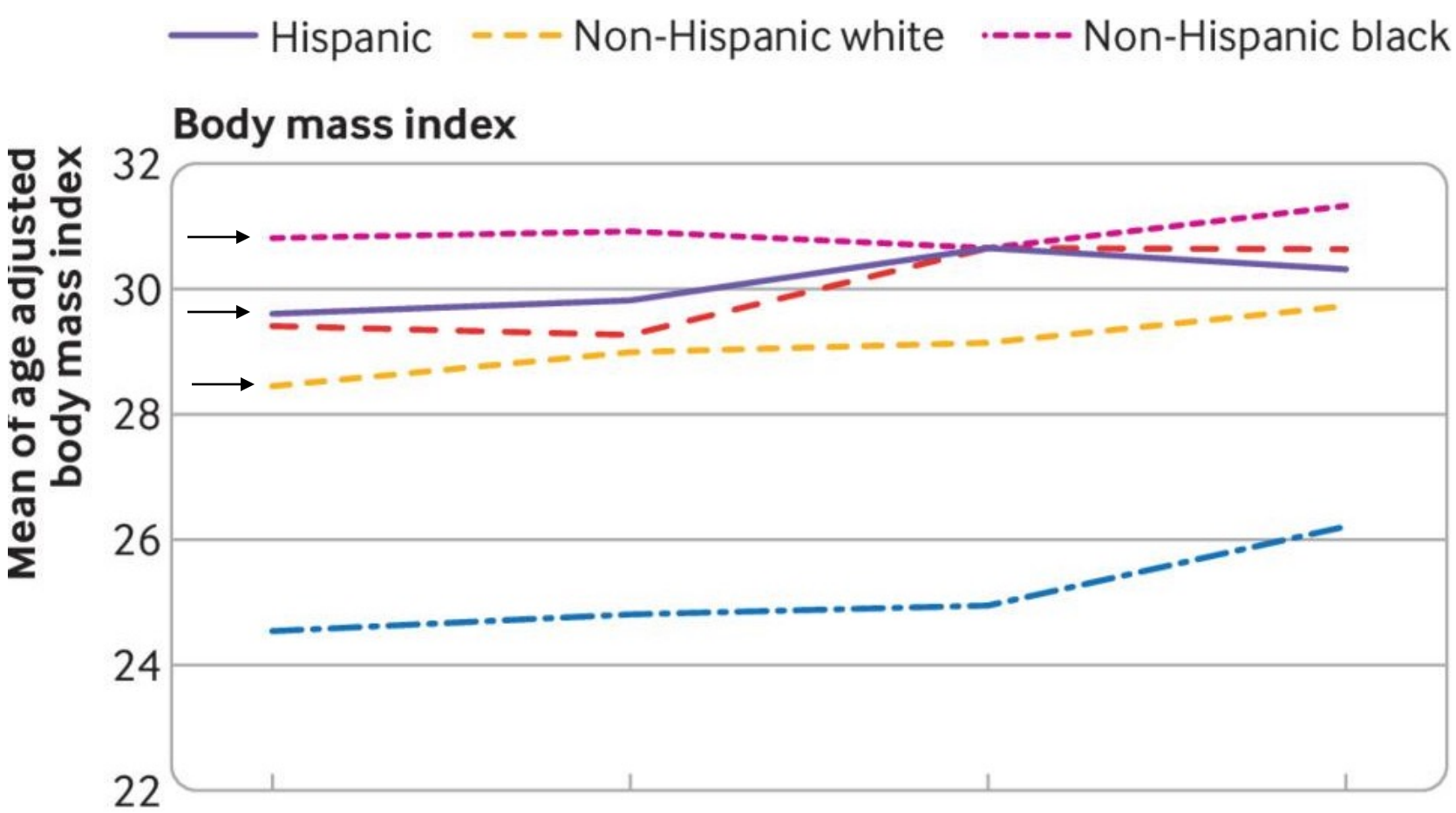

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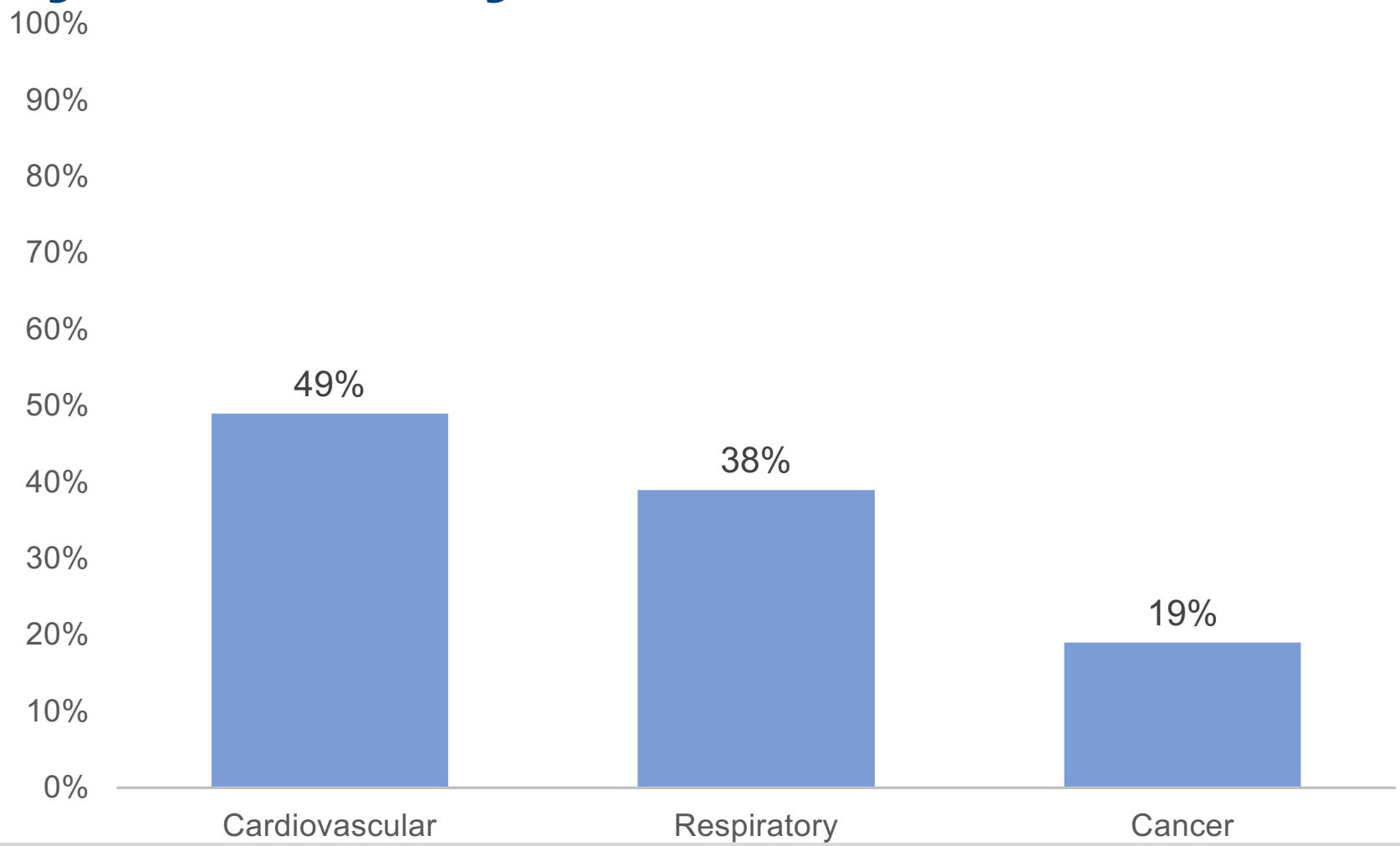
Trends in obesity and adiposity measures by race or ethnicity among adults in the United States 2011-18: population-based study. *BMJ* 2021

Obesity & Mortality



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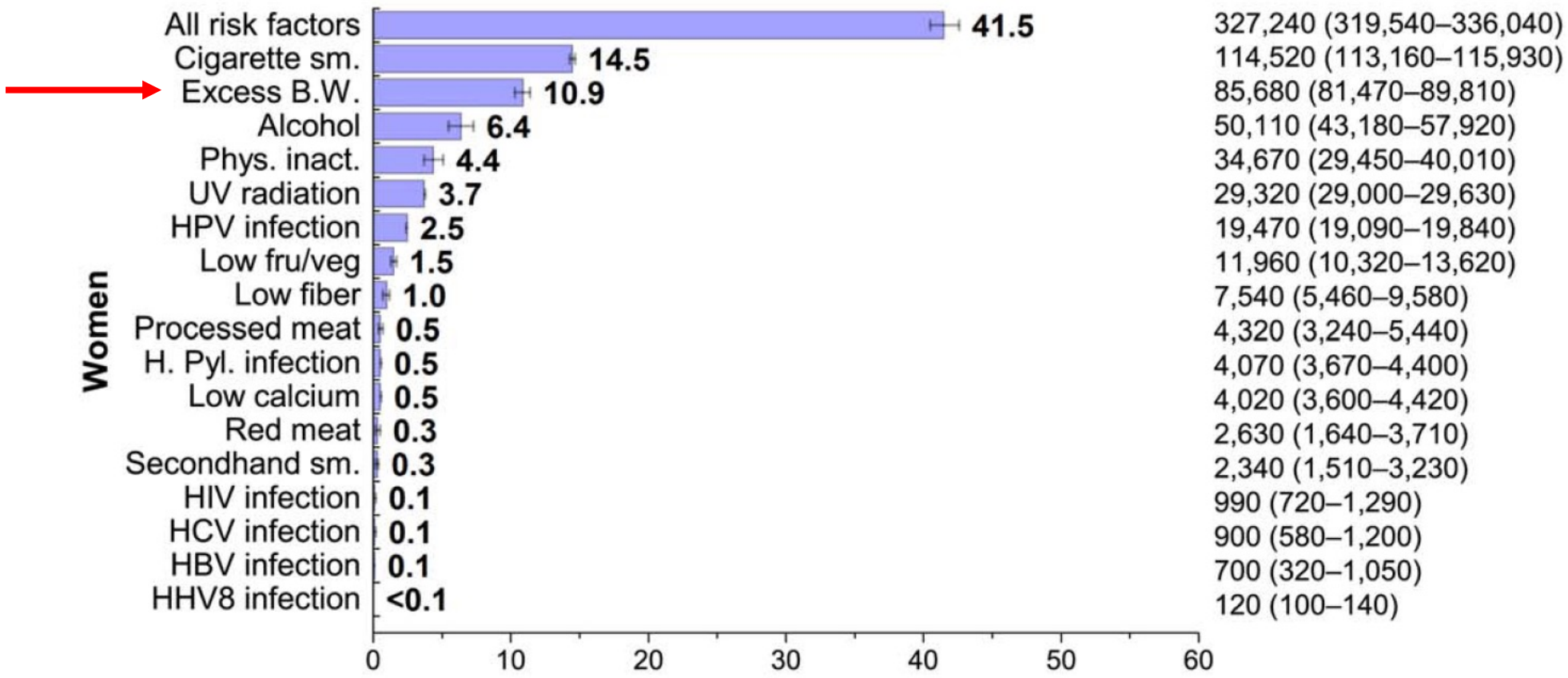
The Global BMI Mortality Collaboration. *The Lancet* 2016

Obesity & Cancer



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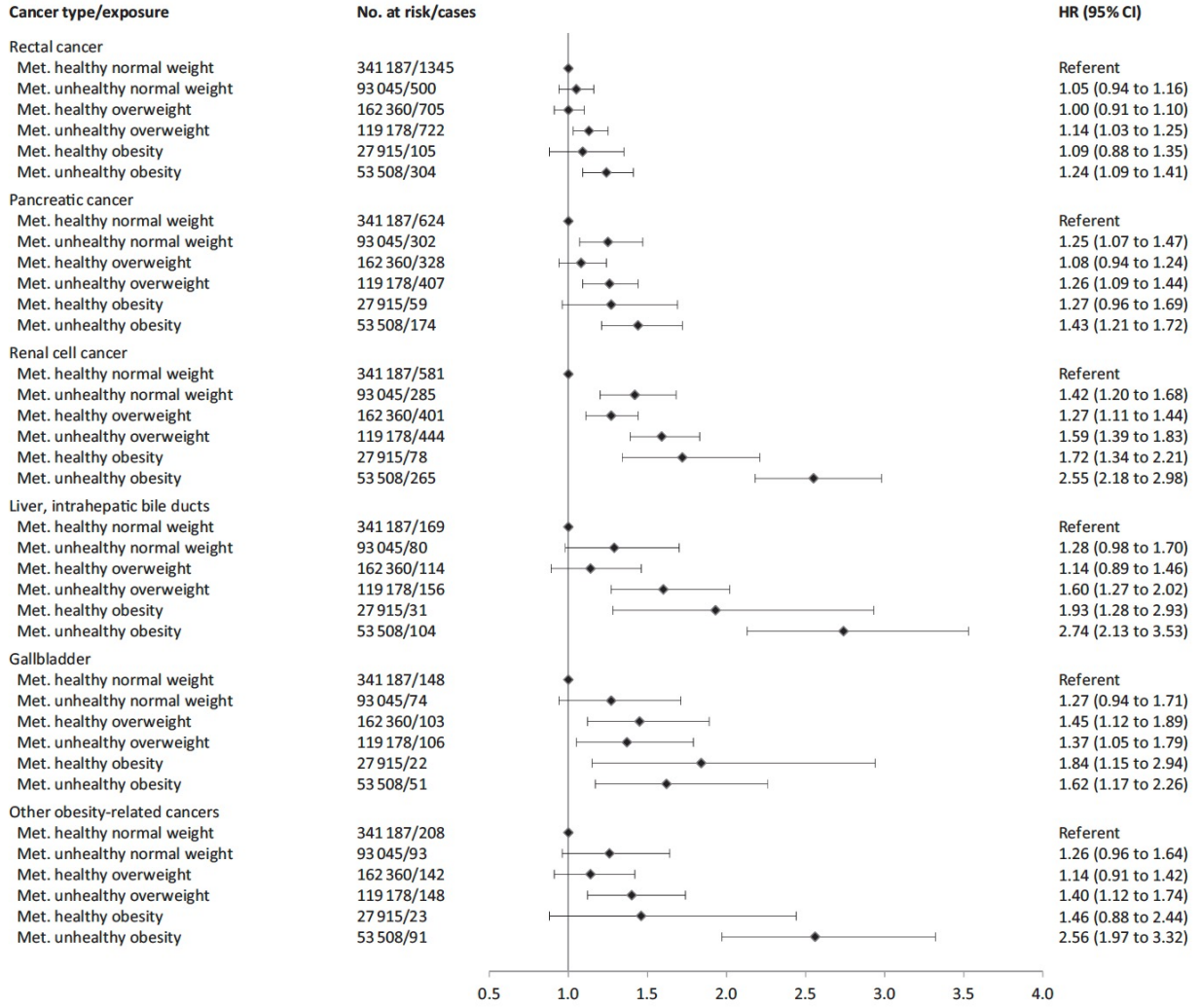
Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. CA Cancer J Clin 2018

Obesity & Cancer

- Aim: evaluate risk of obesity related cancers among metabolically healthy and unhealthy obese individuals
- Metabolically unhealthy individuals defined by a composite score to capture metabolic aberrations of mid-blood pressure, glucose, and triglycerides
- 797,193 individuals with 40 years of follow up
- 35% overweight, 10% obese, 7% metabolically unhealthy obesity
- As compared to metabolically healthy normal, metabolically unhealthy obese patients had higher relative risk of all obesity related cancers



Metabolically (un) healthy obesity and risk of obesity-related cancers: a pooled study. JNCI 2023.

