You Down With GLP?
What Urgent Care Clinicians *Need* to Know About GLP-1 Agents

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Disclosure

I have no financial interests or relationships to disclose.

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Learning Objectives

- Become Familiar with MOA, Indications, Contraindications for GLP-1 Agents
- Recognize Common Side Effects & Clinical Consequences of GLP-1 Agonist Tx
- Develop Comfort in Understanding the Uncommon Adverse Reactions & Unrelated Consequences
- Develop Approaches to Managing Adverse Reactions & Understand When GLP-1 Agents Should be Discontinued

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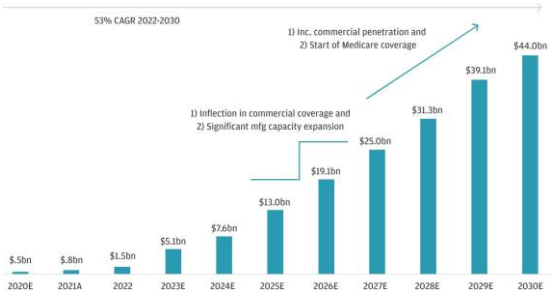
The Rise of GLP-1

41 million (1 in 8) Americans have been prescribed a GLP-1 (May 2024)



Source: PharmaSource

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GLP-1-ophobia

5

What Makes a Crisis?

Hollywood's 'Ozempic face' crisis: Plastic surgeons reveal the celebs suffering from gauntness 'because of weight-loss drug'

By Luke Andrews Senior Health Reporter For Dailymail.Com
16:08 18 Apr 2024, updated 14:34 19 Apr 2024

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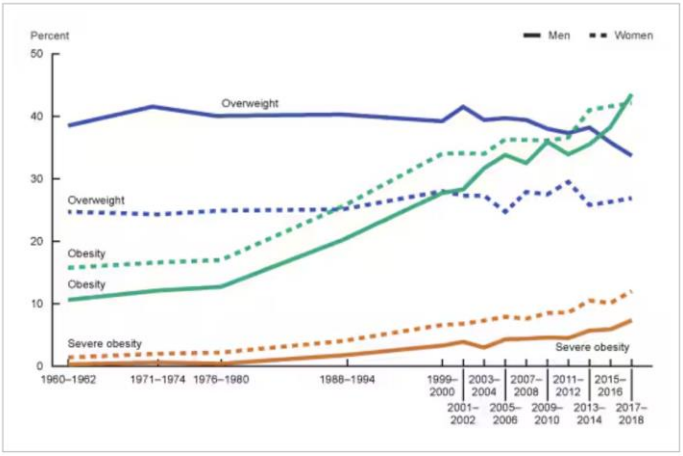
U.S. Trends in Overweight/Obesity



Source: CDC

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What Makes a Crisis?

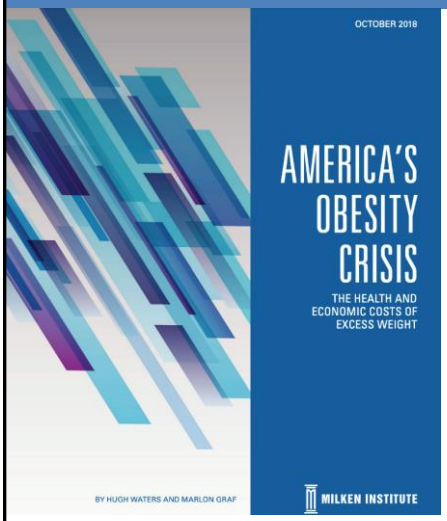

TABLE 1

Total Costs of Obesity and Overweight, 2016

Condition	Costs (in $ Millions) Direct	Indirect	Total
Alzheimer's and Vascular Dementia	$73,572	$32,606	$106,178
Asthma and COPD	$10,564	$16,234	$26,798
Breast Cancer	$5,900	$3,669	$9,569
Chronic Back Pain	$38,476	$217,291	$255,768
Colorectal Cancer	$6,151	$5,425	$11,576
Congestive Heart Failure	$5,201	$2,039	$7,239
Coronary Heart Disease	$22,700	$39,315	$62,015
Diabetes (Type 2)	$120,707	$214,500	$335,208
Dyslipidemia	$28,619	†	$28,619
End Stage Renal Disease	$3,716	††	$3,716
Endometrial Cancer	$189	$158	$347
Esophageal Adenocarcinoma	$970	$92	$1,061
Gallbladder Cancer	$22	$17	$39
Gallbladder Disease	$26,863	$27,401	$54,264
Gastric Cardia Adenocarcinoma	$1,433	$136	$1,568
Hypertension	$29,323	$432,230	$461,553
Liver Cancer	$87	$67	$154
Osteoarthritis	$86,480	$215,303	$301,783
Ovarian Cancer	$1,152	$152	$1,304
Pancreatic Cancer	$146	$738	$884
Prostate Cancer	$1,983	$13,411	$15,393
Renal Cancer	$2,254	$559	$2,813
Stroke	$14,148	$14,527	$28,674
	$480,655	**$1,235,869**	**$1,716,523**

† Included in heart disease, diabetes, and stroke.[1]
†† Included in diabetes and hypertension.

