INFLAMMATORY BOWEL DISEASE AND OBESITY: WHAT DO WE KNOW IN 2024

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DISCLOSURES

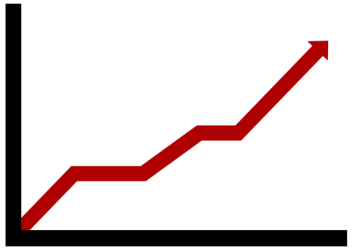
- I have no relevant financial disclosures to report.

OBJECTIVES

- Discuss the prevalence and pathophysiological relationship between obesity and IBD
- Review recent literature on impact of obesity on outcomes of IBD
- Review impact of weight-loss surgery (WLS) and anti-obesity medications (AOM) in patients with IBD

EPIDEMIOLOGY OF OBESITY IN IBD

- 15-40% of adults with IBD have obesity; additional 20-40% are overweight
  - Prevalence higher in US-based studies (~ 1/3rd of patients!)



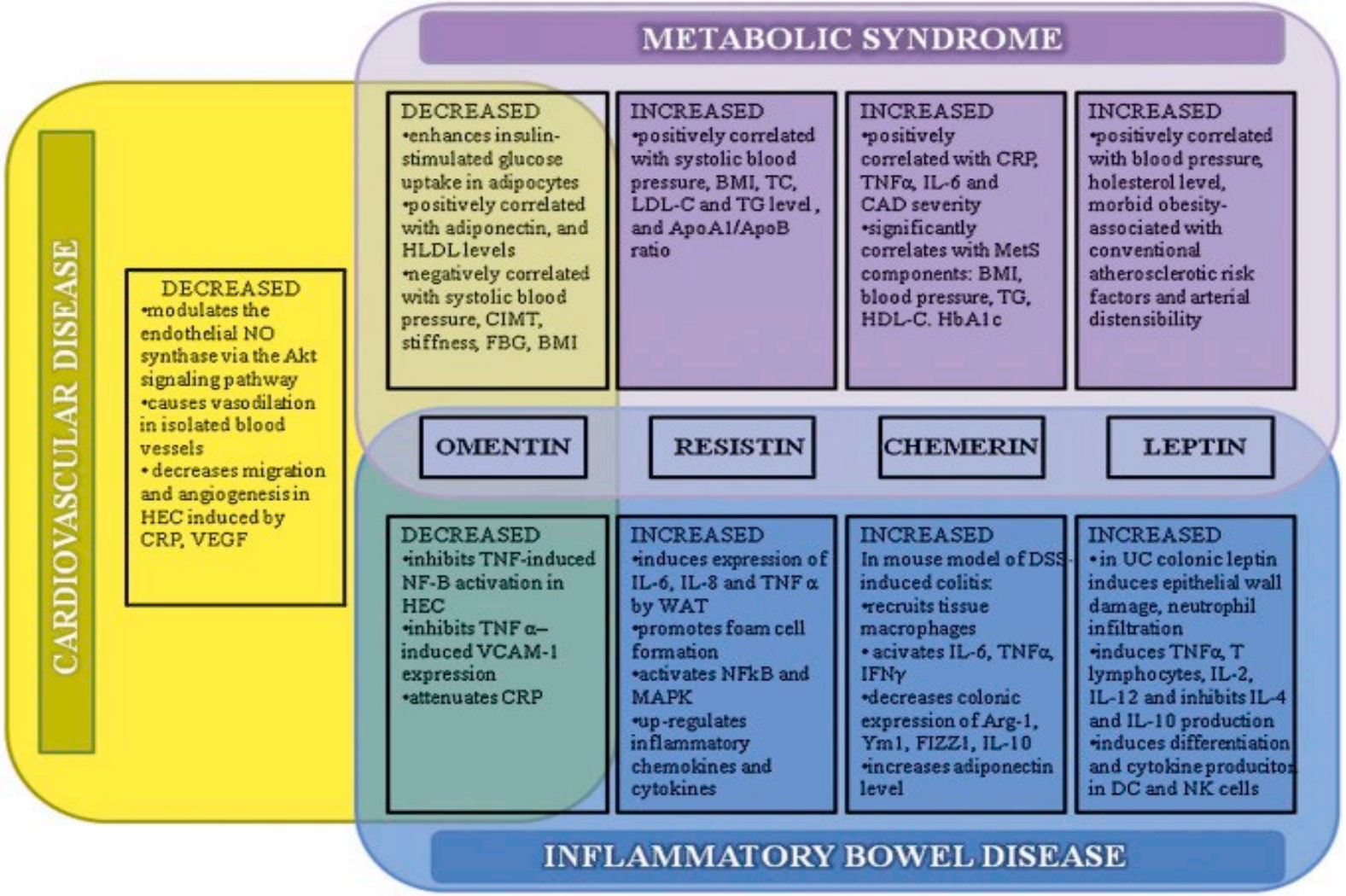
- Overall, rates of obesity in IBD similar to those observed in general population

- 9-10% of children with CD and 20-34% with UC with sex-specific BMI-for-age >85th percentile

- Increased trial participant weight in >10,000 patients across 40 clinical trials of Crohn's disease from 1997-2008
  - Mean weight increase from 57.1 kg in 1997 to 89.1 kg in 2008