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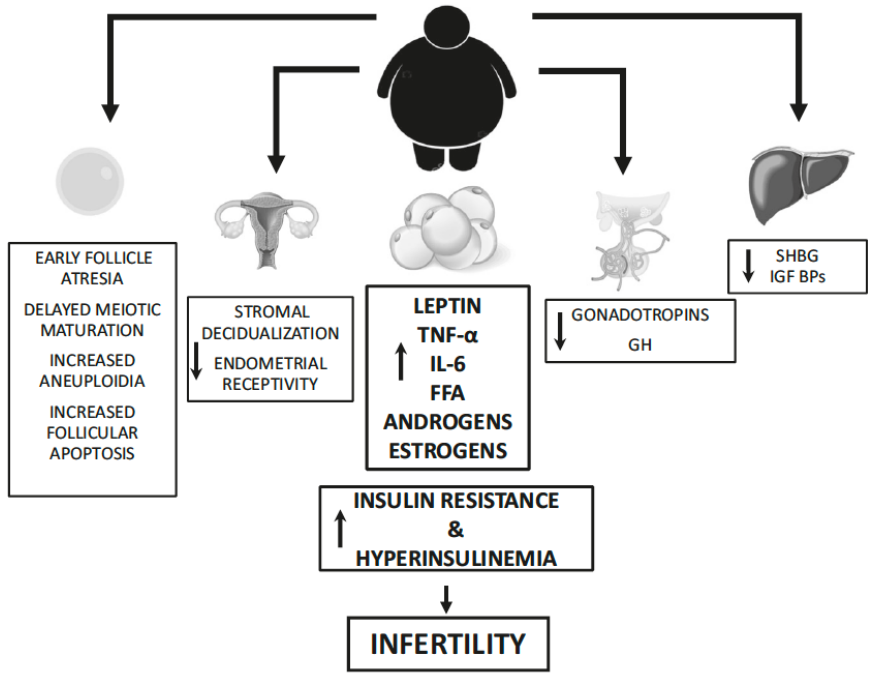
Obesity & Female Infertility

- Adipose tissue will produce leptin and cytokines which affect both ovarian and endometrium function
- Development of peripheral insulin resistance
  - Promotes hyperandrogenism and hyperestrogenism→anovulation
- Obesity also negatively effects assisted reproduction
  - Need for higher doses of gonadotropins
  - Fewer oocytes collected
  - Higher number of cycles cancelled for poor oocytes collected
  - Reduced pregnancy rates

Fig. 1 Mechanisms linking obesity with infertility. TNF-α tumor necrosis factor-α, IL-6 interleukin-6, FFA free fatty acid, GH growth hormone, SHBG sex hormone binding globulin, IGFBPs insulin-like growth factor-binding proteins

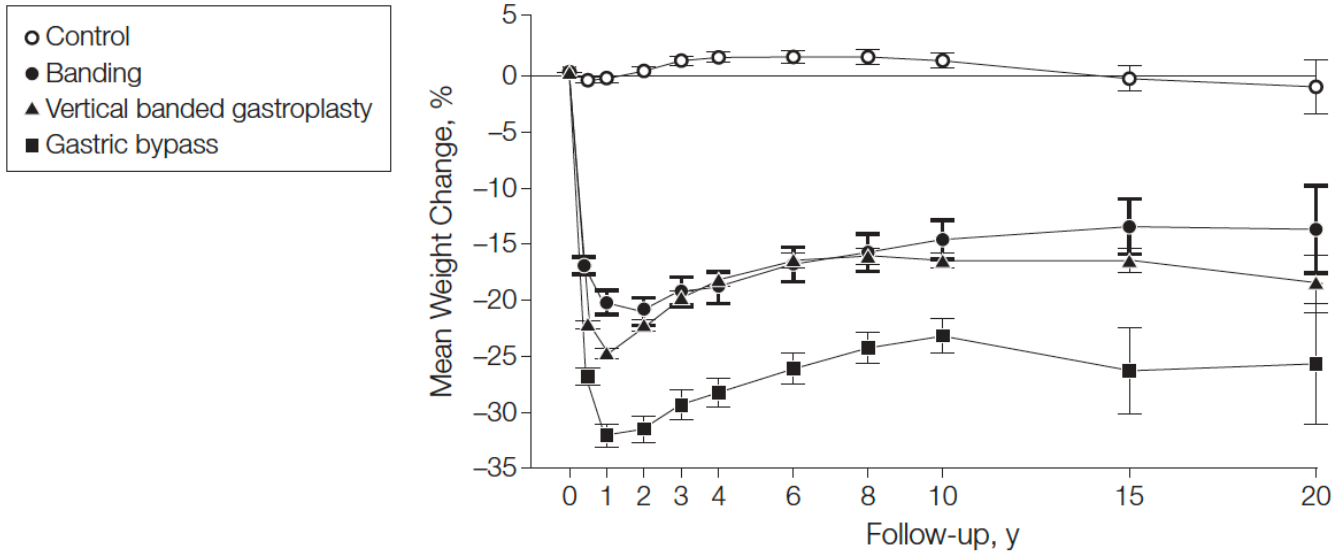


Female Infertility: which role for obesity? International Journal of Obesity Supplements. 2019.

Bariatric Surgery Is Effective For Obesity

- Prospective nonrandomized matched study
- 25 public surgical departments and 480 primary health care centers in Sweden
- 2010 obese participants underwent bariatric surgery. Matched to 2037 obese controls who received usual care.
- Statistically significant difference in weight loss among surgery vs. usual care group.

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

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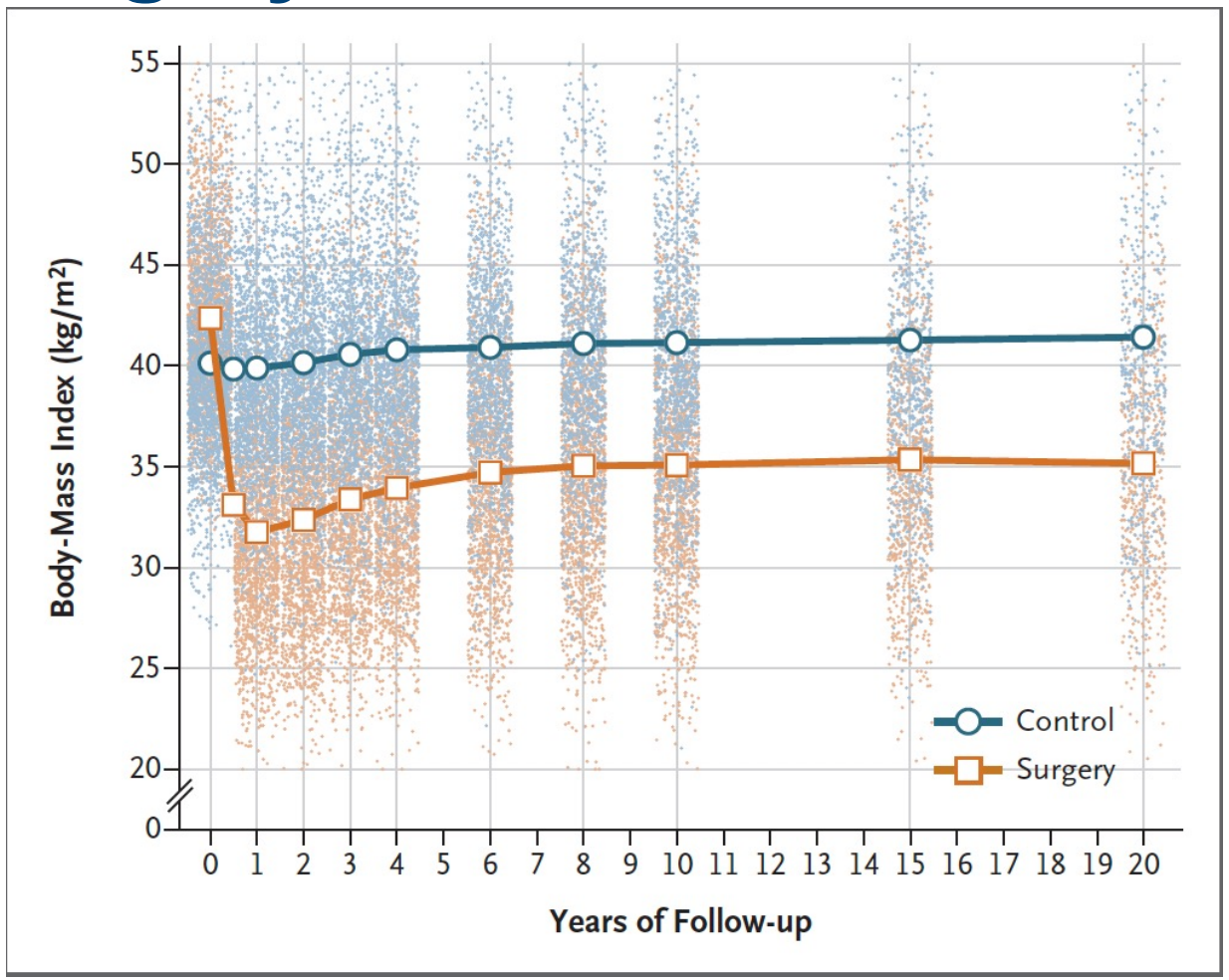
Bariatric surgery and long-term cardiovascular events. JAMA 2012

Bariatric Surgery Is Effective For Obesity



HR for death from CV disease: 0.70 (95% CI 0.57, 0.85)

HR for death from cancer : 0.77 (95% CI 0.61, 0.96)

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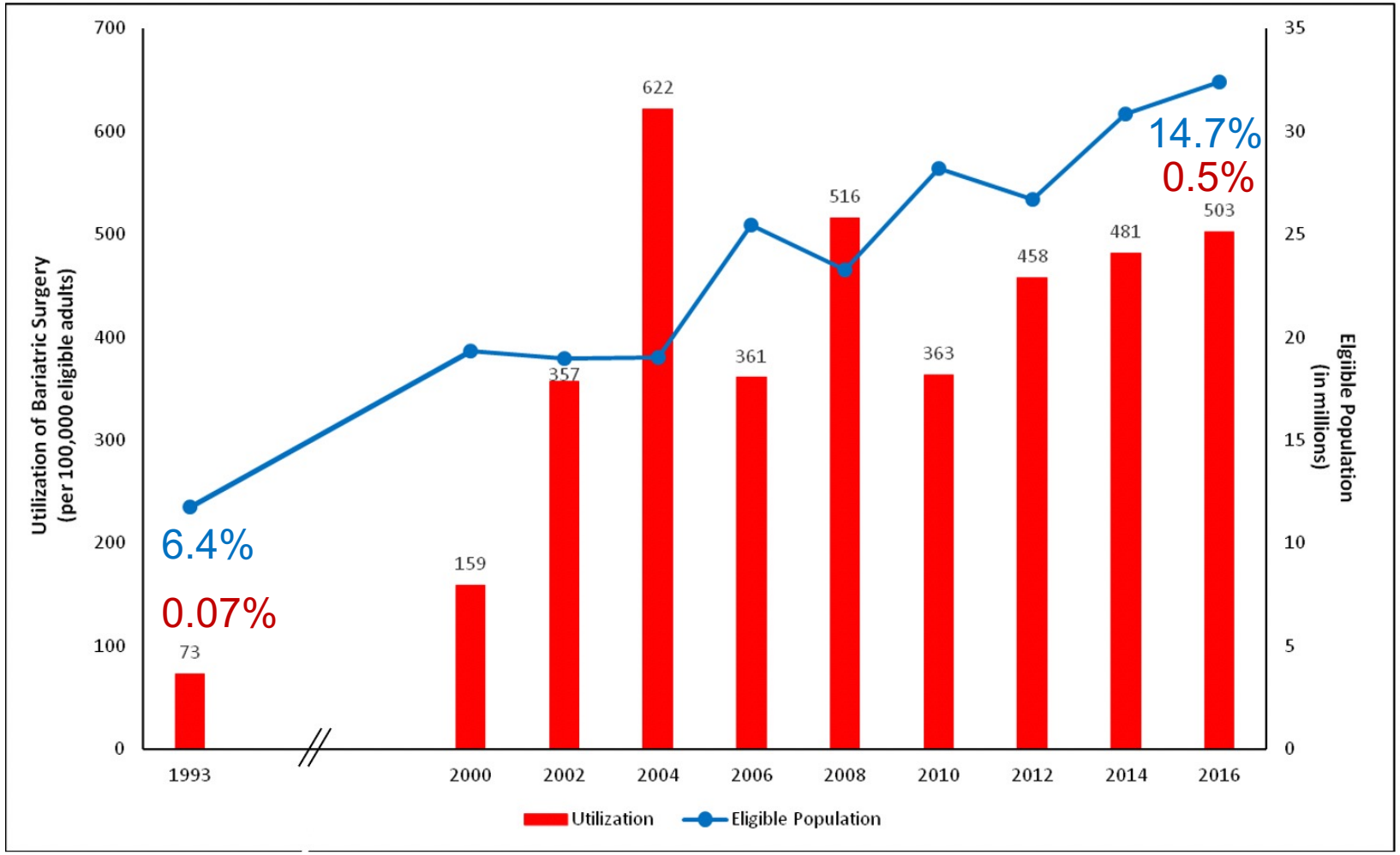
Life Expectancy after Bariatric Surgery in the Swedish Obese Subjects Study. NEJM 2020

Utilization of Bariatric Surgery



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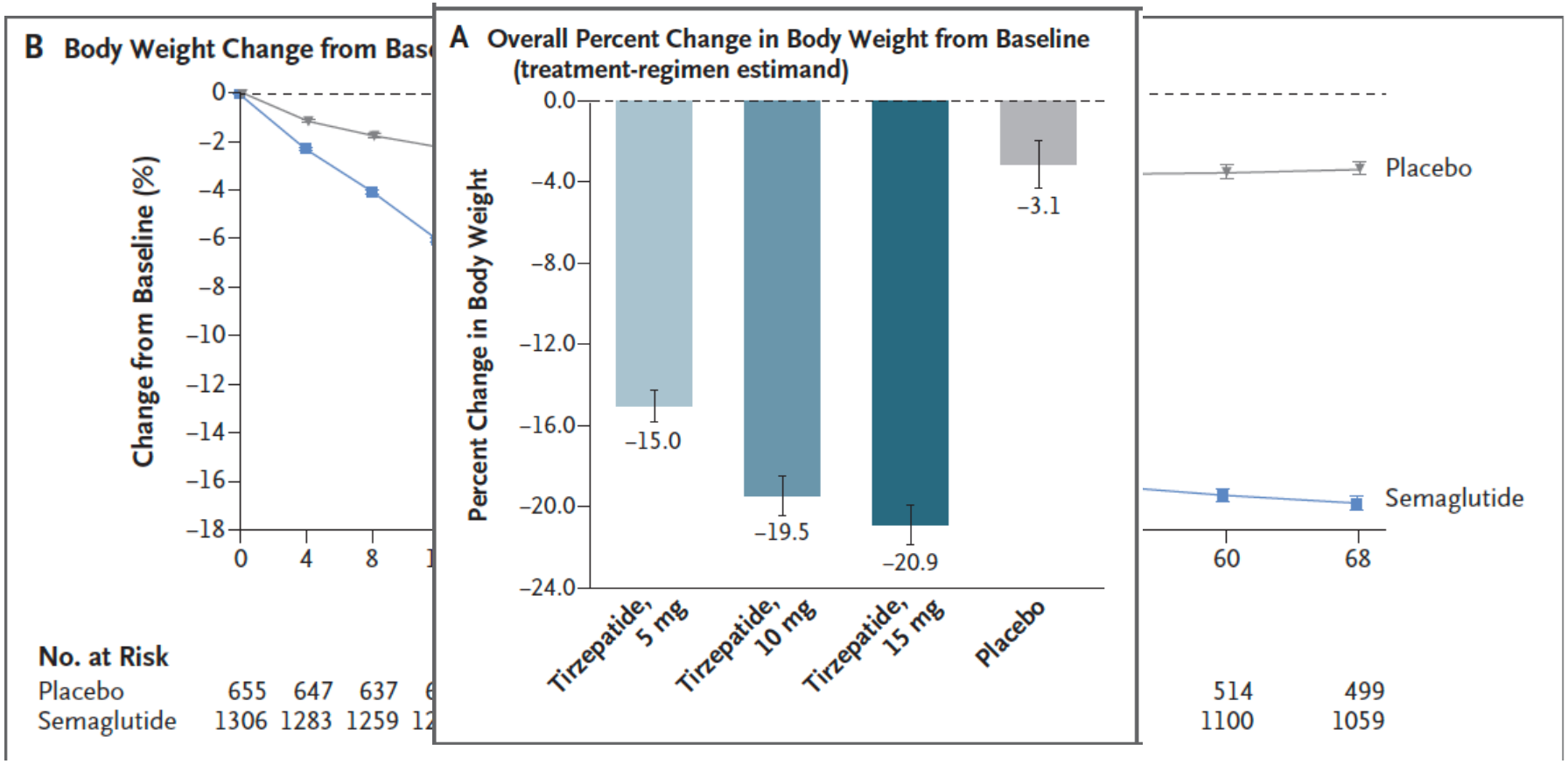
Changes in Utilization of Bariatric Surgery in the United States From 1993 to 2016. Ann Surg 2020

Pharmacotherapy for Obesity



Once-Weekly Semaglutide in Adults with Overweight or Obesity. NEJM 2021
Tirzepatide Once Weekly for the Treatment of Obesity. NEJM 2022

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Pharmacotherapy for Obesity

FEATURE

Ottawa

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DRUG PRICES

High price and demand for semaglutide means lack of access for US patients

The popularity of semaglutide (Ozempic, Wegovy) and its new rival tirzepatide has led to aggressive marketing, shortages, and counterfeits. High drug prices in the United States limit access to these drugs to those who can afford them, denying them from many who could benefit. **Carolyn Brown** reports

Carolyn Brown *freelance journalist*

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High prices and demand for semaglutide means lack of access for US patients. BMJ 2023

