

What's New with IBD, Weight Management and Weight Loss Medications

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Obesity in IBD

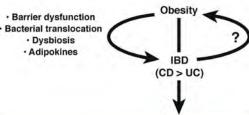
Very Prevalent - Adult IBD patients: 15-40% obese (BMI ≥30) and 20-40% overweight (25-30)

Obesity = chronic low-grade inflammation

VAT not BMI

Possible role in IBD development

Varying data on disease phenotype severity



Disease phenotype and behavior

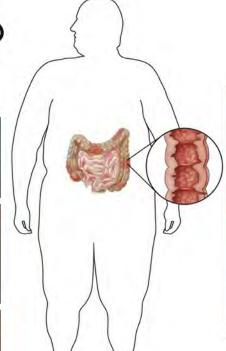
- Milder disease phenotype
- · Lower prevalence of clinical remission
- · Higher anxiety, depression, fatigue, pain

Natural history and treatment response

- · More difficult to achieve remission
- Higher risk of disease relapse (UC > CD)
- Higher burden and costs of hospitalization
- Higher likelihood of failing biologic therapy

Surgical management

- Technical challenges during surgery (stoma-related, and creation of J-pouch)
- · Higher risk of post-surgical complications



Proposed solutions:

Medical management

- Weight-based dosing regimens (infliximab), or targeted small molecule inhibitors (tofacitinib)
- Low threshold for monitoring biologic trough concentrations (?post-induction)
- · Weight-appropriate dosing
- · ?Targeting obesity as adjunctive therapy

Surgical management

- · Optimize weight prior to elective surgery
- Early ambulation, pulmonary hygiene to decrease risk of peri-operative complications
- Bariatric surgery, if needed, appears to be safe and effective in patients with IBD



Obesity

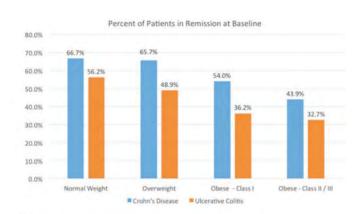
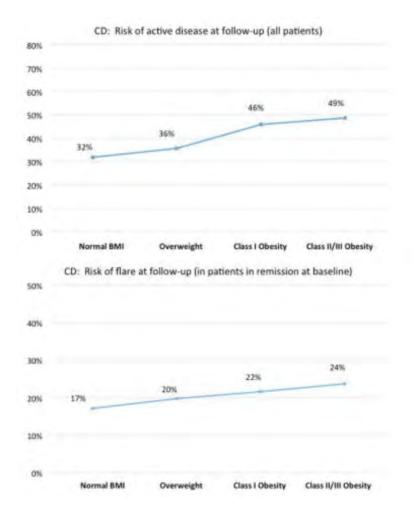
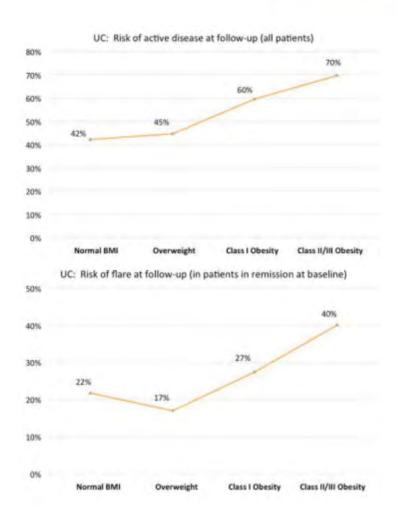


Figure 1. Proportion of patients in clinical remission at baseline, based on body mass index





Jain et al. Impact of Obesity on Disease Activity and Patient-Reported Outcomes Measurement Information System (PROMIS) in Inflammatory Bowel Diseases. Am J Gastroenterol. 2019 Apr;114(4):630-639.