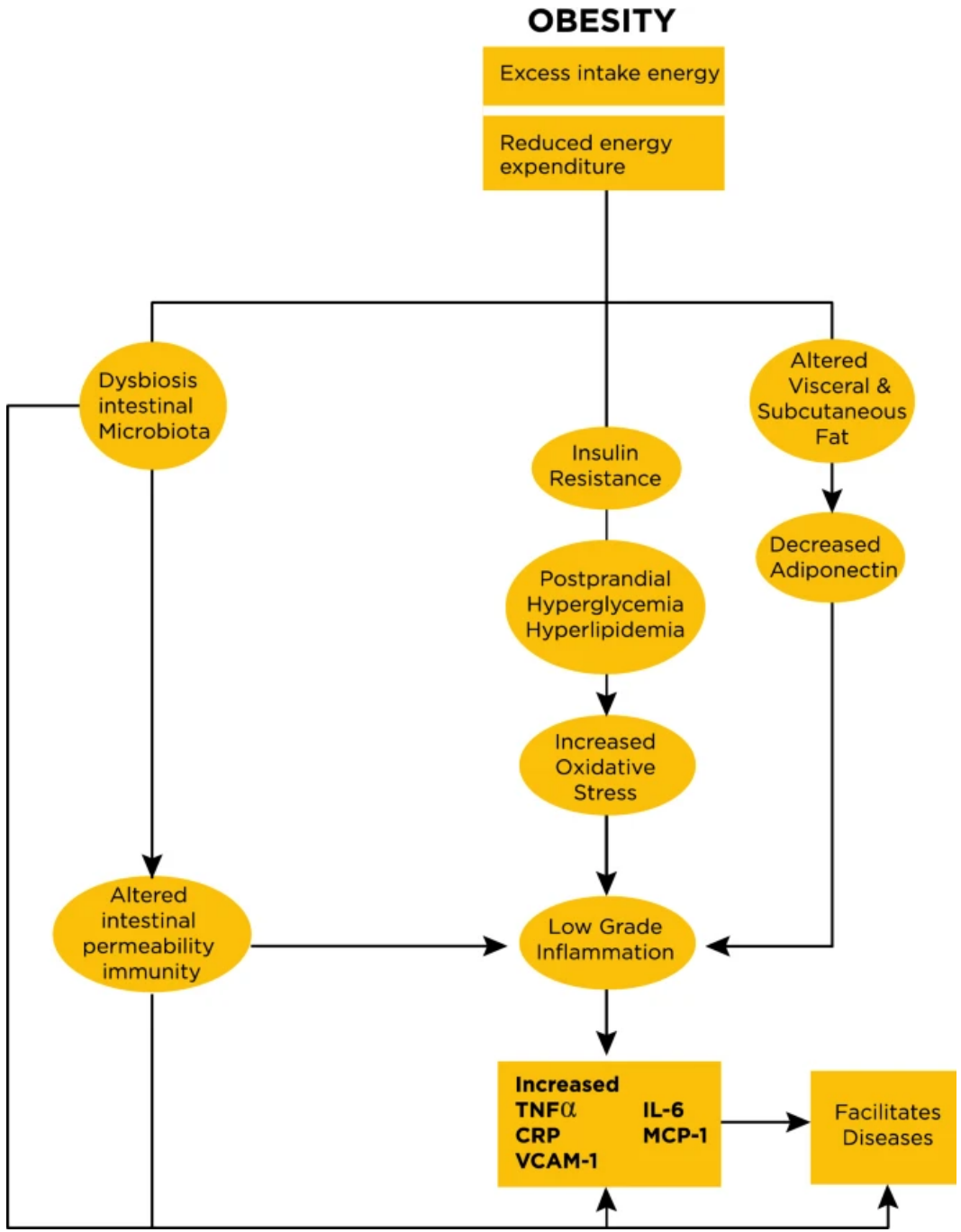
Flores et. al. *Dig Dis Sci*. 2015
Seminerio et. al. *Inflamm Bowel Dis*. 2015
Pringle et. al. . *Inflamm Bowel Dis*. 2015
Hass et. al. *Clin Gastroenterol Hepatol*. 2006
Kugathasan et. al. *J Pediatr*. 2007

ROLE OF ADIPOKINES AND THEIR LEVELS IN METS, IBD AND CVD



Michalak et. al. *Pharmacol Rep*. 2016

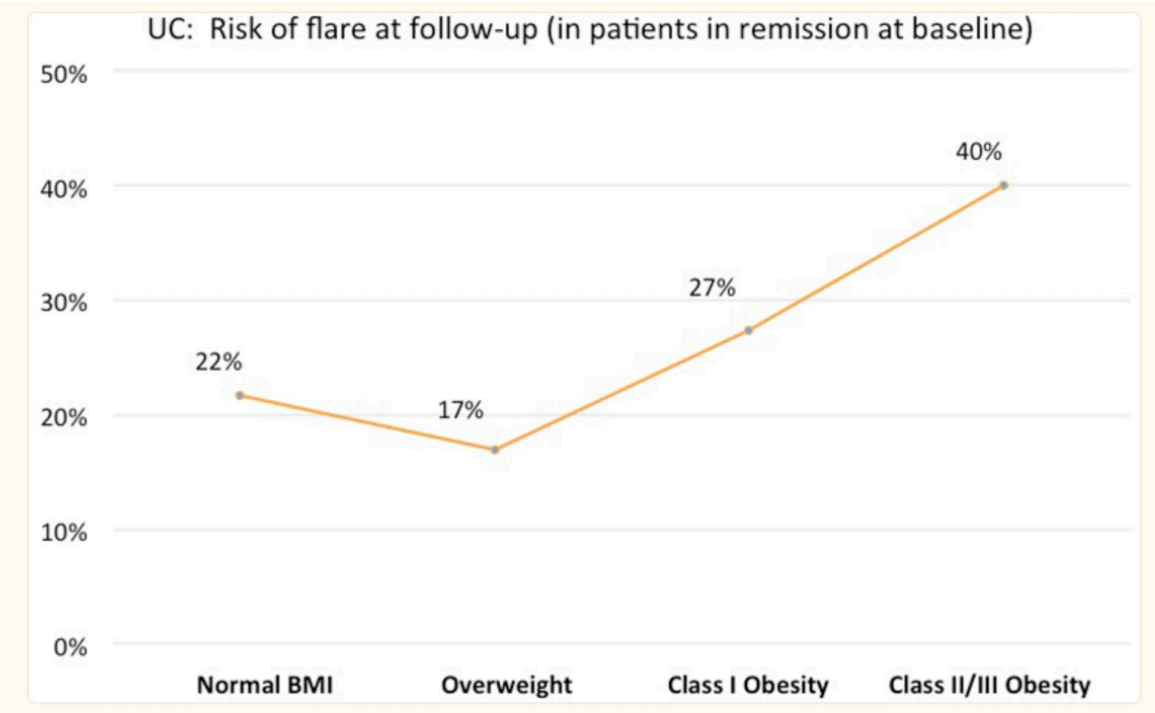
RELATIONSHIP BETWEEN OBESITY AND IBD



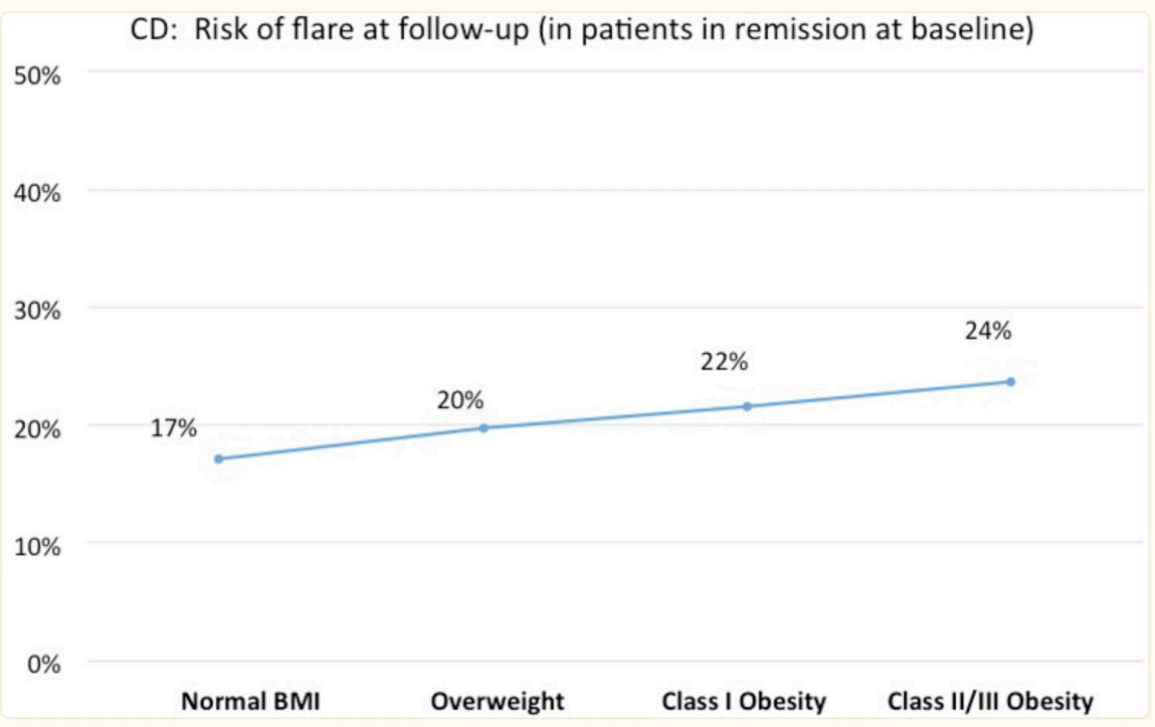
Szilagyi. *Clin J Gastroenterol*. 2019

DOES OBESITY AFFECT OUTCOMES OF IBD?