Management of Obesity

Non-Surgical Options

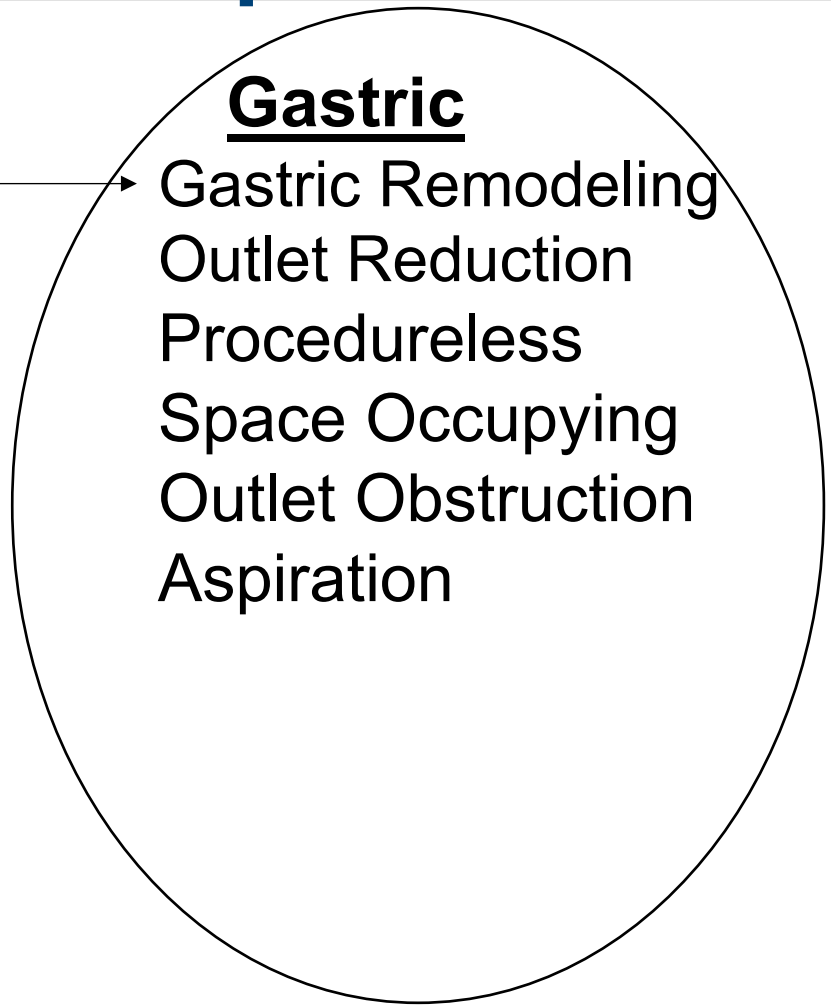
Endoscopy

Surgery

Least Invasive

Most Invasive

Endoscopic Bariatric Therapies (EBTs)



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
  - Ideally reduces stomach volume by 70-80%
  - Outpatient procedure

- **Who Qualifies?**
  - Patients 18 years and older
  - BMI at least 27 kg/m^2
  - 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

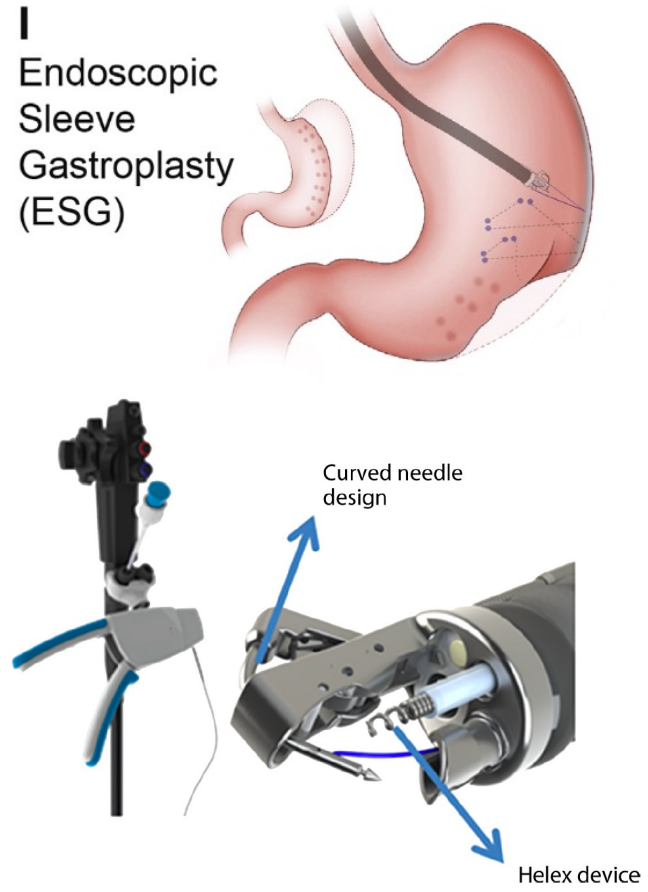
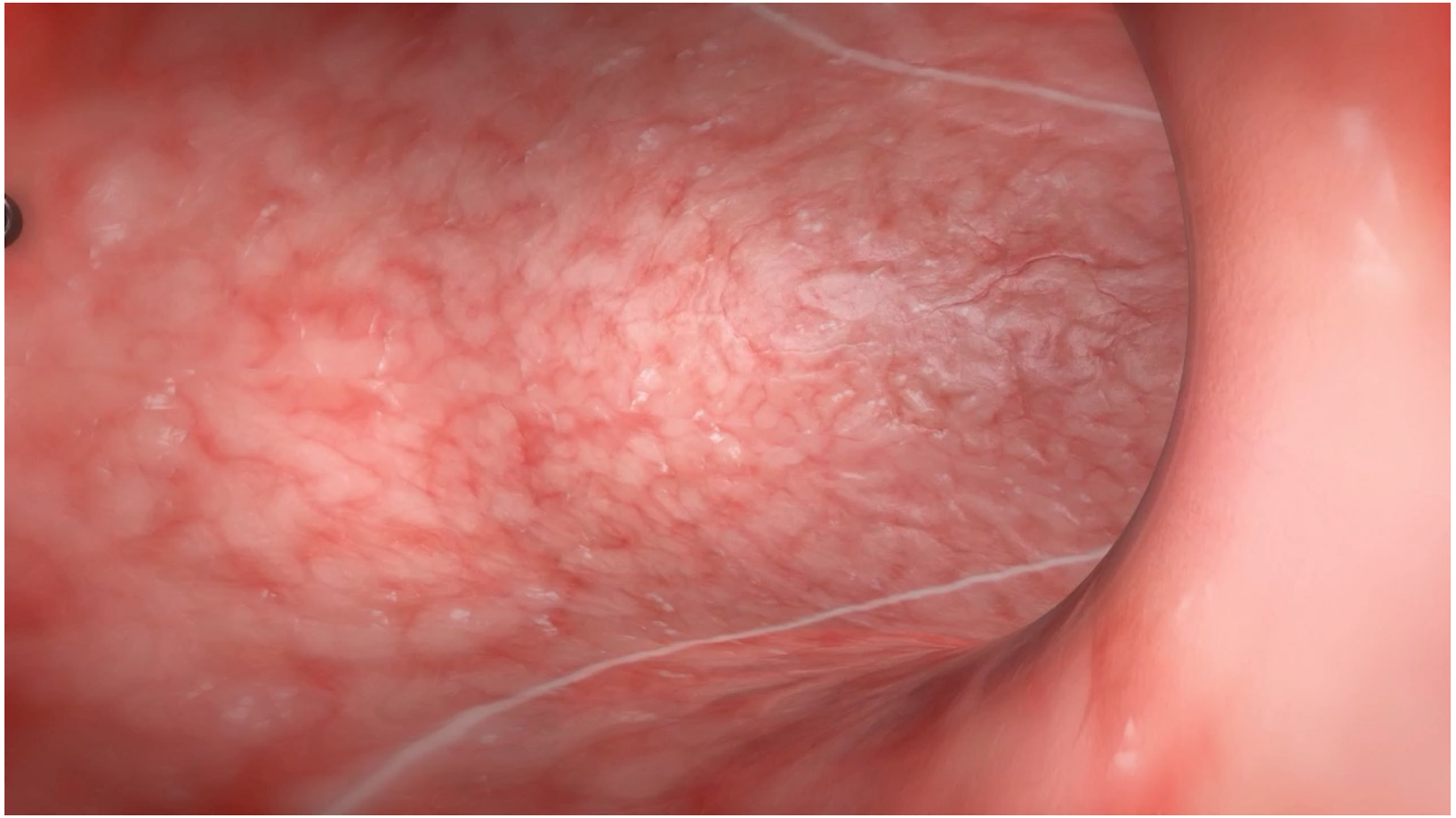
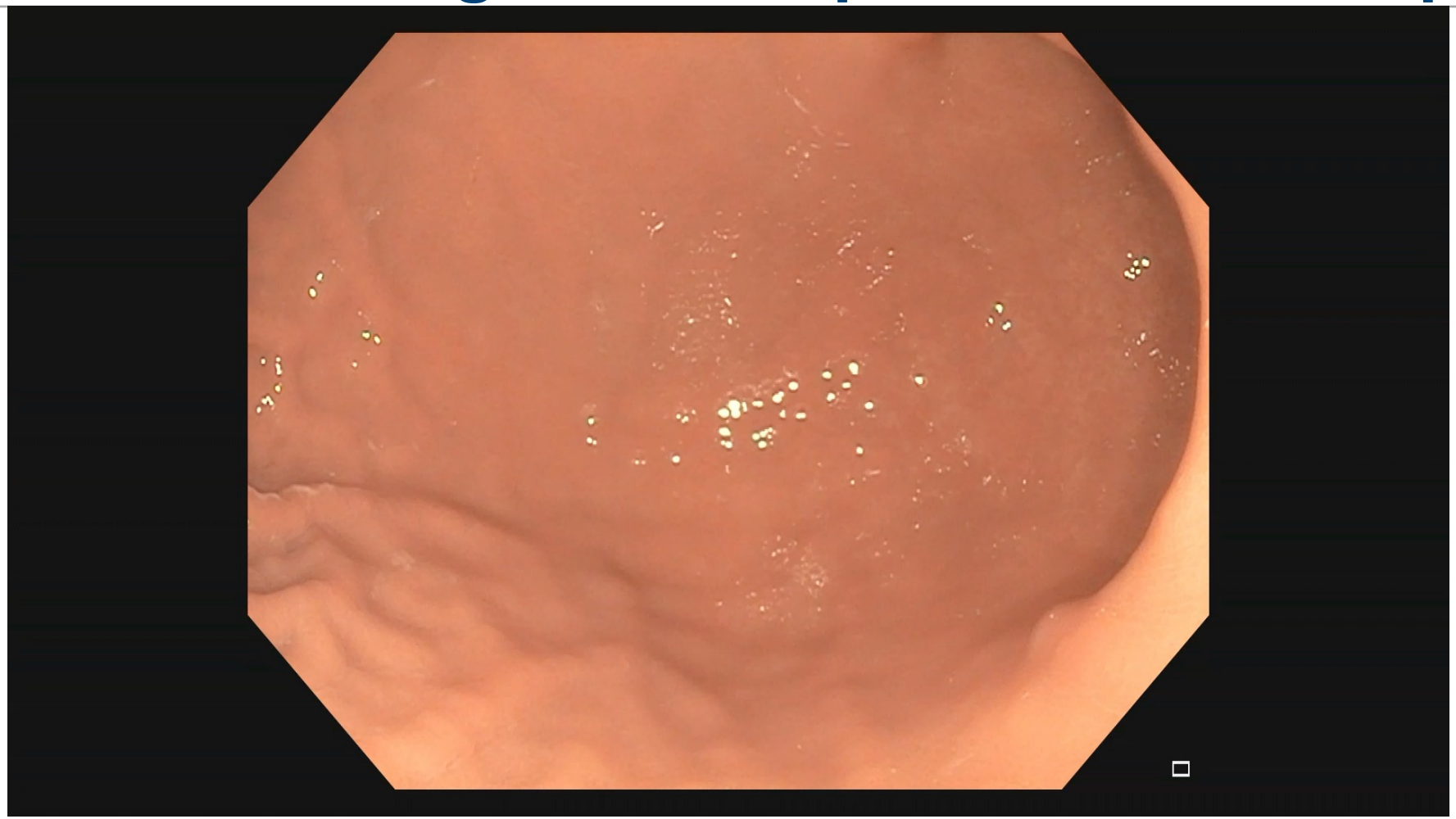


Figure 2. Endoscopic suturing system used in our study.

Gastric Remodeling: Endoscopic Sleeve Gastroplasty



Gastric Remodeling: Endoscopic Sleeve Gastroplasty



Gastric Remodeling: Endoscopic Sleeve Gastroplasty

- First cases done by Chris Thompson and Robert Hawes April 2012 in India

- Pilot of 4 patients:
  - No adverse events

  - BMI : 37.4 →34.8 after 5 months

ESG: Weight Loss & Comorbidity Resolution

- Prospective Series (n=91)

Table 2. Post-ESG Improvement in Weight and Medical Comorbidities at 12 Months (N = 53)

	Before ESG, mean (SD)	12 months after ESG, mean (SD)	*P* value
HgbA1c, % (all patients)	6.1 (1.1)	5.5 (0.48)	.05
HgbA1c, % (only diabetes and prediabetes)	6.6 (1.2)	5.6 (0.51)	.02
Waist circumference, *cm*	119.66 (14.05)	92.75 (5.85)	<.001
SBP, *mm Hg*	129.02 (13.44)	122.23 (11.69)	.023
LDL, *mg/dL*	121.62 (38.61)	124.27 (27.82)	.786
TG, *mg/dL*	131.84 (83.19)	92.36 (39.43)	.017
ALT, *mg/dL*	32.28 (16.43)	20.68 (11.44)	<.001

- SAE: 1 perigastric leak

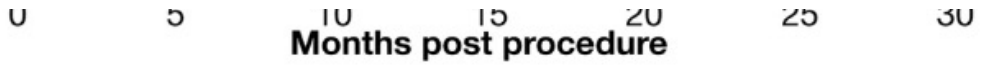


Figure 3. Percentage TBWL after ESG.

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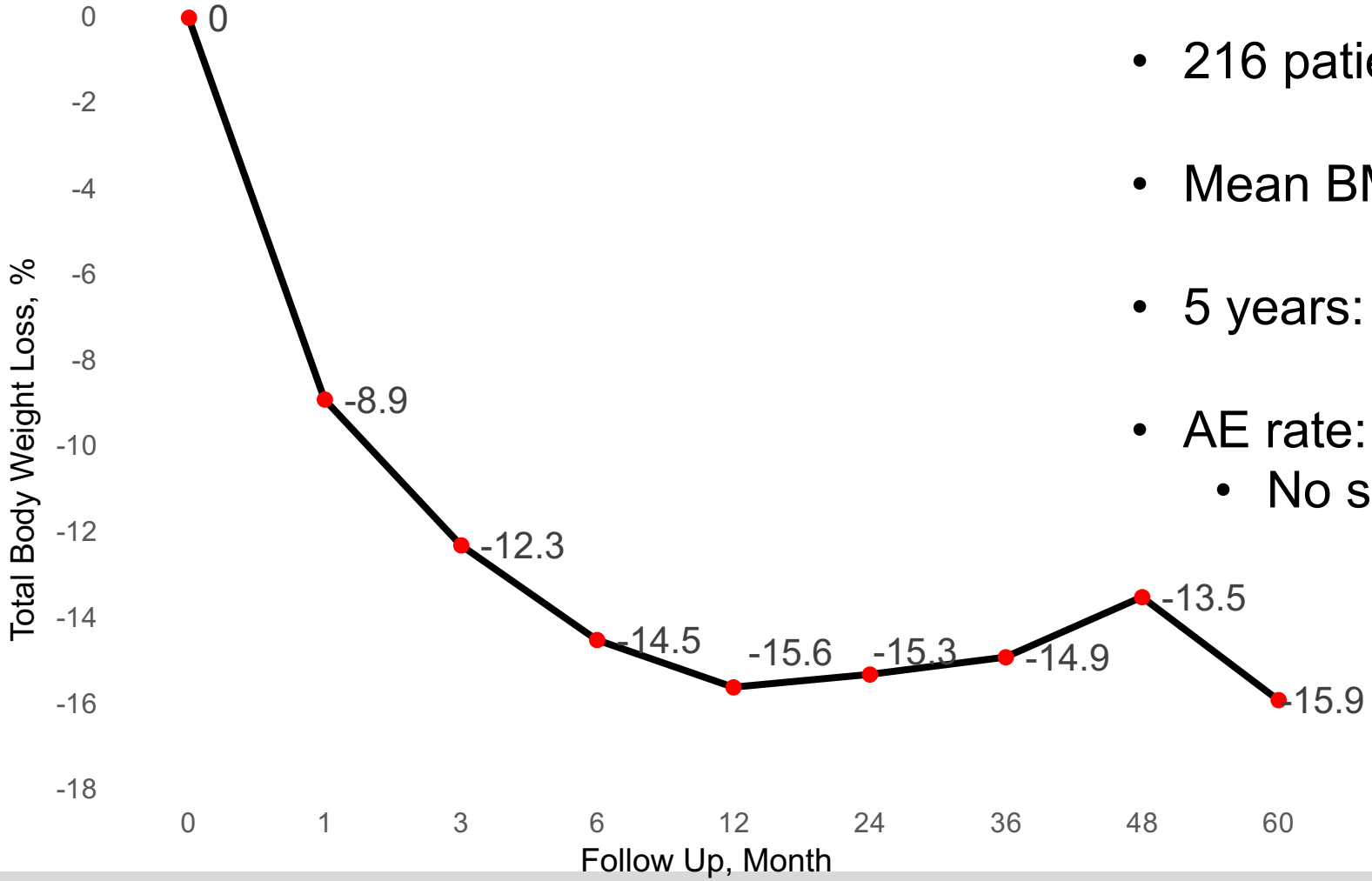
Endoscopic Sleeve Gastroplasty Significantly Reduces Body Mass Index and Metabolic Complications in Obese Patients. Clin Gastro Hepatol 2017

ESG: Weight Loss Outcomes



- 216 patients
- Mean BMI 39
- 5 years: TBWL 15.9%
- AE rate: 1.3%
  - No severe or fatal AE