Source: Milken Institute.

Total Annual Cost: **$1.72 trillion**
(10% GDP, 40% of Total Health spending)

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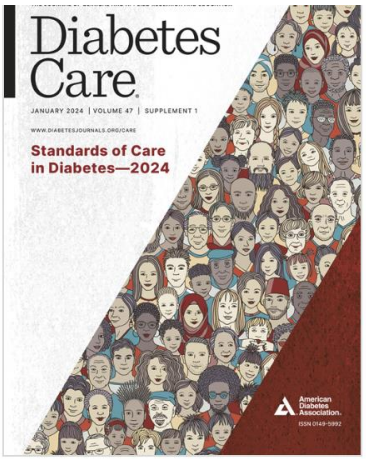
Don't Forget About Diabetes!



- **Metformin no longer 1st line!**
  - SGLT-2 for CHF, CKD
  - GLP-1 for Obese, ASCVD, other vascular dz
    - Hgb A1c reduction better than insulin
    - Significantly less hypoglycemia

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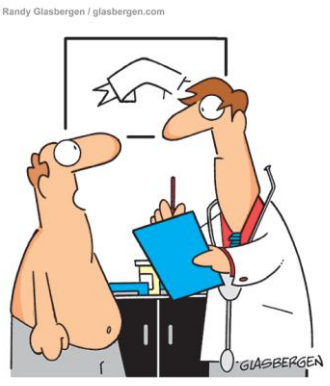
"Diet & Exercise"?: The World Before GLP-1's

Obesity: multifactorial, chronic disease
- Leptin resistance
- Polygenic inheritance

Lifestyle Change (i.e. diet & exercise)
- <5% long-term weight loss

+ Cognitive Behavioral Tx:
~5 kg extra weight loss



"Everyone knows food is bad for you, but I don't know what else to eat!"

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Steel to Heal?: The World Before GLP-1's

Bariatric Surgery
+ Very Effective **Short Term**: ~35kg @ 2 yrs
+ Reduction in HTN, DM

BUT...**Long-Term**: Weight Regain Common
Complications also common:
¾ regain 10+% @5yrs

Plus...Nutrient Deficiencies, Limited Reversibility

- ***Most Bariatric Surgeries - 280,000***
- ***BMI >35 + complications (or 40)***
  23+ million morbidly obese & 108+ million obese American adults

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A Magic Pill?: The World Before GLP-1's

Anti-Obesity Medications (AOM)

- **Phentermine/Topiramate**: 7% @ 1yr
  - 30% non-responder, 20% AE/DC
- **Bupropion/Naltrexone:** 5-10% @ 1yr
  - 30-40% DC for AE or non-responder
- **Orlistat:** 6 kg @ 1 yr
  - 30% of patients DC related to GI "side effects"
- **Metformin & SGLT-2:** 2.5% @ 1 yr

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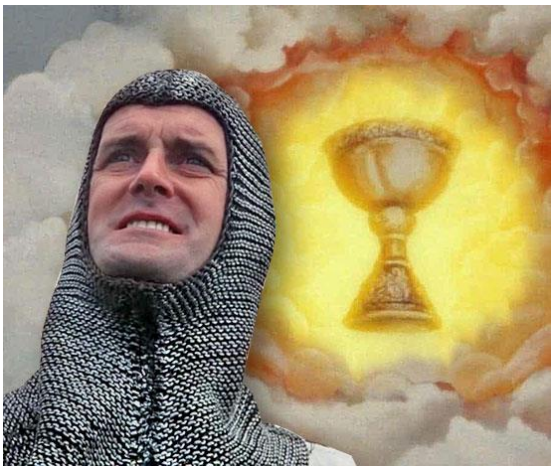
A Magic Pill?: The World Before GLP-1's

Anti-Obesity Medications (AOM)

- Total AOM spending 2020: $750 mil
  - 2022: $5.7 billion GLP-1 Medicare D alone (diabetes)
- **What happened?**
  - Late 90's Pharma "gave up" AOM
  - Phen-Fen Disaster – 1997
  - Obesity blamed on "lifestyle"
- **"Holy Grail" = Safe & Effective**
  - No Free Lunch?
  - Affordable…?



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What Happens If We Do Nothing?

- **Overweight/obesity is a chronic, stigmatized disease**
- **Diet/Exercise rarely works**
- **Deck increasingly stacked against us**
- **Obesity now affects over 1 billion people (and rising)**
- **30% increase in premature death for every 5 BMI pts >25**

LETTER FROM THE EDITOR-IN-CHIEF

'What Happens If We Do Nothing?' Is Still the Right Question

"It only hurts right here," Rich told me, pointing to a tender spot on his ribs under his arm pit.

I palpated his chest wall and observed as he winced when I hit the spot.

"I just need to make sure I'm okay to go back to work."

Rich was middle-aged and had a mustache with hints of grey. He was a large man, but his potbelly was overshadowed by his towering height. He had a polite, unassuming demeanor and came in wearing his uniform for the mechanic shop he worked in, complete with his name embroidered on the chest and a collage of grease stains. He'd left work to come to urgent care (UC) to get a note clearing him for work after slipping and falling on some steps the night before. It was clear he didn't want to be here.