OBESITY INDEPENDENTLY ASSOCIATED WITH WORSENING DISEASE ACTIVITY AND PROMIS MEASURES IN IBD



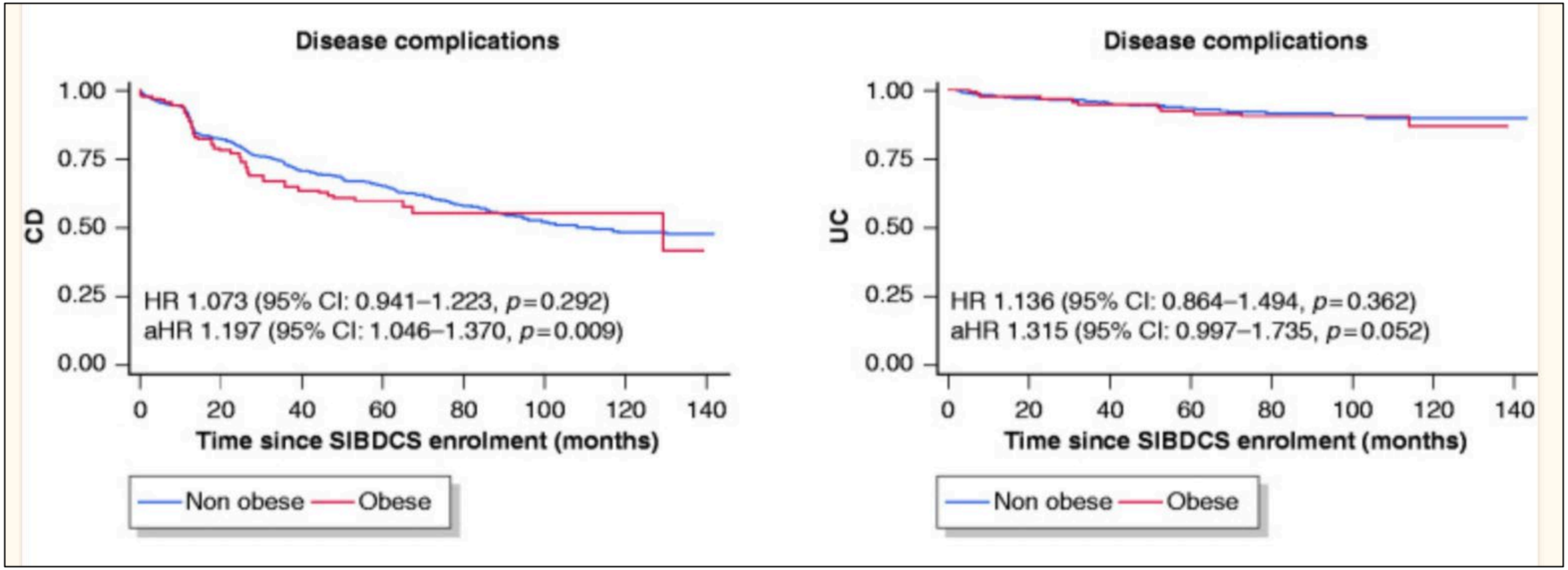
Class I obesity: OR 1.50 (1.07-2.09), p=0.02
Class II or III obesity: OR 1.86 (1.30-2.68), p=<0.01



Class I obesity: OR 1.65 (1.0—2.61), p=0.03
Class II or III obesity: OR 2.97 (1.75-5.17), p=<0.01

Jain et al. *Am J Gastroenterol*. 2019

OBESITY ASSOCIATED WITH DECREASED RATES OF DISEASE REMISSION AND INCREASED RISK OF COMPLICATED DISEASE IN CD



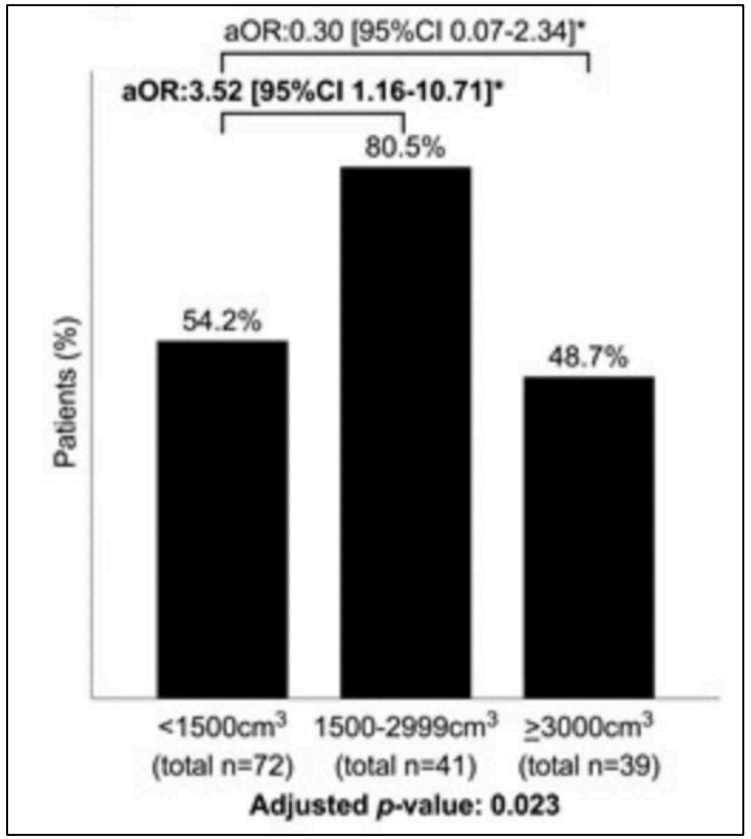
BMI ≥ 30 kg/m2 was an independent negative predictor for presence of disease remission defined as CDAI <100 (OR 0.61, 95% CI 0.40-0.92, p=0.02) for CD but not UC.