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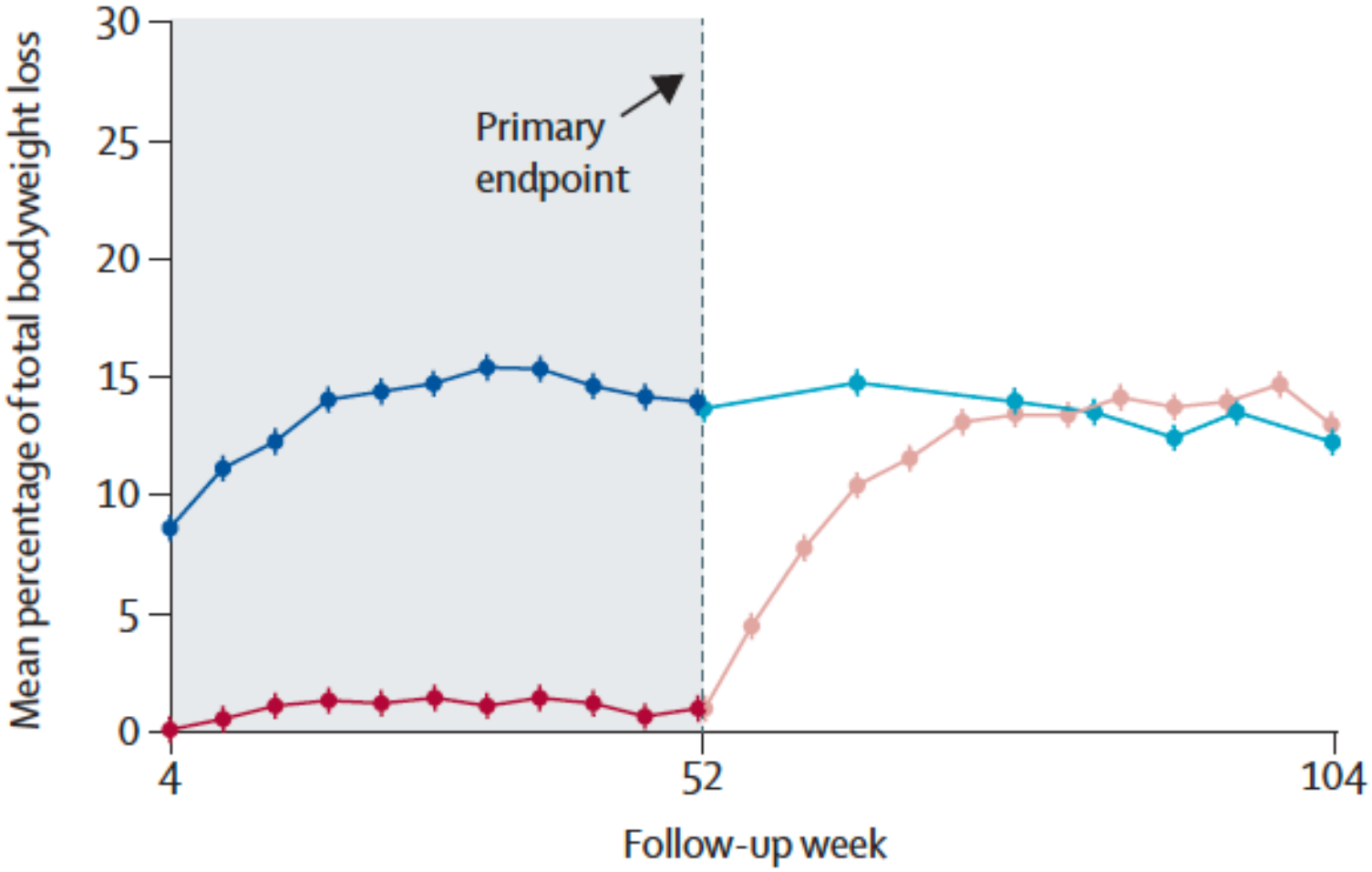
Endoscopic Sleeve Gastroplasty Significantly Reduces Body Mass Index and Metabolic Complications in Obese Patients. Clin Gastro Hepatol 2017

Gastric Remodeling: Endoscopic Sleeve Gastroplasty

- 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 or lifestyle modifications only
  - Allowed for potential retightening or crossover to ESG at 52 weeks
- Endpoints: % excess weight loss (primary) and change in metabolic comorbidities (secondary)

Gastric Remodeling: Endoscopic Sleeve Gastroplasty



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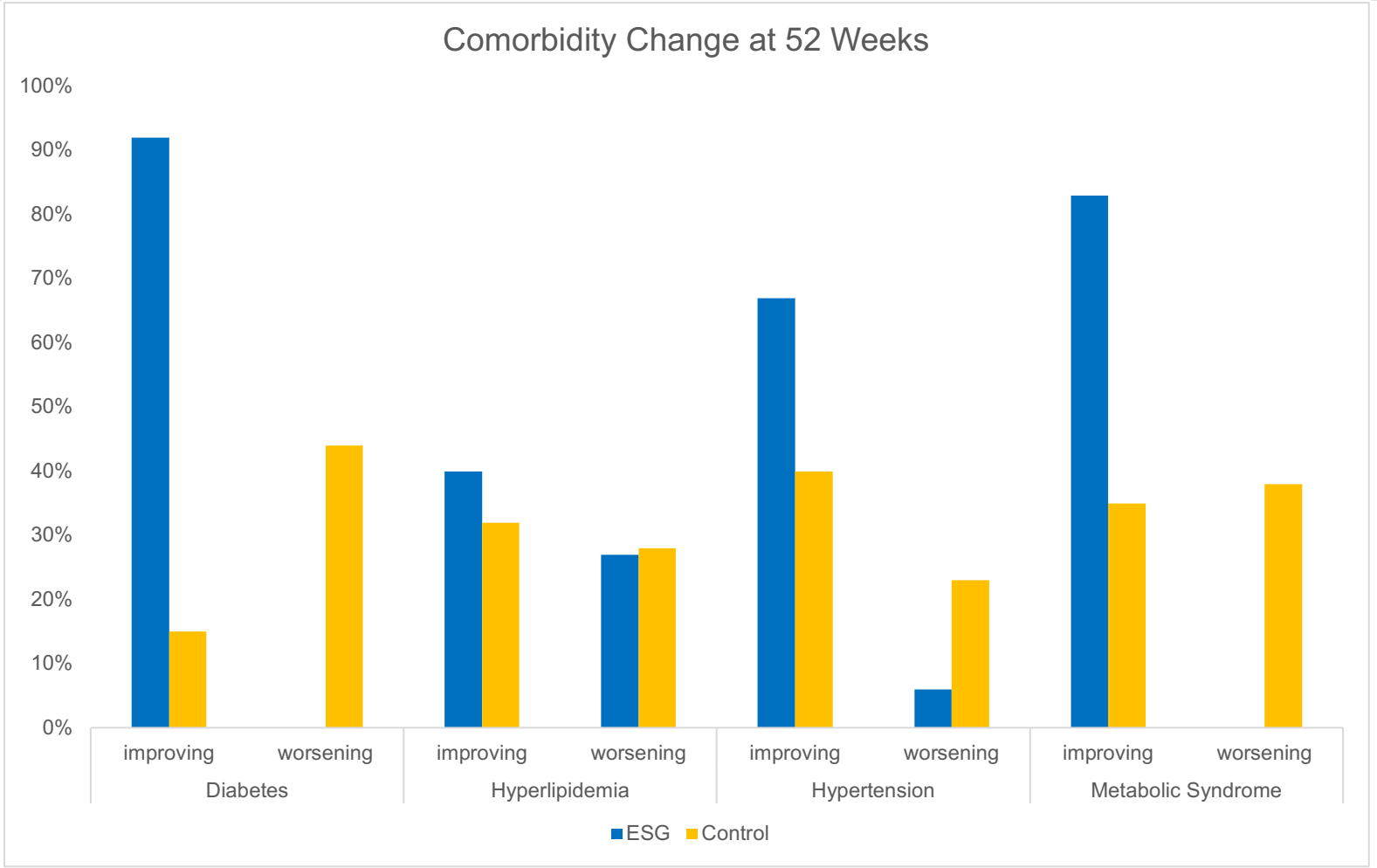
Endoscopic sleeve gastroplasty for treatment of class 1 and 2 obesity (MERIT): a prospective, multicentre, randomised trial. The Lancet 2022

Gastric Remodeling: Endoscopic Sleeve Gastroplasty



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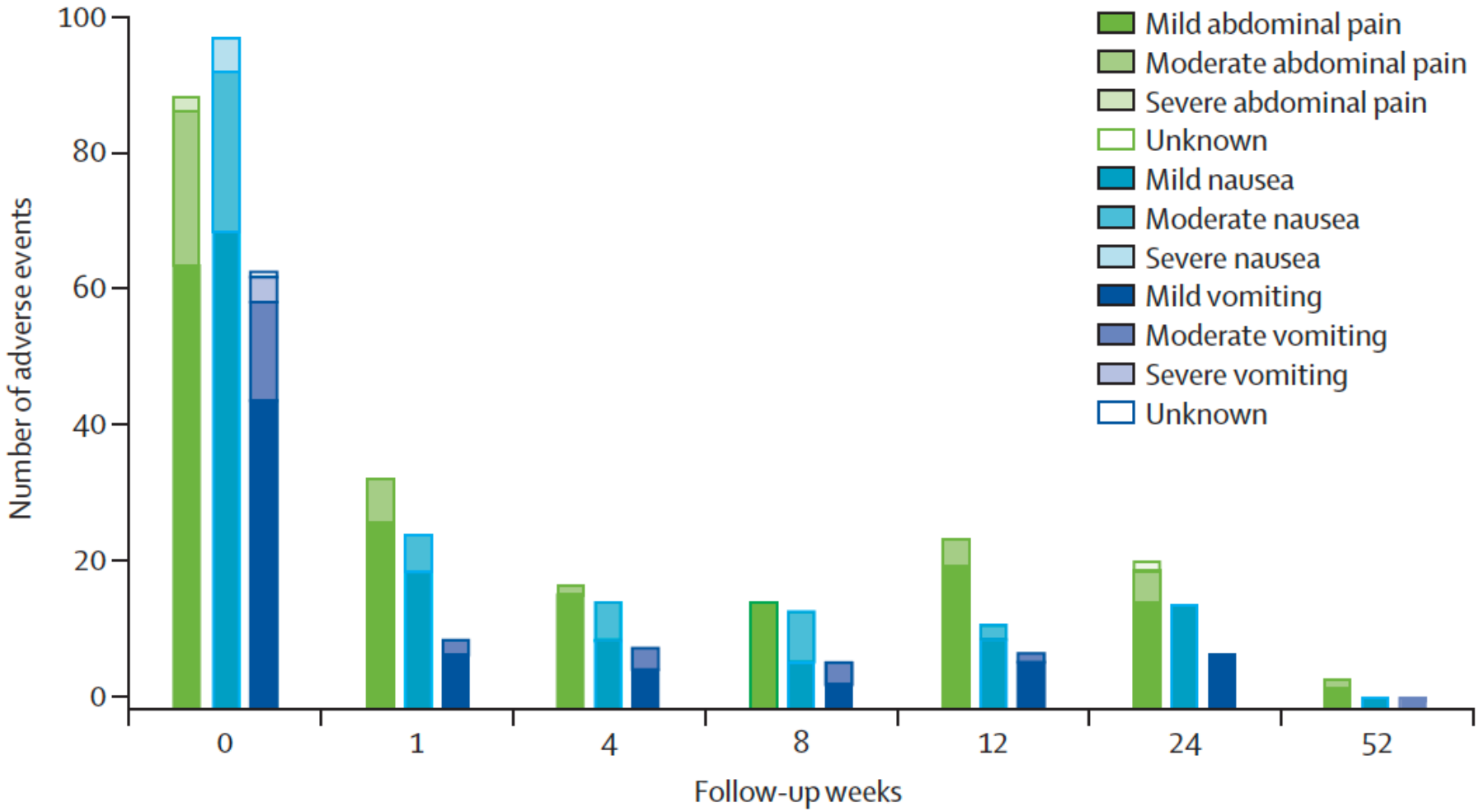

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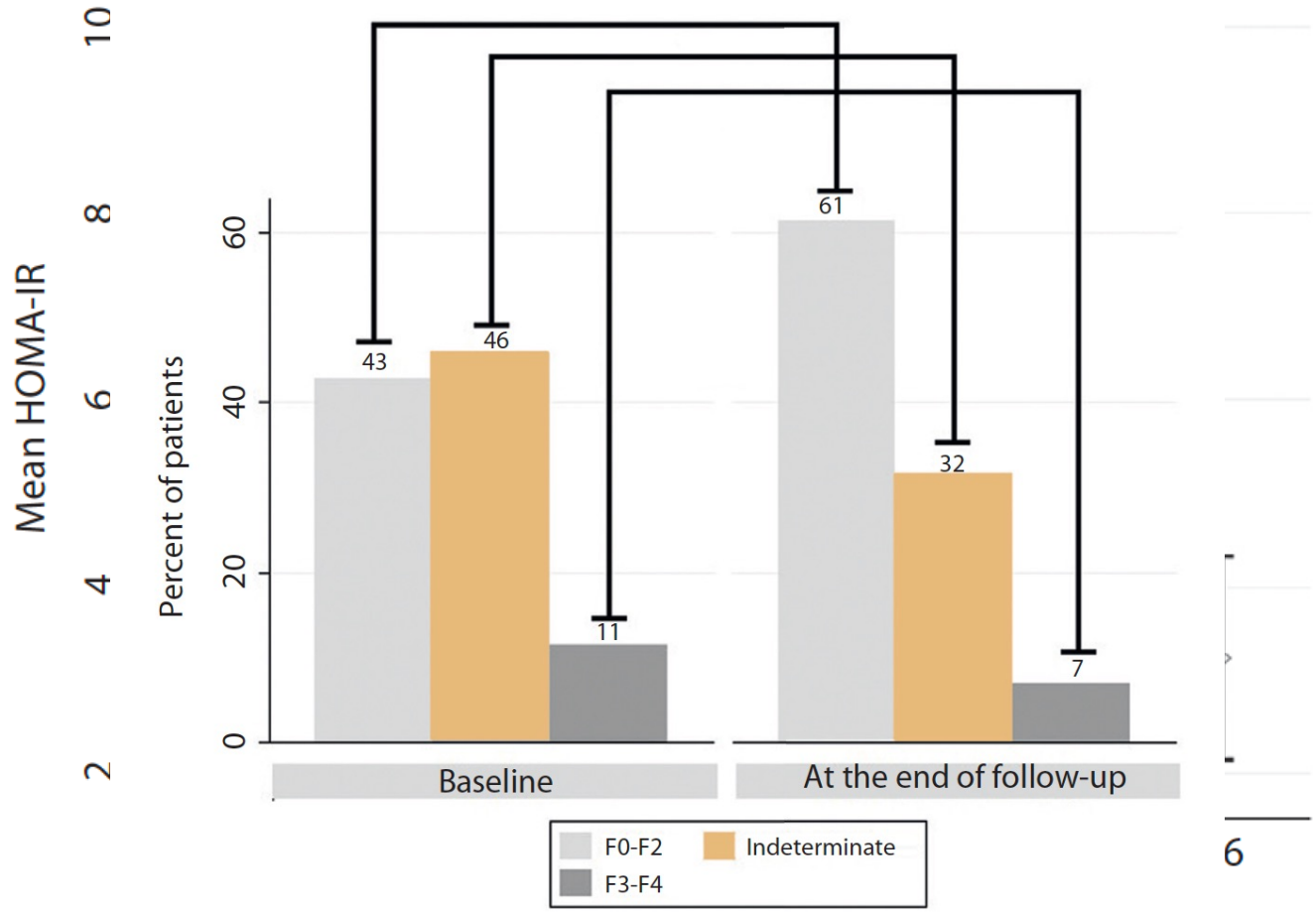
Endoscopic sleeve gastroplasty for treatment of class 1 and 2 obesity (MERIT): a prospective, multicentre, randomised trial. The Lancet 2022

Gastric Remodeling: Endoscopic Sleeve Gastroplasty

- Other Key-Takeaways from MERIT trial
  - 18 patients were eligible for retightening of their sleeve
    - 4 did not have retightening because sleeve was intact on endoscopy
- Found no worsening of reflux symptoms and improvement in QOL and depression in ESG group based on surveys sent to patient