Seminerio et al. Impact of obesity on the management and clinical course of patients with

IBD. Inflamm Bowel Dis. 2015;21:2857-2863



GLP-1 Medications in IBD

- Not a lot of data
- No signal for IBD exacerbation
- Could \(\) obesity improve IBD outcome ??
- My approach



Weight Loss Medications

Medication Name (Generic/Brand)	Potential Side Effects
Metformin / Glucophage	Diarrhea, nausea, passing gas, vomiting, abdominal pain
Orlistat / Xenical or Alli	Abdominal pain, bowel urgency, stool leakage, headache, passing gas
Phentermine and Topiramate / Qsymia	Increased heart rate and blood pressure, constipation, headache, sleep issues
Naltrexone and Bupropion / Contrave	Nausea, constipation, sleep issues, headache, vomiting
Liraglutide / Saxenda Semaglutide / Wegovy	GLP-1 Medications
Tirzepatide / Zepbound	Same as GLP-1 agents above + risk of low blood sugar

	DOSAGE	DOSAGE FORM	SUITABLE FOR LONG-TERM USE	EFFICACY*	COVERED BY INSURANCE"	COVERED BY MEDICARE**
Metformin***	1-2 DAILY	0	YES	i	99%	100%
Contrave (NALTREXONE/BUPROPION)	2 DAILY	00	YES	7	11%	0%
Phentermine	1-3 DAILY	00	NO	,	47%	0%
Diethylpropion	1-3 DAILY	0	NO	,	43%	0%
Qsymia рнемтермое порядамате его	1 DAILY	0	YES	7	23%	0%
Saxenda LIRAGIUTION	1 DALY	1	YES	7	16%	0%
Wegovy SEMAGUUTIDES	1 WEEKLY	1	YES	7	20%	0%
Tirzepatide***	1 WEEKLY	1	YES	4	13%	43%

Palmer C and Aungst C. From GoodRx (2023, November 28). Can tirzepatide help you lose weight? https://www.goodrx.com/conditions/weight-loss/tirzepatide-and-weight-loss

1.



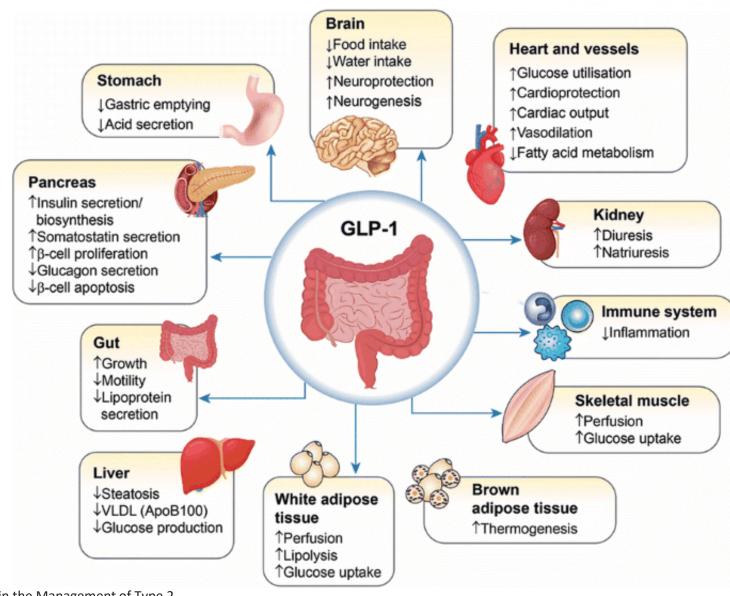
What GLP-1 medications are on the market and what are they used for?

Generic Name	Brand Name	Dosage Form	Dosing Schedule	Indication For Use	FDA Approval
Liraglutide	Victoza®	Injection	Daily	Type 2 Diabetes	2010
Liraglutide	Saxenda®	Injection	Daily	Weight loss	2014
Dulaglutide	Trulicity®	Injection	Weekly	Type 2 Diabetes	2014
Semaglutide	Ozempic [®]	Injection	Weekly	Type 2 Diabetes	2017
Semaglutide	Rybelsus®	Oral	Daily	Type 2 Diabetes	2019
Semaglutide	Wegovy®	Injection	Weekly	Weight Loss	2022
Tirzepatide	Mounjaro®	Injection	Weekly	Type 2 Diabetes	2022
Tirzepatide	Zepbound®	Injection	Weekly	Weight loss	2023
Retatrutide	TBD	Injection	Weekly	Weight loss	TBD
Orforglipron	TBD	Oral	Daily	Weight loss	TBD