Greuter et al. *United European Gastroenterol J.* 2020

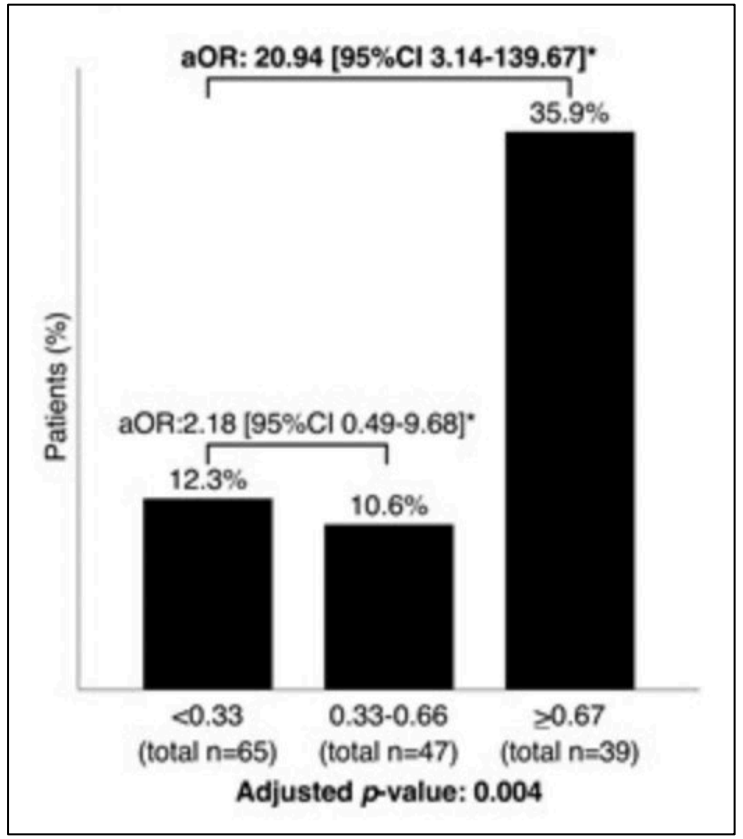
HIGH VAT VOLUME ASSOCIATED WITH RESPONSE TO TNF INHIBITOR AND RISK OF SURGERY

- Patients with VAT volume 1500-2999 cm^3 had higher odds of response to TNFi at 12 months compared to <1500 cm^3 but not >3000 cm^3
- Patients with visceral to subcutaneous adipose tissue ratio (VFI) > 0.67 had higher odds of surgery at 6 and 12 months compared to VFI <0.33

TNFi response at 12 months



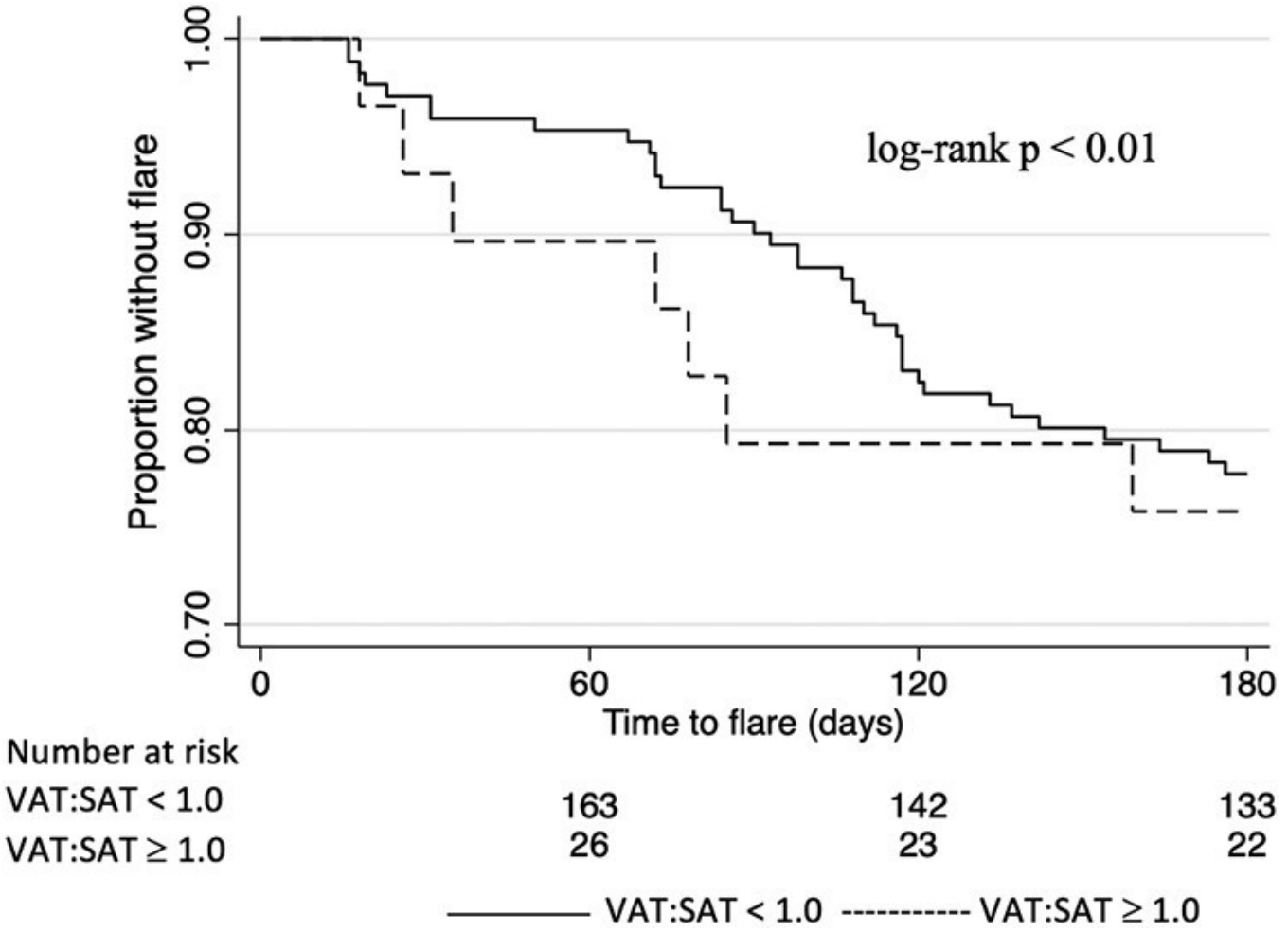
Surgery at 12 months



Gu et al. *Inflamm Bowel Dis*. 2022

VISCERAL ADIPOSITY ASSOCIATED WITH DECREASED TIME TO IBD FLARE

- Primary exposure = ratio of visceral adipose tissue to subcutaneous adipose tissue (VAT:SAT)
- Higher VAT:SAT associated with shorter time to IBD flare (HR 4.8, 95% CI 1.7-13)
- No relationship between BMI and time to IBD flare (aHR 0.73, 95% CI 0.32-1.67)