ESG: Metabolic Outcomes



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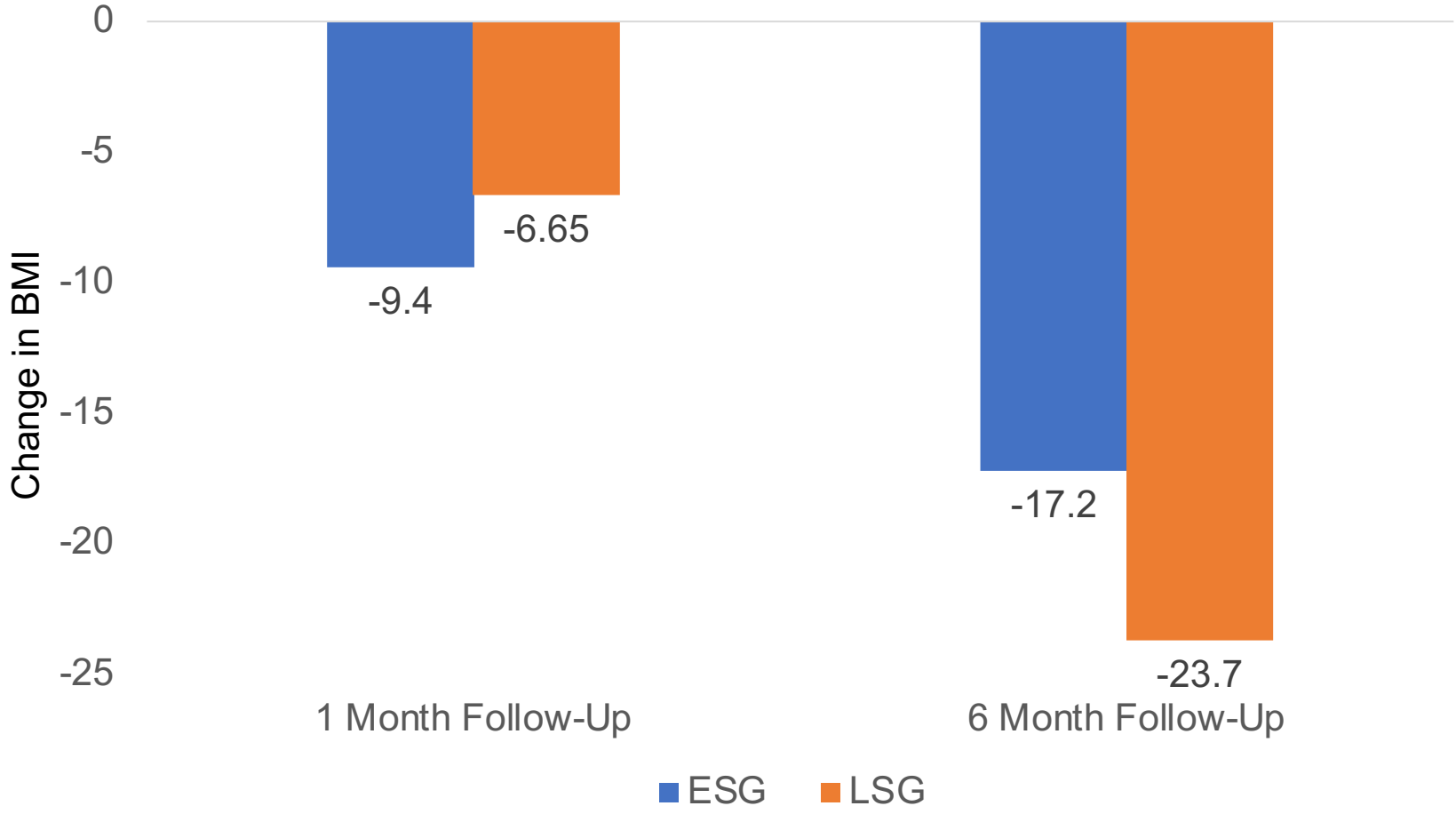
Improvement in insulin resistance and estimated hepatic steatosis and fibrosis after endoscopic sleeve gastroplasty. GIE 2021

ESG vs. LSG



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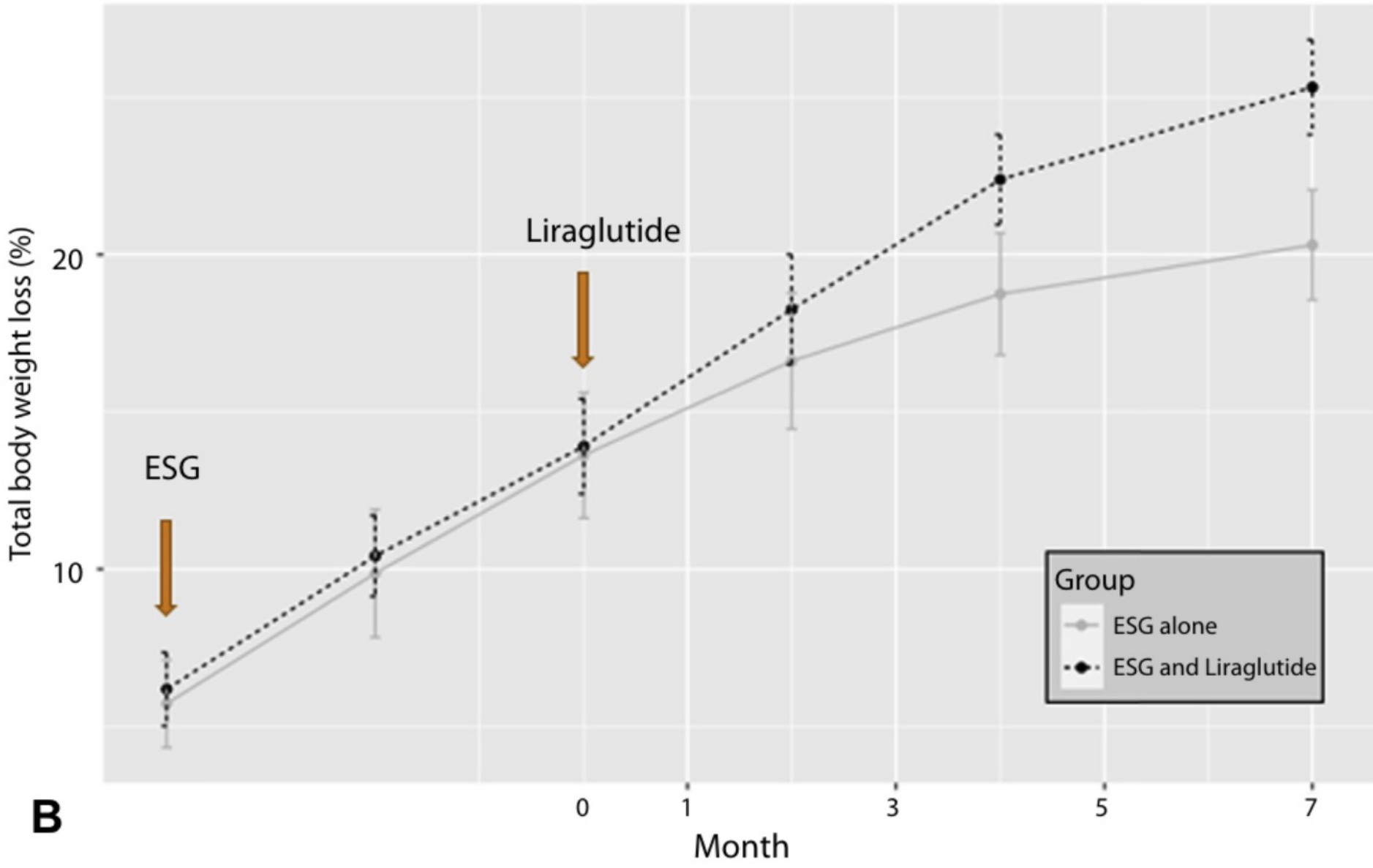
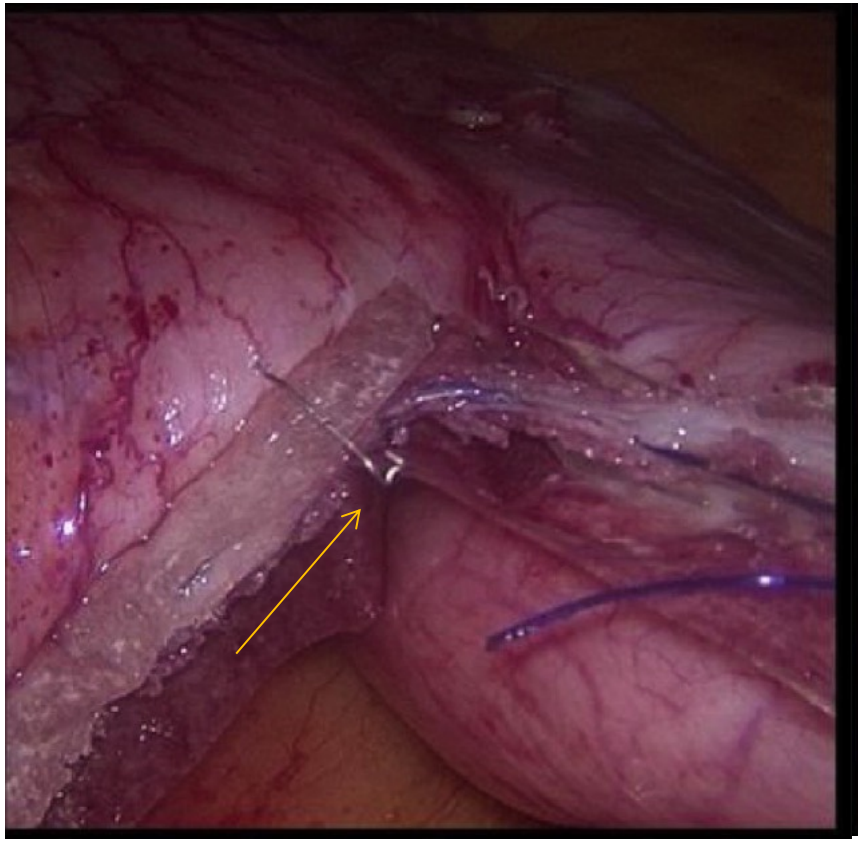
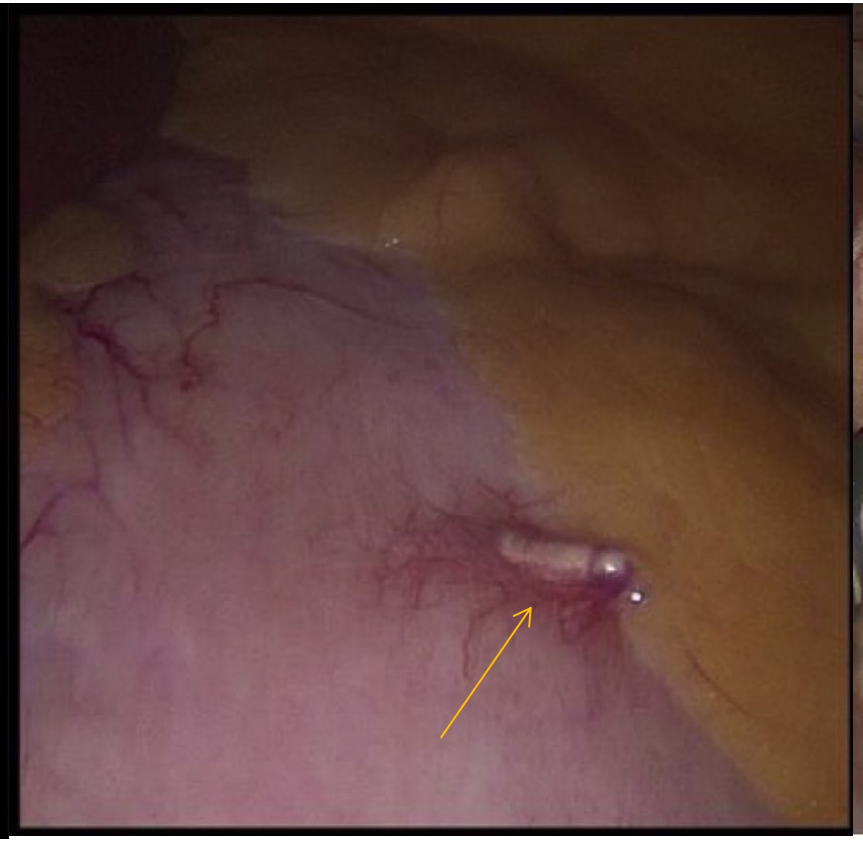
Endoscopic sleeve gastroplasty versus laparoscopic sleeve gastrectomy: a case-matched study. GIE 2019

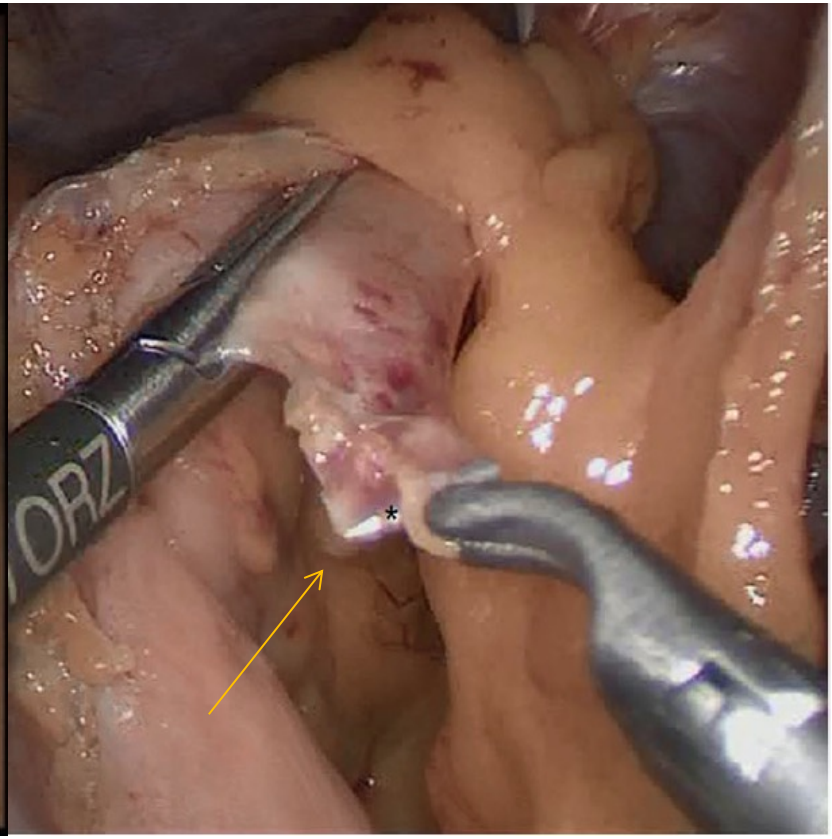


Conclusions: Addition of liraglutide at 5 months results in superior weight loss and improved efficacy as demonstrated by decreased body fat 12 months after ESG. Further studies are imperative to determine optimal dose, timing, and duration of liraglutide. (Gastrointest Endosc 2021;93:1316-24.)

ESG to LSG







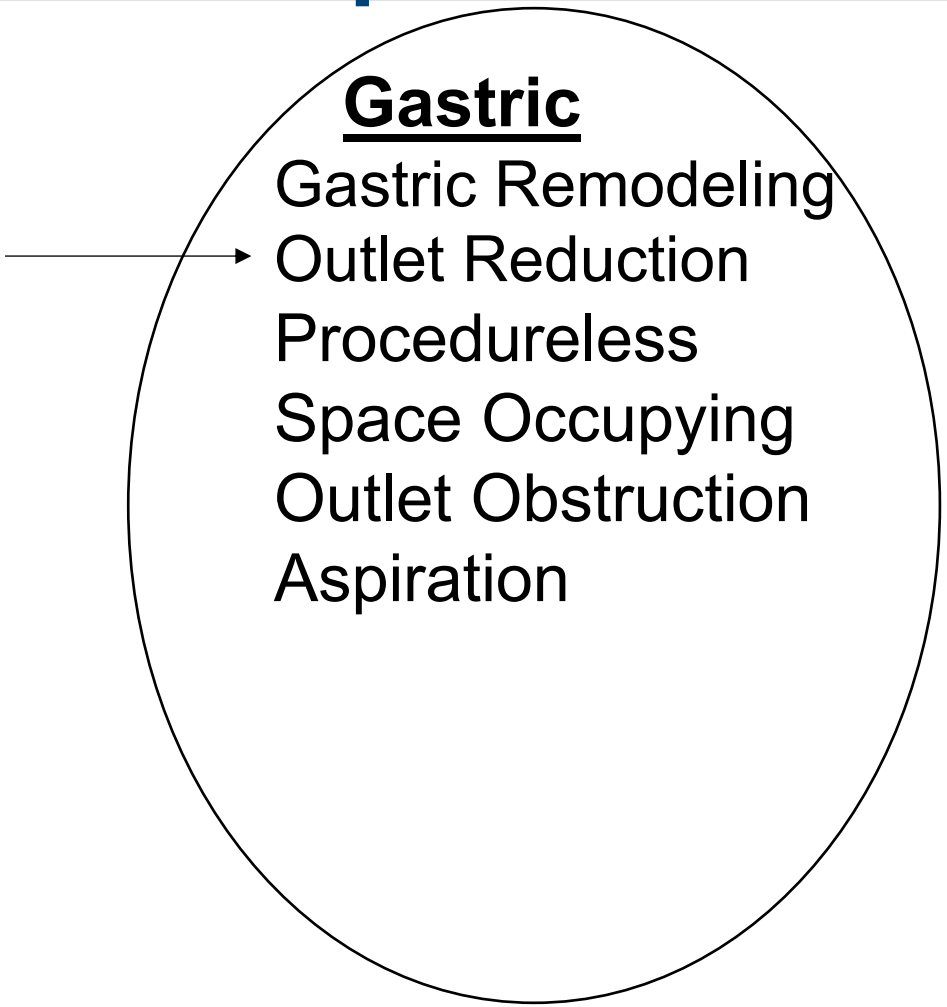
ESG: Insurance Coverage and Next Steps

- Medicare HCPCS code for procedure now available

- Improve access to patient populations that lack data on efficacy
  - Cancer survivors
  - Minorities, including Hispanic and non-Hispanic Blacks

- Ideal timing to augment weight loss with medications

Endoscopic Bariatric Therapies (EBTs)