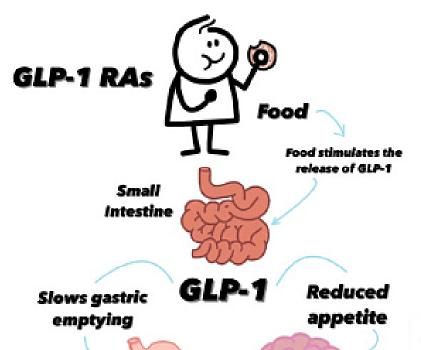


What are GLP-1 medications?

- Glucagon-like peptide-1 receptor agonists
- Mechanism of action:
 - Binds to and activates the GLP-1 receptor
 - GLP-1: hormone that plays a key role in blood glucose control
- When activated this causes:
 - Slowed gastric emptying
 - Increased insulin production
 - Reduced food intake
 - Many other systemic effects







How GLP-1 medications work







GLP-1





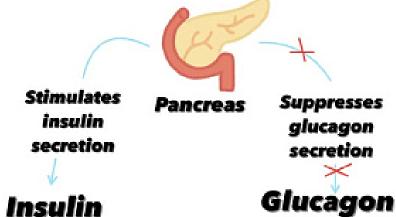
INSULIN REGULATION

BLOOD SUGAR CONTROL

APPETITE

WEIGHT MANAGEMENT

CARDIOVASCULAR HEALTH



Brain

Stomach





Appetite/Weight



.. Muskiet MHA, Tonneijck L, Smits MM, et al. GLP-1 and the Kidney: From Physiology to Pharmacy and Outcomes in Diabetes. *Nat Rev Nephrol*. 2017;13(10):605-628.



Possible side effects of GLP-1 medications

Common

- Nausea (15-45%)
- Vomiting (5-25%)
- Diarrhea (10-30%)
- Constipation (3-24%)
- Abdominal pain (6-20%)
- Headache (14-17%)

Note: most side effects are mild and improve as your body gets used to the medication

These side effects are more common with higher doses of the medication and when starting treatment

Rare to very rare

- Low blood sugar (2-6%)
- Gallbladder issues (1-4%)
- Pancreatitis (inflammation of the pancreas) (less than 1%)
- Intestinal obstruction (less than 1%)
- Allergic reactions (not defined)
- Increased risk of certain cancers

Avoid use if there is a personal or family history of medullary thyroid carcinoma (MTC) or in patients with multiple endocrine neoplasia syndrome type 2 (MEN2)



Strategies to Minimize GLP-1 RA Side Effects



Smaller, more frequent meals



Separate fluids from foods, take small sips



Decrease high fat meals



Choose well balanced meals containing fiber



Avoid eating close to bedtime



Physical activity as tolerated

1. Gorgojo-Martínez JJ, Mezquita-Raya P, Carretero-Gómez J, et al. Clinical Recommendations to Manage Gastrointestinal Adverse Events in Patients Treated with Glp-1 Receptor Agonists: A Multidisciplinary Expert Consensus. *J Clin Med*. 2022;12(1):145. Published 2022 Dec 24. doi:10.3390/jcm12010145

Sarcopenia and IBD





Dhaliwal A, et al. Nutrients. 2021

BMI>25 can still be malnourished

19% of patients with sarcopenia and IBD have a BMI >25 and 41% have a normal BMI

^{1.} Dhaliwal A, Quinlan JI, Overthrow K, et al. Sarcopenia in Inflammatory Bowel Disease: A Narrative Overview. *Nutrients*. 2021;13(2):656. Published 2021 Feb 17. doi:10.3390/nu13020656

^{2.} Adams DW, Gurwara S, Silver HJ, et al. Sarcopenia Is Common in Overweight Patients with Inflammatory Bowel Disease and May Predict Need for Surgery. *Inflamm Bowel Dis*. 2017;23(7):1182-1186. doi:10.1097/MIB.00000000001128



Preserve Muscle Mass

- Adequate protein lean protein sources such as chicken, turkey, fish
- Resistance training body weight exercise, weightlifting as tolerated