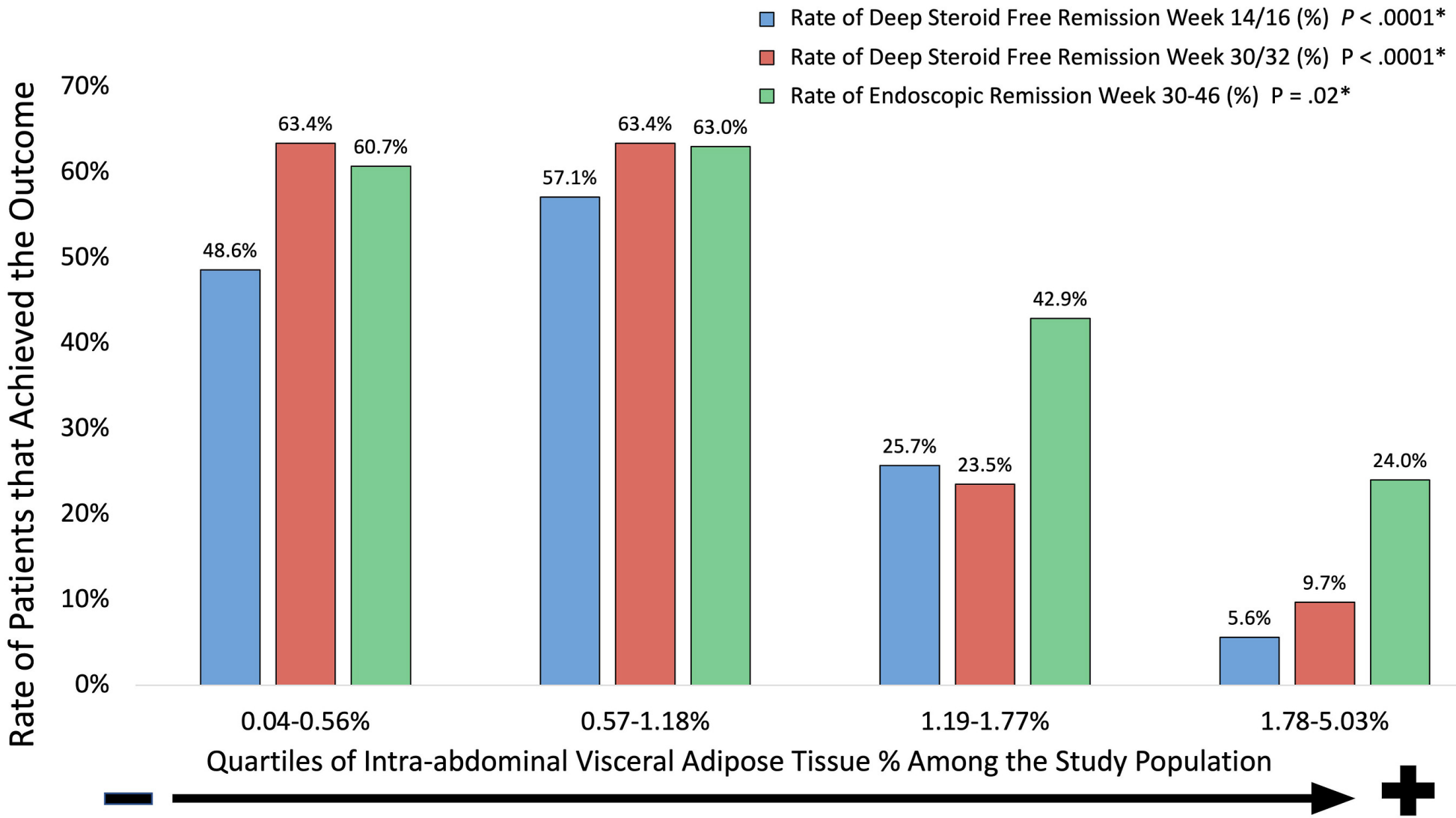


Sehgal et al. *Inflamm Bowel Dis*. 2024

HIGHER INTRA-ABDOMINAL VAT % IS INDEPENDENTLY ASSOCIATED WITH WORSE IBD OUTCOMES

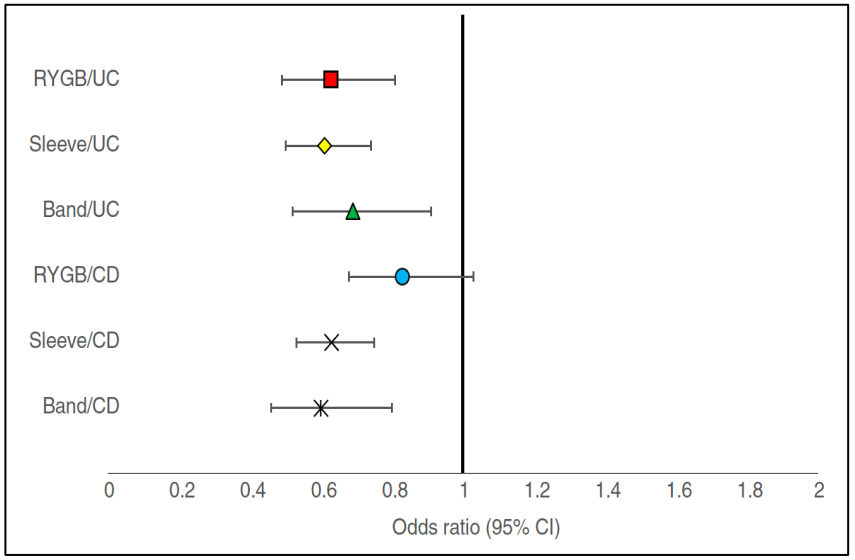
- Prospective observational cohort study in 141 patients with active IBD initiating infliximab, vedolizumab or ustekinumab and 51 healthy controls
- Higher IA-VAT% was associated with decreased likelihood of corticosteroid-free deep remission (wk 14-16) and endoscopic remission (wk 30-46) compared to lower IA-VAT%
- No significant difference in drug concentrations of infliximab, vedolizumab and ustekinumab in high vs low IA-VAT%
- Higher serum IL-6 and TNF levels observed at baseline in non-responders with high IA-VAT% compared with low IA-VAT%