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Gastric Remodeling

Outlet Reduction

Procedureless

Space Occupying

Outlet Obstruction

Aspiration

Small Bowel

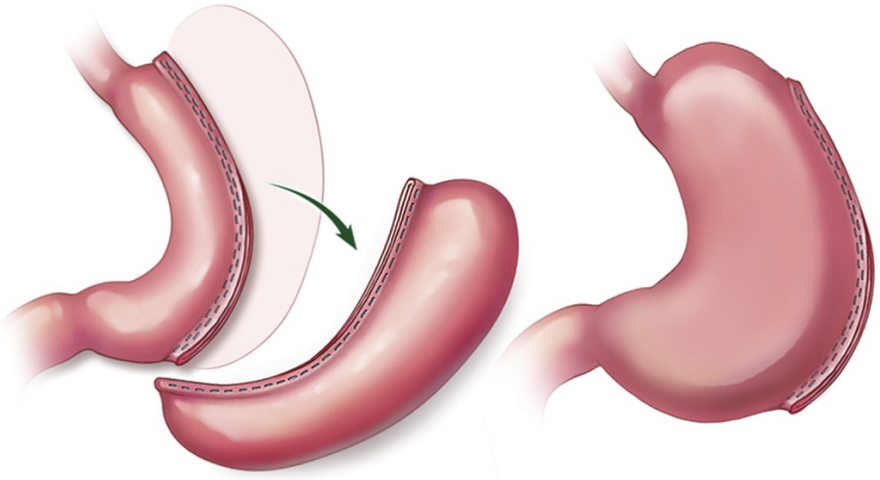
Sleeves

Duodenal Resurfacing

Flow altering

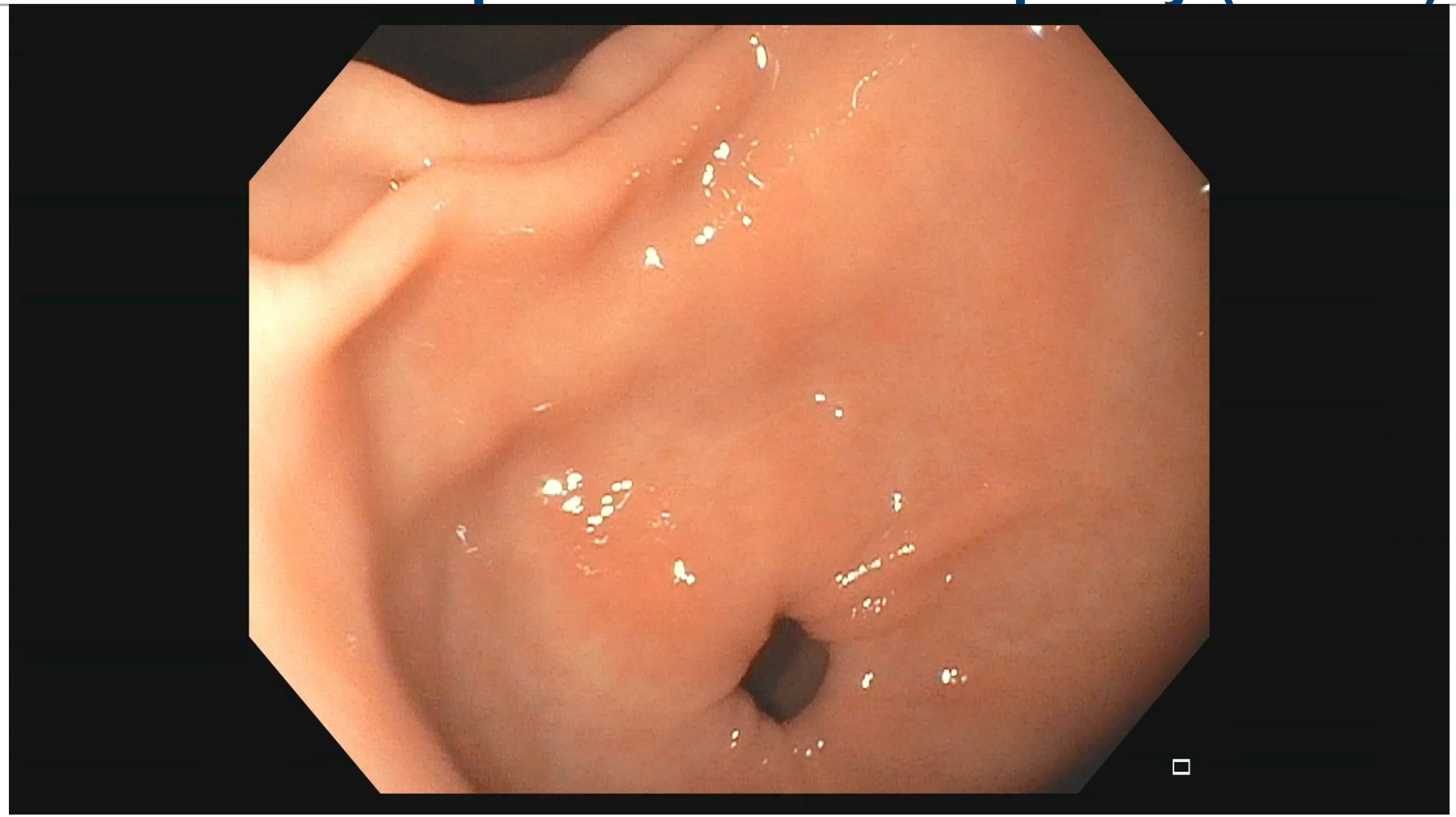
Revisional Endoscopic Sleeve Gastroplasty (r-ESG)

- **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.

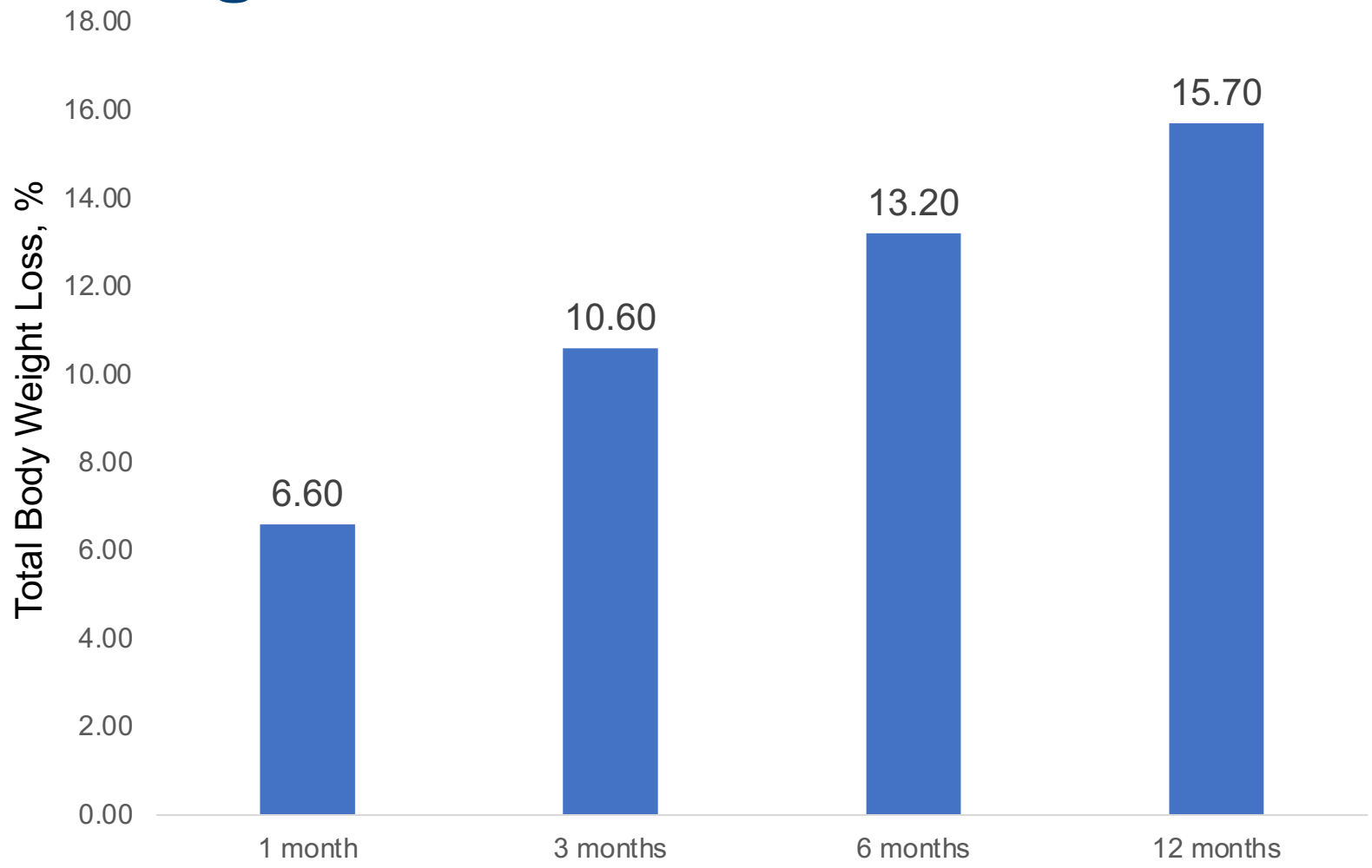


- **Who Qualifies?**
  - Weight regain after laparoscopic sleeve gastrectomy with a BMI of at least 27 kg/m^2
  - High risk for surgical revision to Roux-en-Y gastric bypass or do not want to pursue surgery

Revisional Endoscopic Sleeve Gastroplasty (r-ESG): Video



r-ESG: Weight Loss Outcomes



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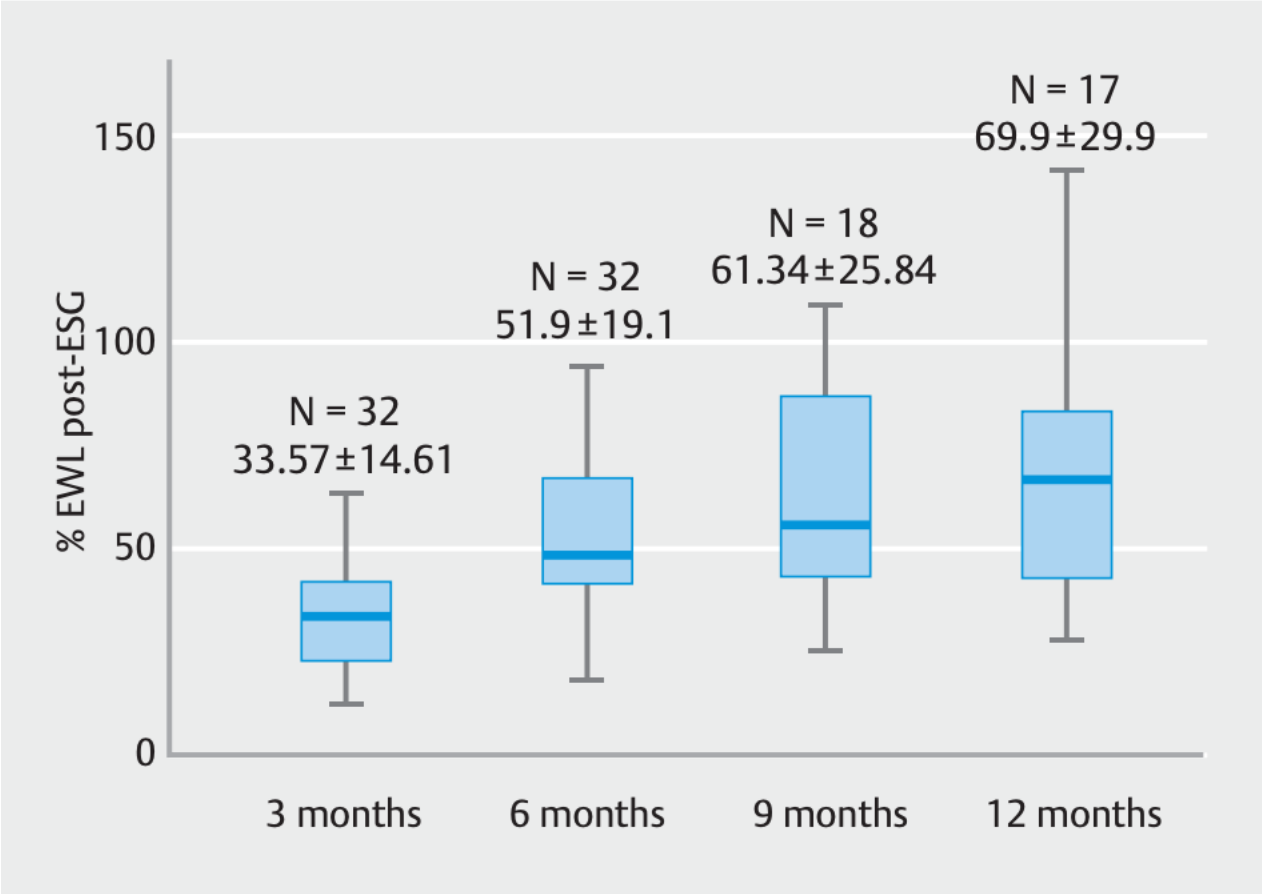
Revisional endoscopic sleeve gastroplasty of laparoscopic sleeve gastrectomy: an international, multicenter study. GIE 2021

r-ESG: Weight Loss Outcomes



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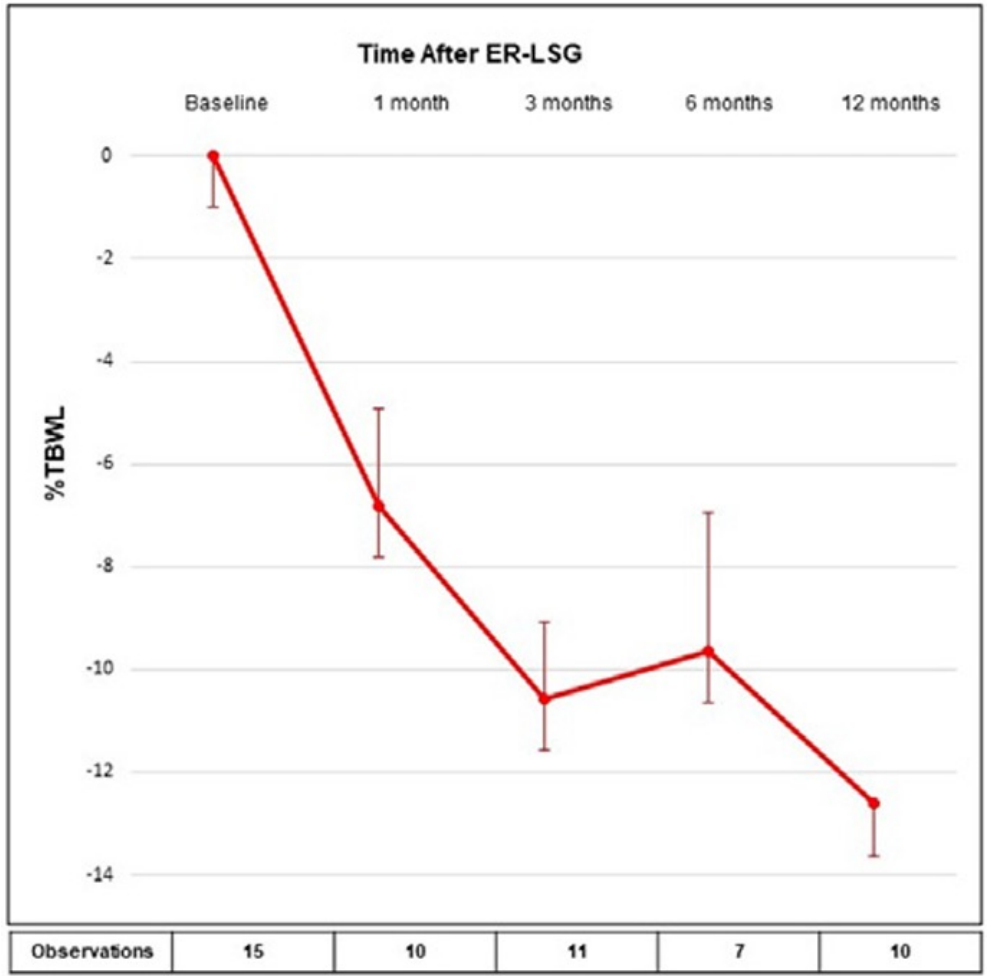
Endoscopic sleeve gastroplasty in the management of weight regain after sleeve gastrectomy. Endoscopy 2020