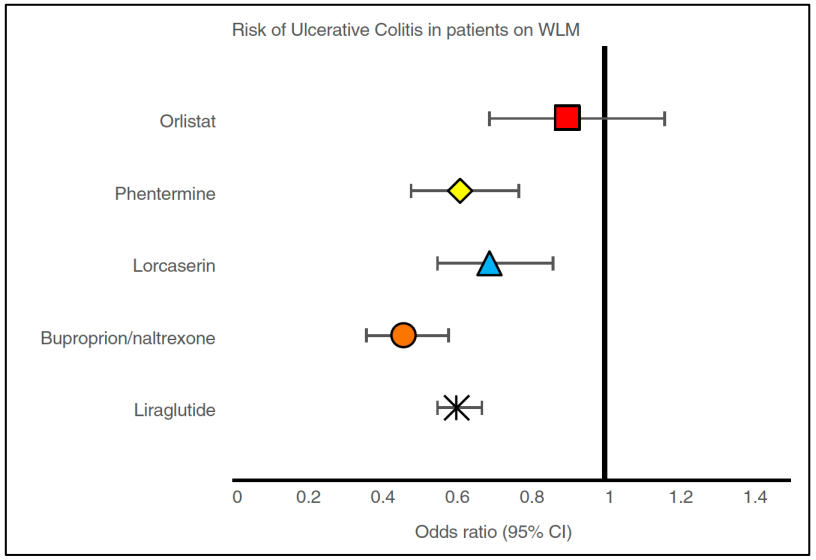
Yarur et al. *Gastroenterology*. 2023

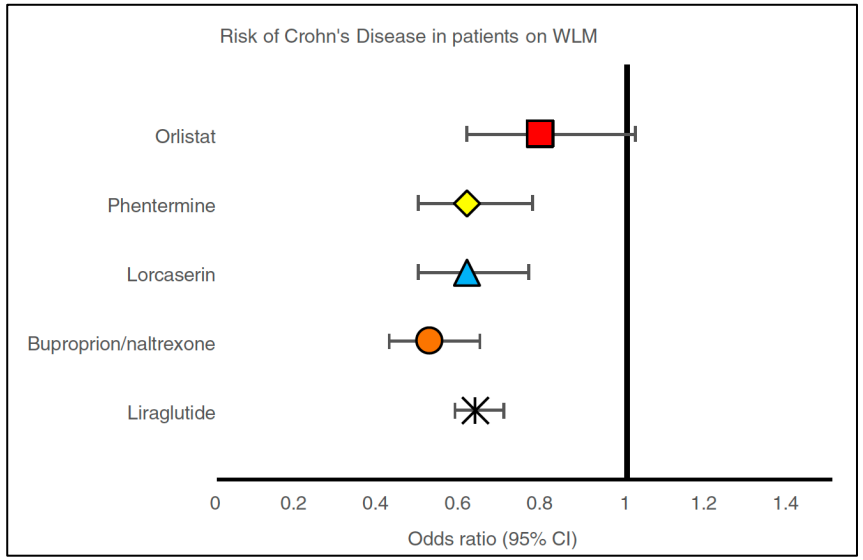


Yarur et al. *Gastroenterology*. 2023

OBESITY TREATMENTS AND IBD



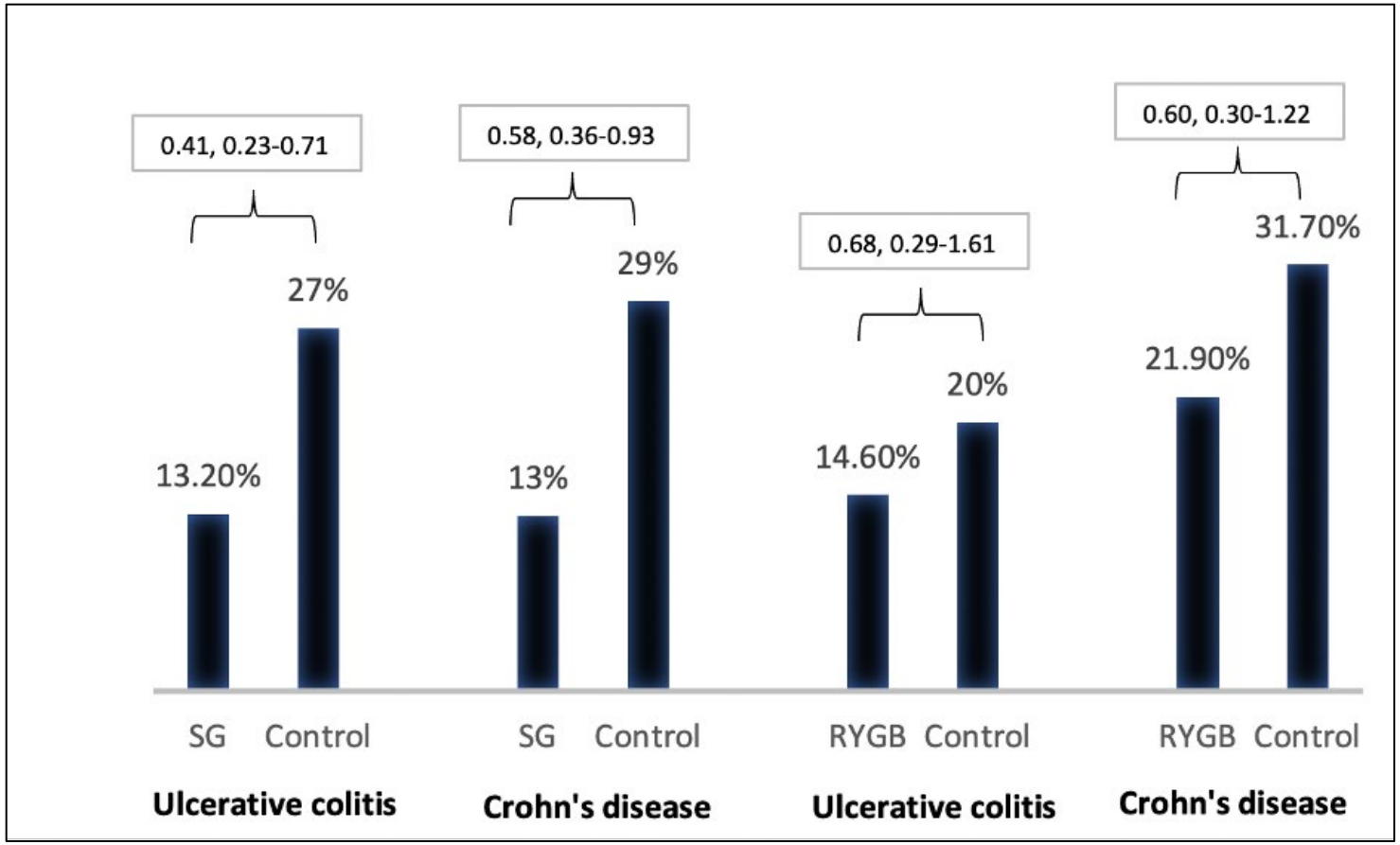




WLS AND AOM ASSOCIATED WITH LOWER RISK OF DE-NOVO IBD COMPARED WITH PATIENTS WITH OBESITY NOT EXPOSED TO THESE INTERVENTIONS