r-ESG: Weight Loss Outcomes



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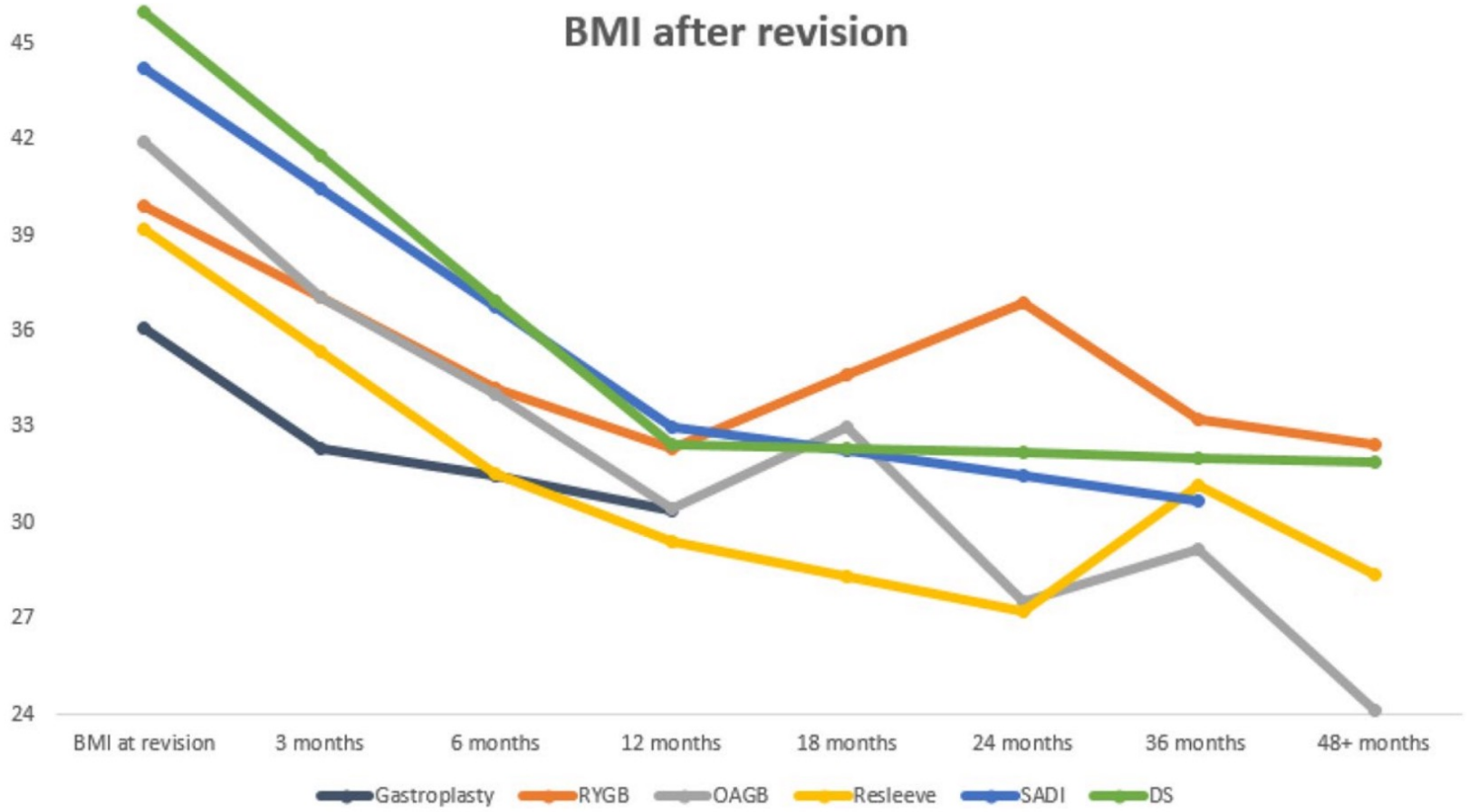
Endoscopic revision of laparoscopic sleeve gastrectomy: a single center experience of weight loss outcomes and safety. GIE 2023.

r-ESG: Weight Loss Outcomes



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Treatment Options for Weight Regain or Insufficient Weight Loss After Sleeve Gastrectomy: a Systematic Review and Meta-analysis. Obes Surg 2022

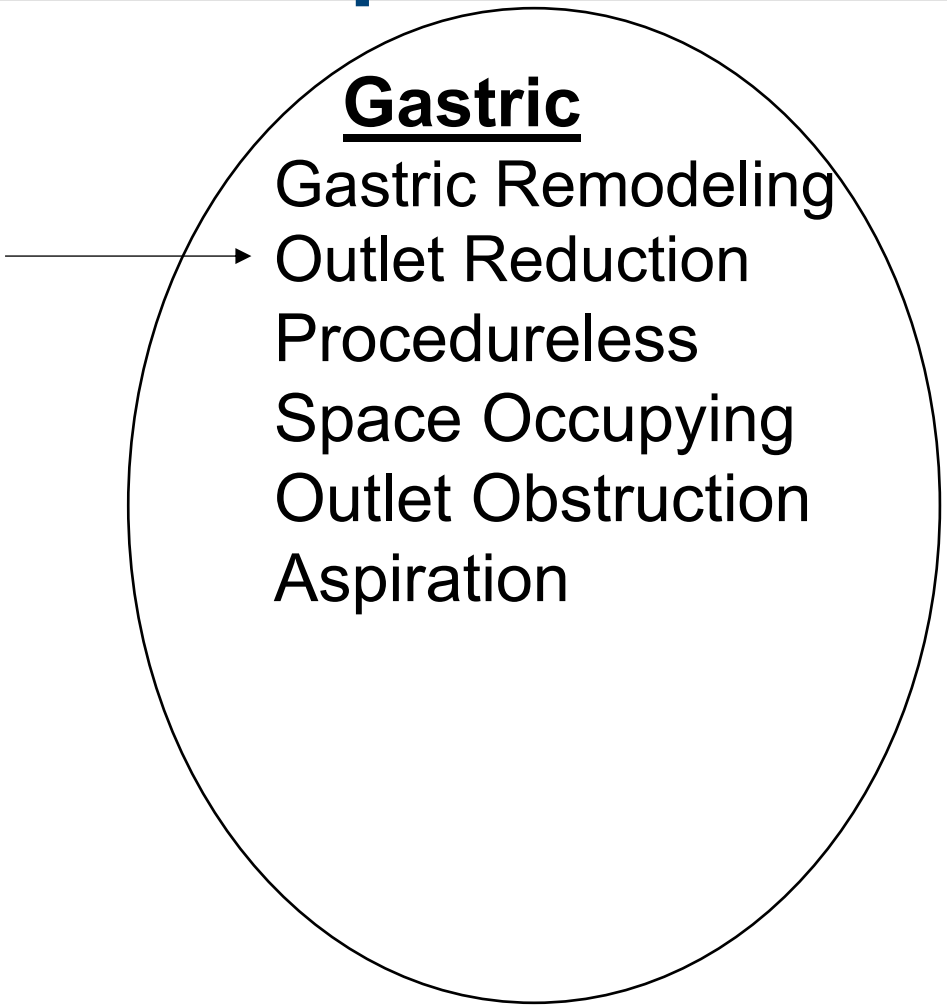
r-ESG: Adverse Events

- Similar adverse events to ESG
  - Dehydration
  - GERD
  - Nausea
  - Vomiting

r-ESG: Next Steps

- Long term efficacy > 1 year

Endoscopic Bariatric Therapies (EBTs)



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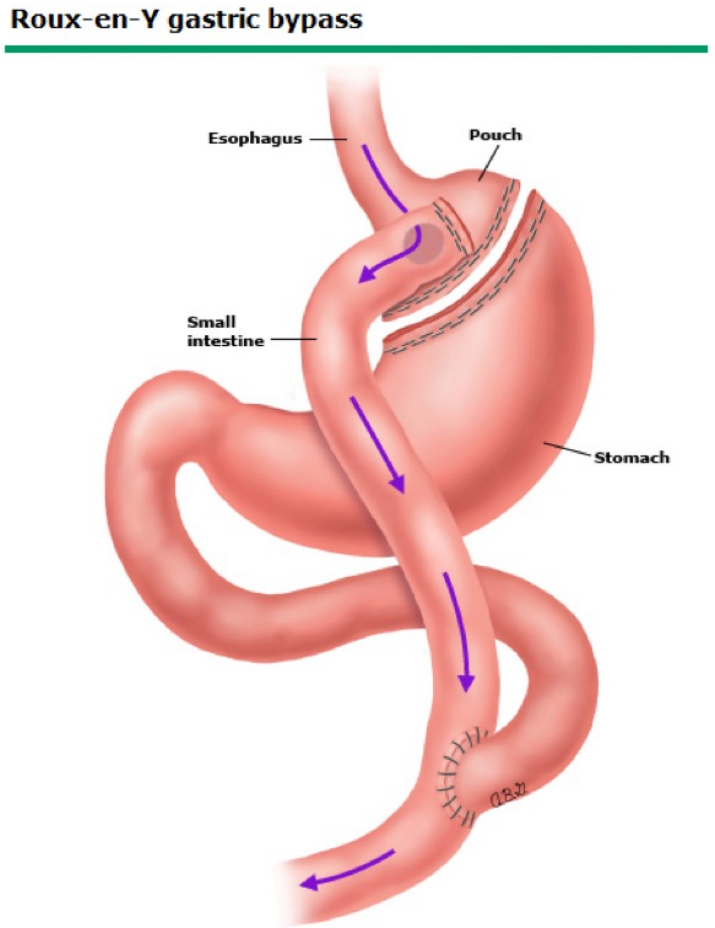
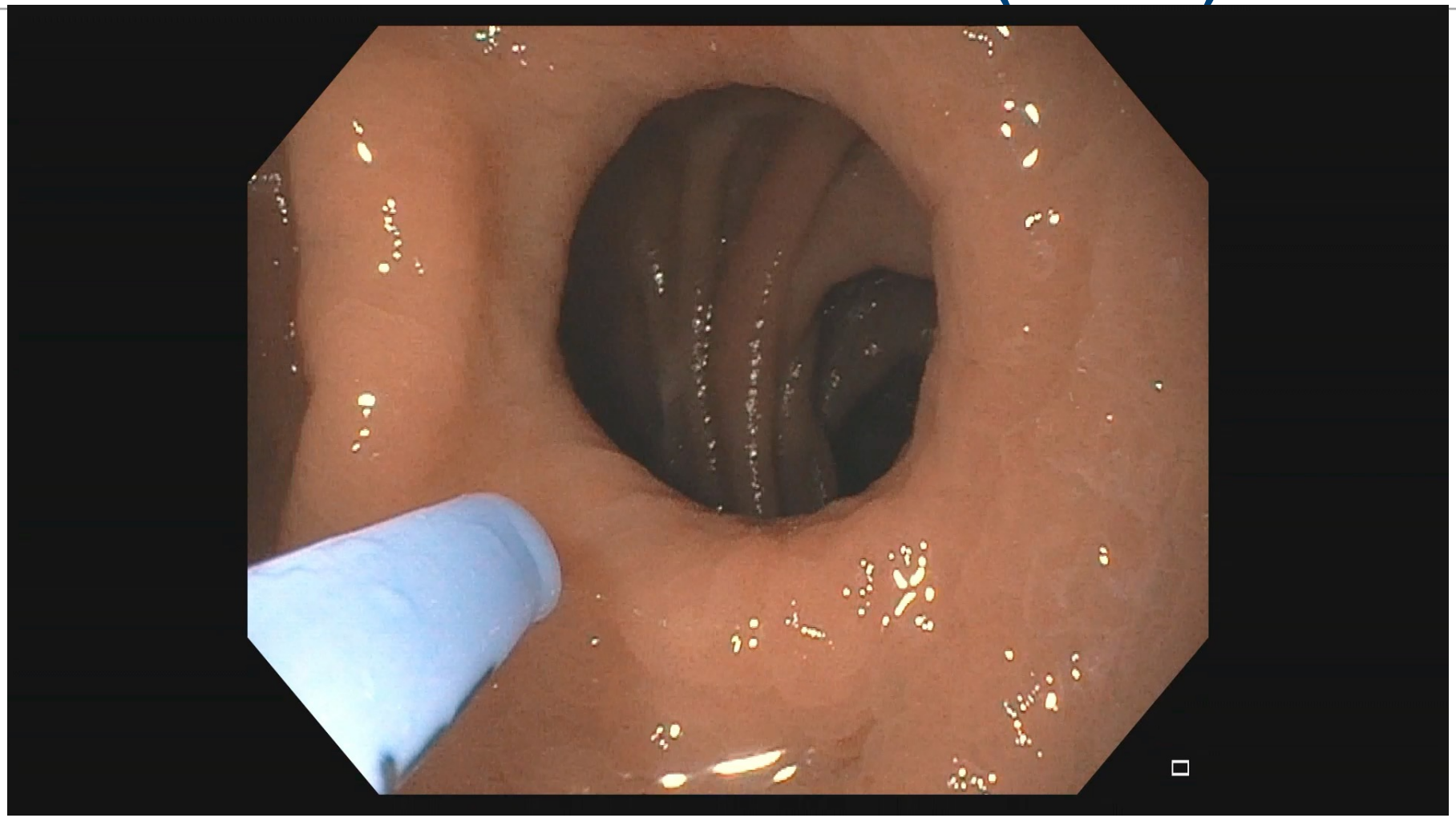
Transoral Gastric Outlet Reduction (TORE)

- **What is it:**
  - Transoral outlet reduction (TORe) uses APC and the OverStich Device to reduce the size of the GJ anastomosis.

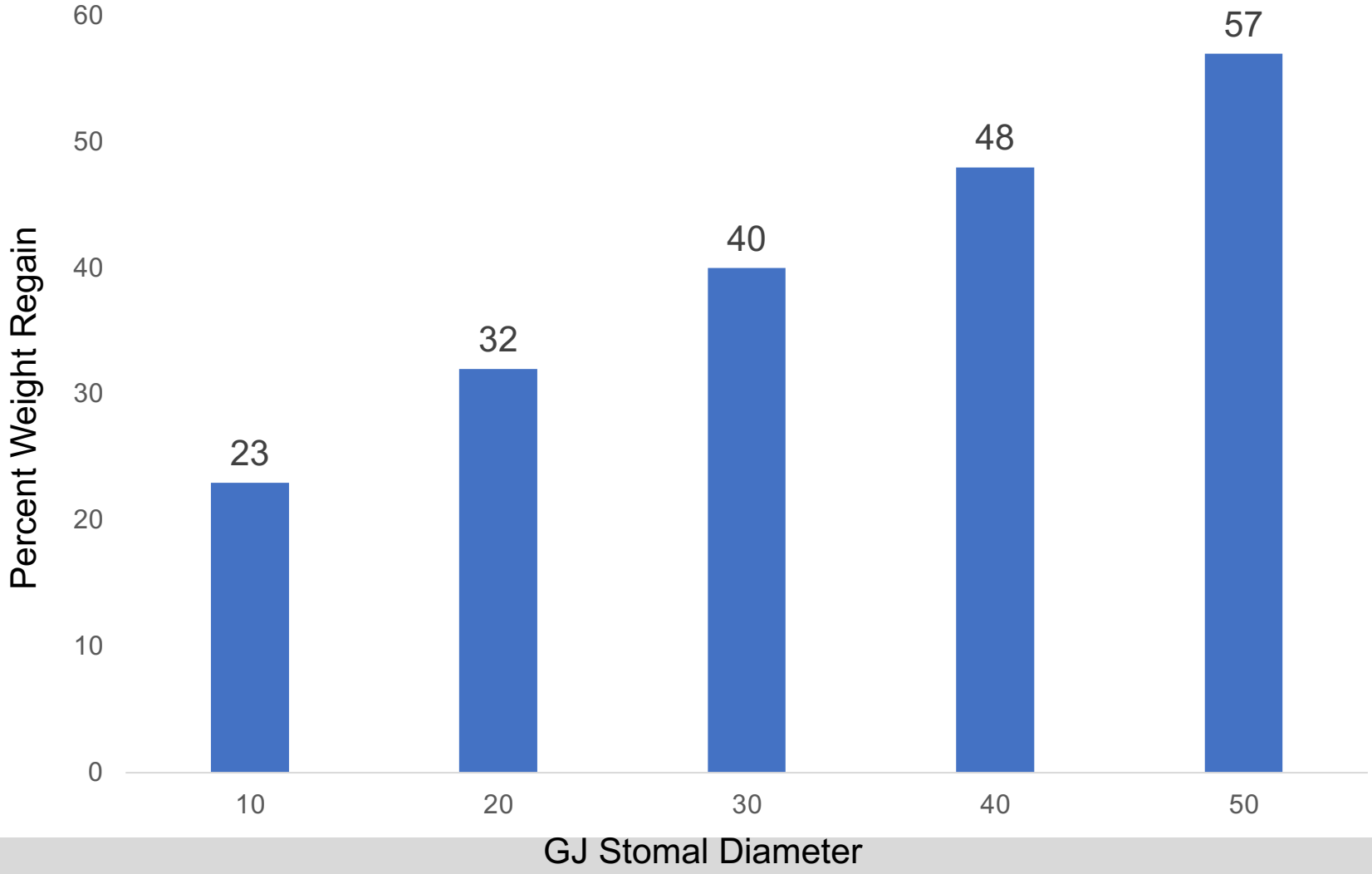
- **Who Qualifies?**
  - Weight regain after Roux-en-Y gastric bypass with BMI of at least 27 kg/m^2
  - Dumping syndrome and/or reactive hypoglycemia after Roux-en-Y gastric bypass
  - Dilated gastrojejunal anastomosis