Kochhar et al. *Aliment Pharmacol Ther*. 2020

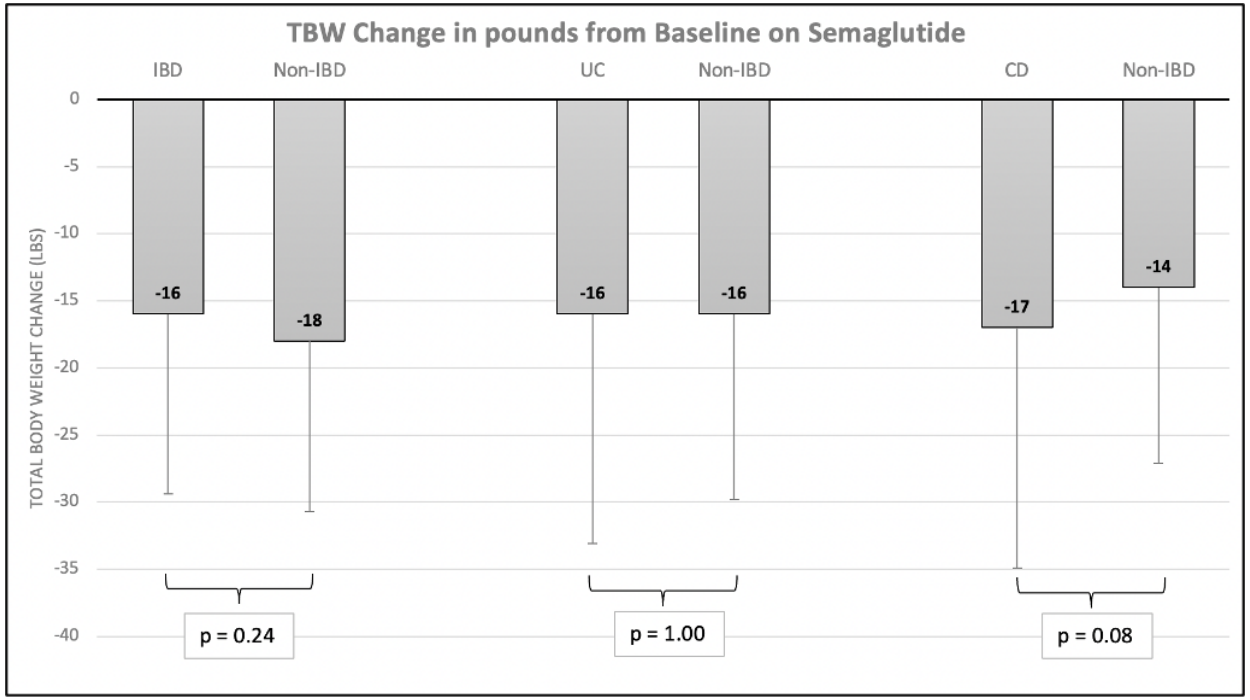
IBD OUTCOMES AFTER WEIGHT-LOSS SURGERY

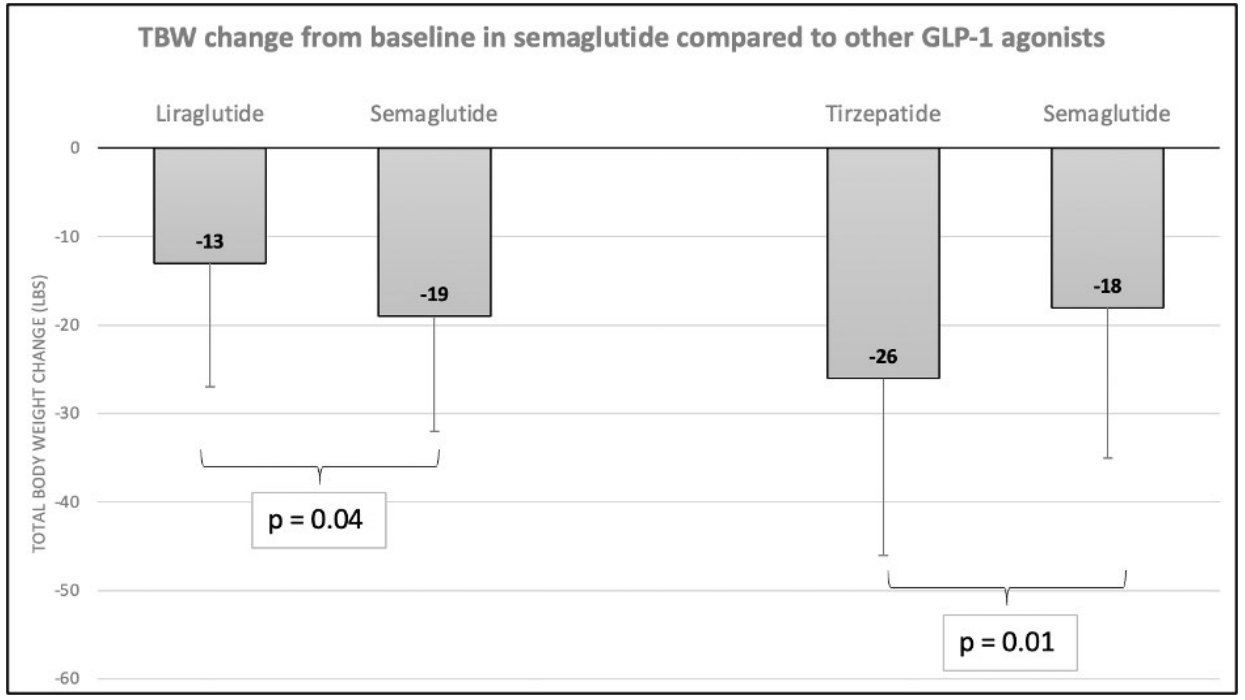


- 482 patients with IBD and morbid obesity (mean BMI 42, 60% CD, 68% SG)
- Lower risk of IV steroid use and surgery in WLS group compared to controls within 2 years (aOR 0.31, 95% CI 0.17-0.56)
- Sleeve gastrectomy (SG) but not Roux-en-Y gastric bypass (RYGB) associated with improved disease specific outcomes
- Similar findings noted in a prior case control study and systematic review and meta-analysis

Desai et al. *J Clin Gastroenterol*. 2023
Neto et al. *Inflamm Bowel Dis*. 2020
Garg et. al. Obes Surg. 2020

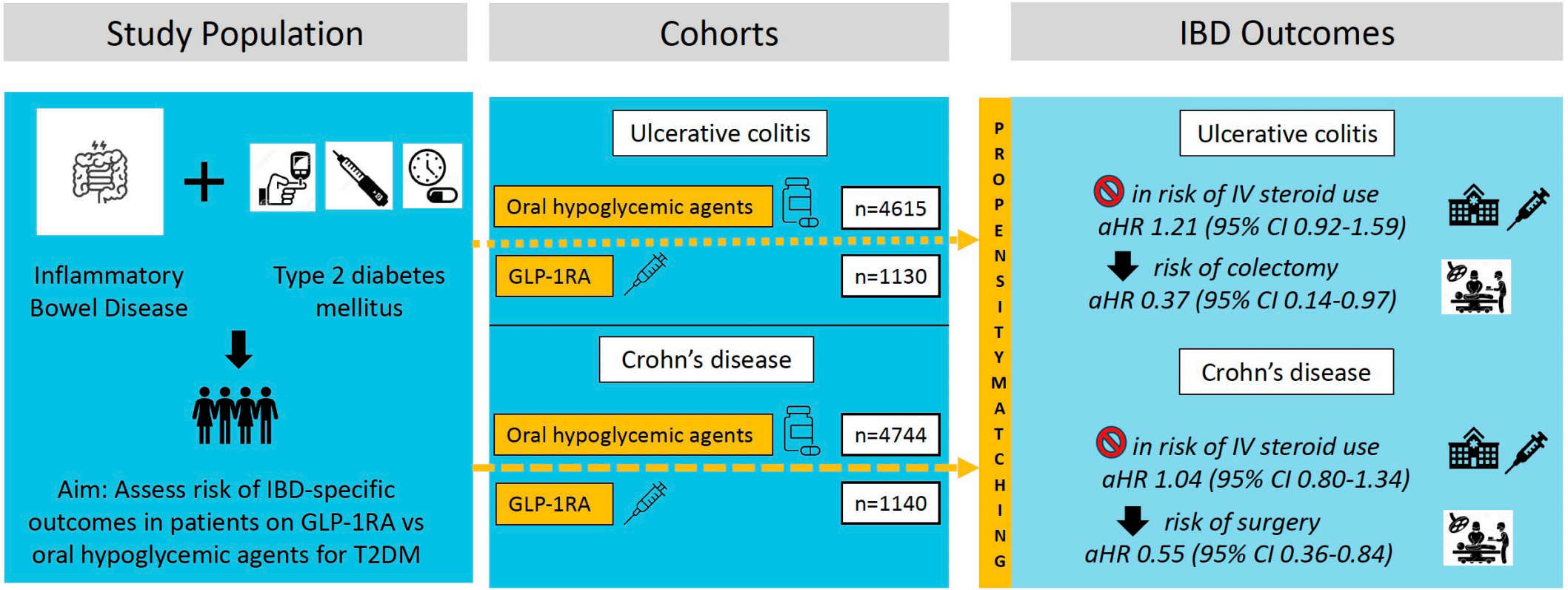
SEMAGLUTIDE FOR OBESITY TREATMENT IS ASSOCIATED WITH >5% WEIGHT LOSS IN IBD





Desai et al. *Inflamm Bowel Dis*. 2024

OUTCOMES OF IBD IN PATIENTS ON GLP-1RA FOR T2DM



Desai et al. *Aliment. Pharmacol. Ther.*

AP&T

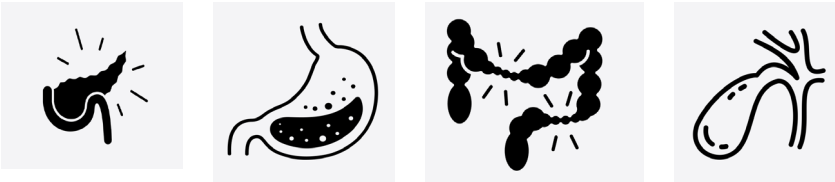
SAFETY OF GLP-1RA IN IBD

- We did not observe any difference in the risk of corticosteroid use or initiation of advanced therapy in patients on semaglutide compared to patients with IBD and obesity who were not on any GLP-1RA[1]

- No patients required surgery in the IBD semaglutide cohort during 1-year follow up[1]

- No patients in the IBD semaglutide cohort developed acute pancreatitis or ileus. Rates of gastroparesis and gallbladder disease were very low (<0.06%)[1]

- No difference in the risk of de-novo acute pancreatitis, gastroparesis, ileus/SBO and gallbladder/biliary disease in patients with IBD on GLP-1RA compared to oral hypoglycemic agents[2]



1. Desai et al. *Inflamm Bowel Dis*. 2024
2. Desai et al. *Aliment Pharmacol Ther*. 2024

WHAT ABOUT ENDOSCOPIC BARIATRIC THERAPIES IN IBD?

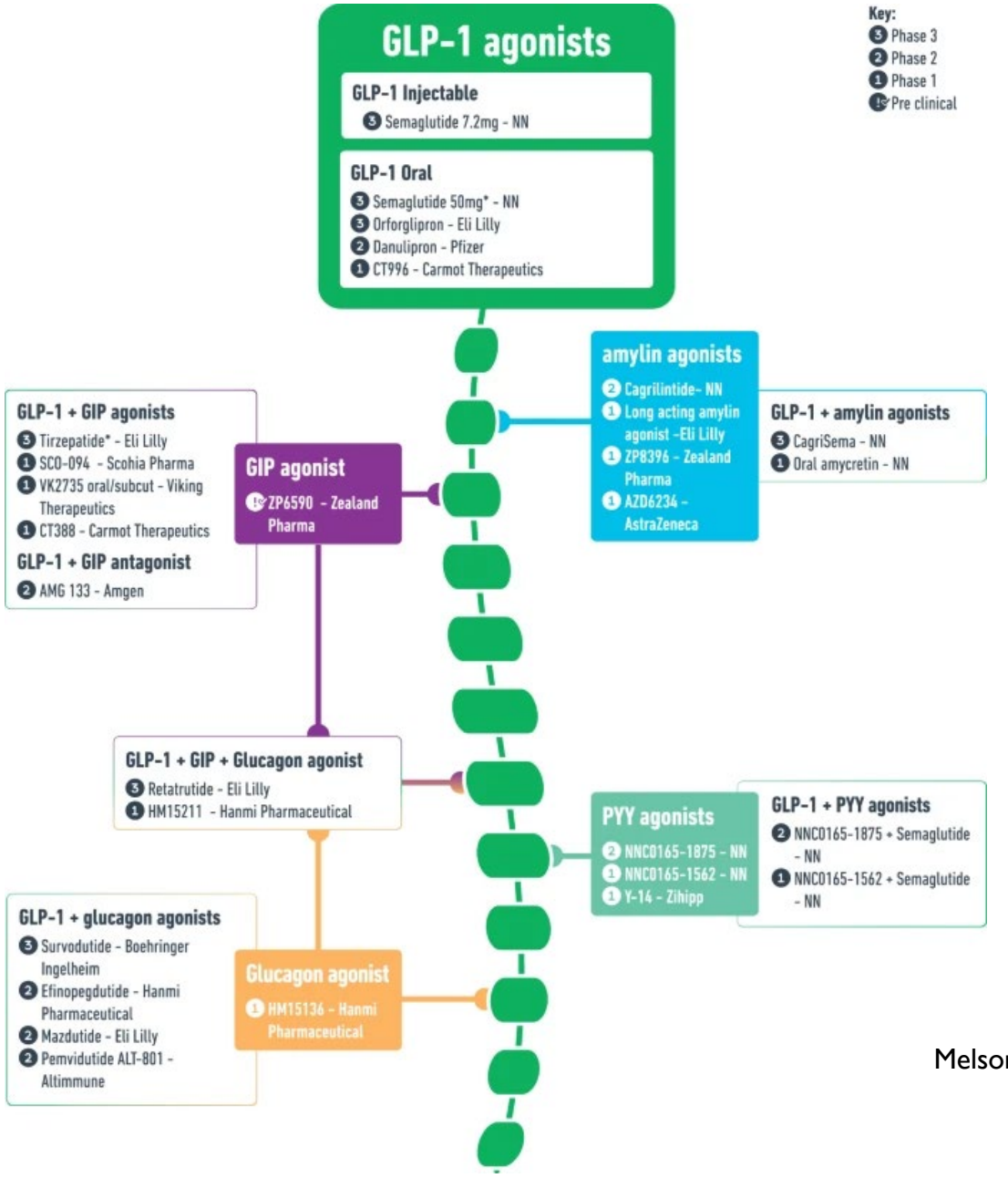
- Case series of 7 patients with IBD (86% with CD) from Mayo Clinic
  - 3 patients treated with intragastric balloon and 4 treated with ESG
  - 3 patients with previous IBD surgery, 6 patients in clinical remission

- % estimated weight loss (EWL) at 6 months was 27.5% (IQR 7-46.4%) in 5 patients with follow up data

- 4/5 patients had improvement in obesity-related co-morbidities

- Favorable IBD outcomes and no procedure or device related adverse events

Johnson et al. *Obes Surg*. 2023



WHAT'S IN THE PIPELINE FOR OBESITY PHARMACOTHERAPY?

Melson et al. *Int J Obes*. 2024

TAKE-HOME POINTS

- Obesity is common in patients with IBD, however prevalence is likely under-reported
- Recent evidence strongly suggests that obesity/visceral adiposity leads to worsened IBD outcomes
- Management of obesity is key in patients with MetS/IBD and requires a multi-disciplinary team-based approach
- Weight-loss surgery and obesity pharmacotherapy is the present and future however, the importance of dietary and lifestyle interventions cannot be understated for sustained weight-loss