Transoral Gastric Outlet Reduction (TORE): Video



Transoral Gastric Outlet Reduction (TORE): Weight Loss Outcomes



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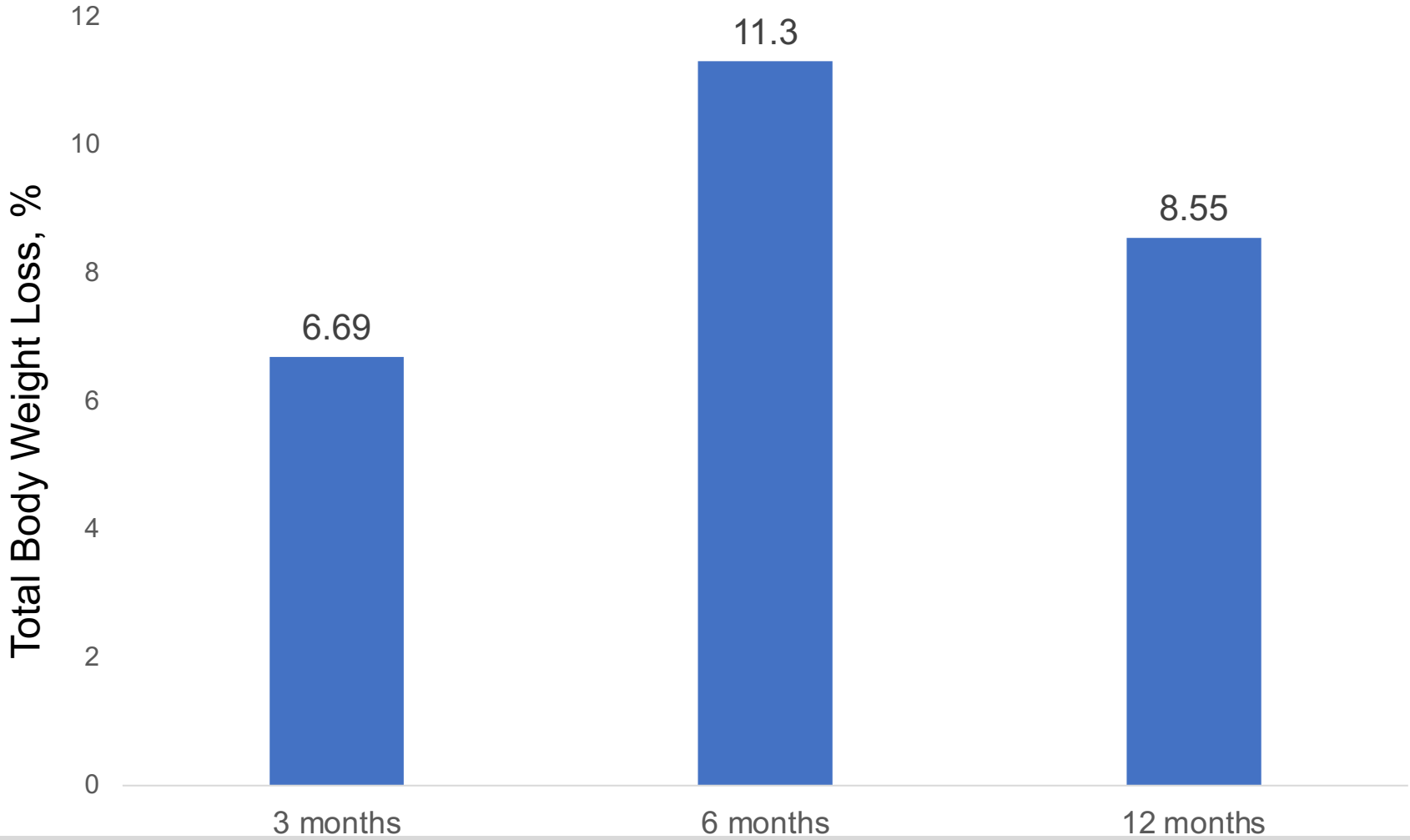
Gastrojejunal stoma diameter predicts weight regain after Roux-en-Y gastric bypass. Clin Gastroenterol Hepato 2011

Transoral Gastric Outlet Reduction (TORE): Weight Loss Outcomes



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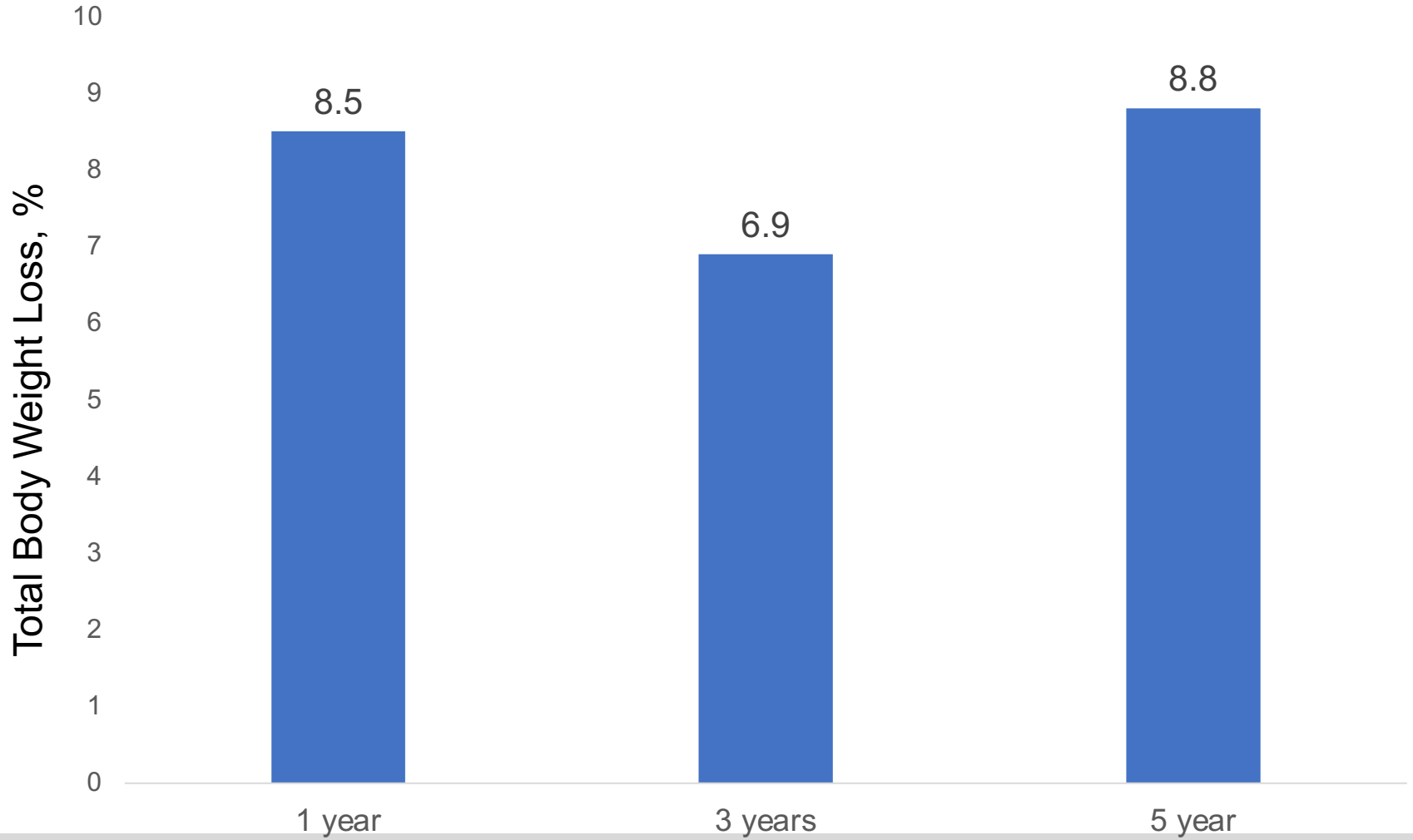
Five-year outcomes of transoral outlet reduction for the treatment of weight regain after Roux-en-Y gastric bypass. GIE 2020

Transoral Gastric Outlet Reduction (TORE): Weight Loss Outcomes



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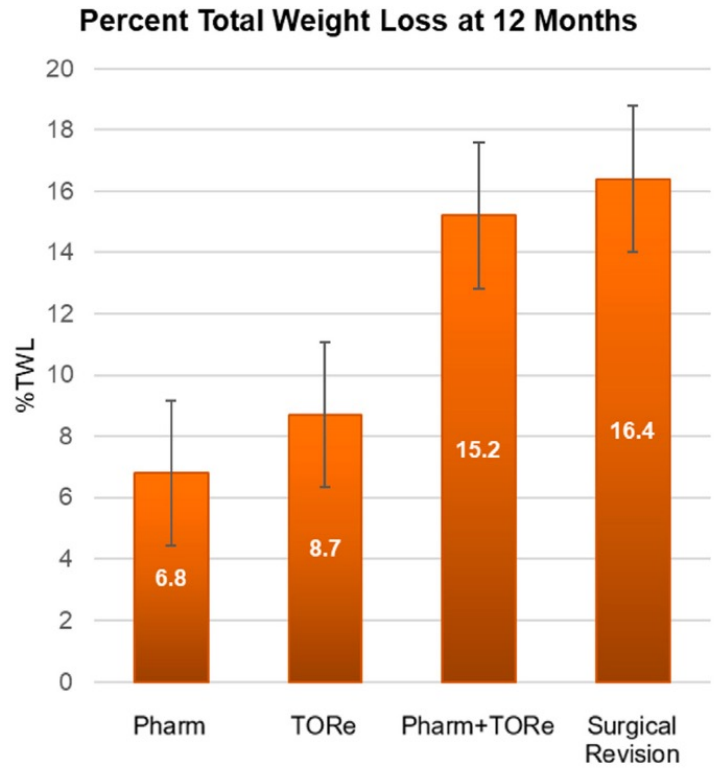
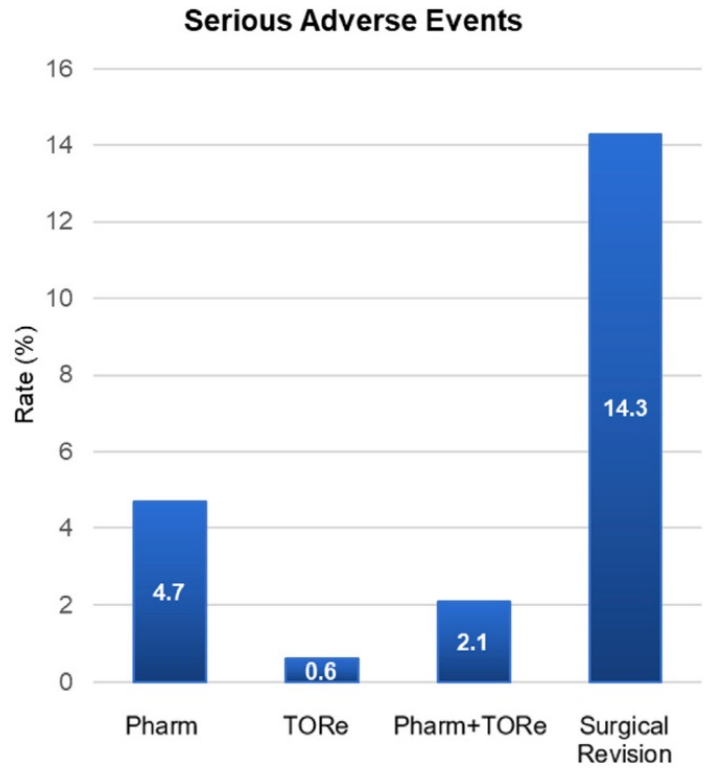
Efficacy of transoral outlet reduction in Roux-en-Y gastric bypass patients to promote weight loss: a systematic review and meta-analysis. Endosc Int Open 2020

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)





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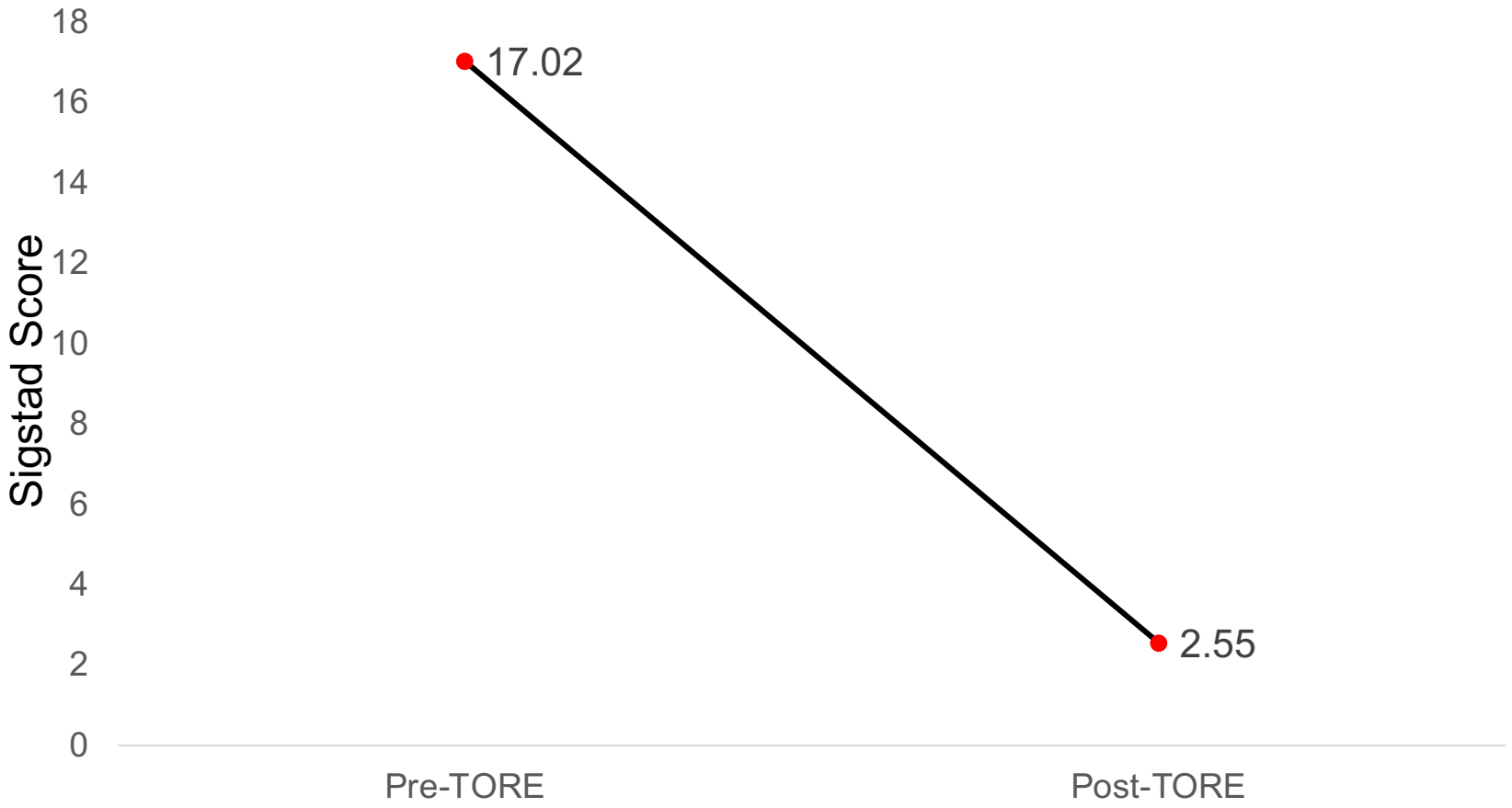
Combining transoral outlet reduction with pharmacotherapy yields similar 1-year efficacy with improved safety compared with surgical revision for weight regain after Roux-en-Y gastric bypass. GIE 2023.

Transoral Gastric Outlet Reduction (TORE): Dumping Syndrome



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Endoscopic management of dumping syndrome after Roux-en-Y gastric bypass: a large international series and proposed management strategy. GIE 2020

Transoral Gastric Outlet Reduction (TORE): Reactive Hypoglycemia

Obesity Surgery (2019) 29:3773–3775
https://doi.org/10.1007/s11695-019-04113-x

MULTIMEDIA ARTICLE

Endoscopic Gastrojejunal Revision (Transoral Outlet Reduction) for Persistent Hypoglycemia After Gastric Bypass

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Abstract

Background The patient presented with symptomatic postprandial biweekly hypoglycemic seizures. Her hypoglycemic episodes were aggravated by stress and also occurred during sleep. She managed these hypoglycemic episodes with an endocrinologist, trying both nutritional and medical management without successful control of her symptoms. An endoscopic gastrojejunal revision (EGJR) was recommended to provide more restriction and prolong transit time into the Roux limb to decrease the chance of postoperative dumping syndrome and subsequent hypoglycemia.

Methods This video is a case study of an EGJR done for persistent postoperative hypoglycemia. The gastroscope was introduced and using Argon Plasma Coagulation at a flow of 8 liters/min and 30 watts; the mucosa around the gastrojejunal stoma was ablated circumferentially. This was done to decrease bleeding from needle placement and to promote adherence of the mucosa after the sutures were placed. The purse-string technique was favored for this procedure due to an inherent reduction in suture tension. Several full-thickness bites were taken to narrow the stoma from 20 to 4 mm in diameter.

Results The patient was discharged home the same day following the procedure. She was placed on a two week liquid bariatric postoperative diet. At two week follow-up, the patient reported normal blood sugars and no hypoglycemic episodes since surgery. At six month follow-up, the patient reported significant improvement in her hypoglycemia symptoms, and no further syncopal episodes or seizures.

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TORE: Adverse Events

- Adverse events are uncommon
- Abdominal pain and nausea occur the most frequently
- Other less common: Bleeding and gastrojejunal stenosis

Conclusion

- There are many endoscopic bariatric procedures available for patients who either do not qualify or do not want bariatric surgery
- Careful discussion of risks, benefits, and expectations is important prior to performing any of these procedures
- Having support with endocrinologists, dieticians, behavioral psychologists, and surgery is vitally important
- There are options to help patients continue to lose weight after a prior bariatric procedure

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