"How's the pain? Have you taken anything for it?" I asked.

"Just some ibuprofen. It's manageable," he said.

I recommended we get a chest x-ray to make sure he hadn't punctured his lung. He somewhat reluctantly agreed. It was clear anything I suggested was going to seem like overkill to him.

Not surprisingly, his x-ray showed no pneumothorax, hemothorax, or lung contusion. I thought I might be was more than just the adrenaline from his rib pain driving this. Looking through his chart further, I found no mention of his elevated blood pressure or any documented history of hypertension. He was only taking metformin for diabetes. Then I saw his last HbA1c; it was over 10. It seemed like there was more than the rib fracture I needed to discuss with Rich.

I went back to the exam room and found him standing at the doorway with his coat on. He was clearly only waiting for his note for work. "How often do you check your blood pressure and blood sugar?" I asked.

"I don't check either. They check them for me if I go to the doctor's," he said. It turned out this wasn't very often.

We see patients like Rich every day in UC, and we find ourselves in similar situations as this almost as frequently. He was in a hurry, I was in a hurry. The immediate issue had been assessed, and we both had other things to do.

I imagine if you polled a group of UC clinicians about how they'd address his undiagnosed hypertension and poorly controlled diabetes, many would say they wouldn't. Perhaps some would comment on his high BP and that he should see his primary care provider about it. However, I am certain that most UC practitioners would spend several minutes—likely the vast majority of the interaction—discussing the suspected rib fracture and things like bracing, incentive spirometry, pain control, and cautions around developing pneumonia. After all, it's why he came in that day. But while it's undeniable Rich presented for his rib injury, it was arguably the least important topic to discuss.

My October 2023 editorial entitled "What Happens If

Our greatest perpetual duty is to spend each moment in the most meaningful way possible.

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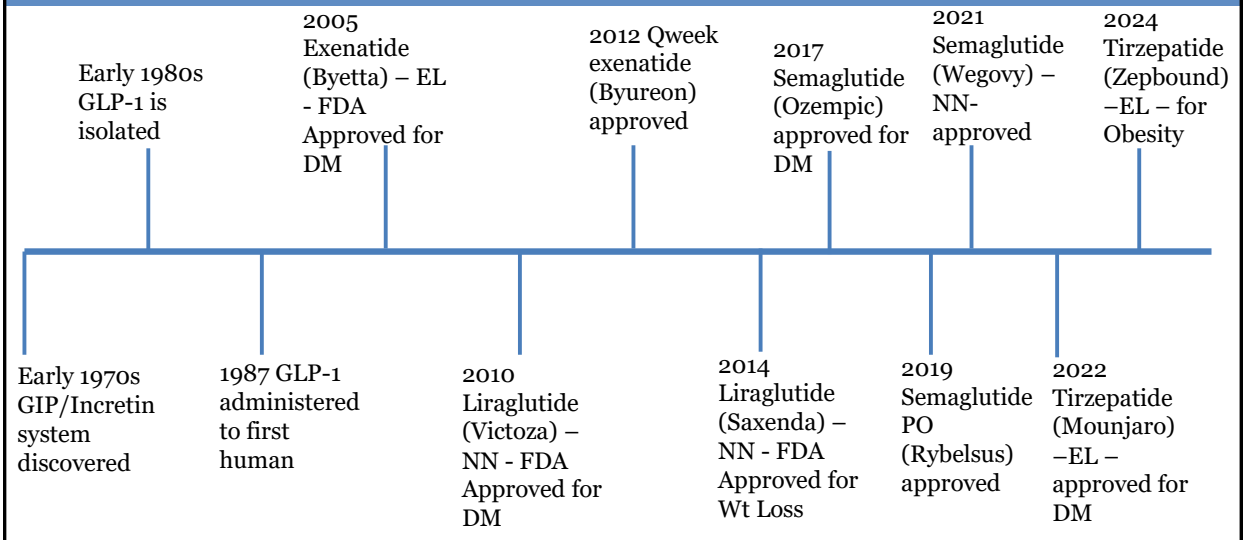
A Brief History of GLP-1 – Novo Nordisk & Eli Lilly



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GLP-1 Medications

- Liraglutide (Victoza/Saxenda) – Daily
- Semaglutide (Ozempic/Wegovy) – Weekly
- Tirzepatide (Mounjaro/Zepbound) - Weekly

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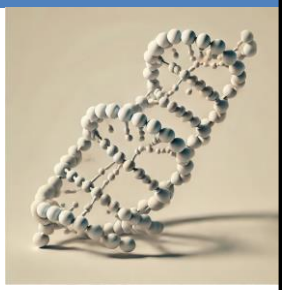
GLP-1



- Glucagon-like Peptide-1
- 30 AA peptide from proglucagon
- L-cells of the bowel
- Receptors throughout body and brain
- Inc Insulin, Dec Glucagon, Dec Gastric Emptying
- T1/2 = 2 min
- DPP-4 metabolism (safe w/ renal, hepatic dz)

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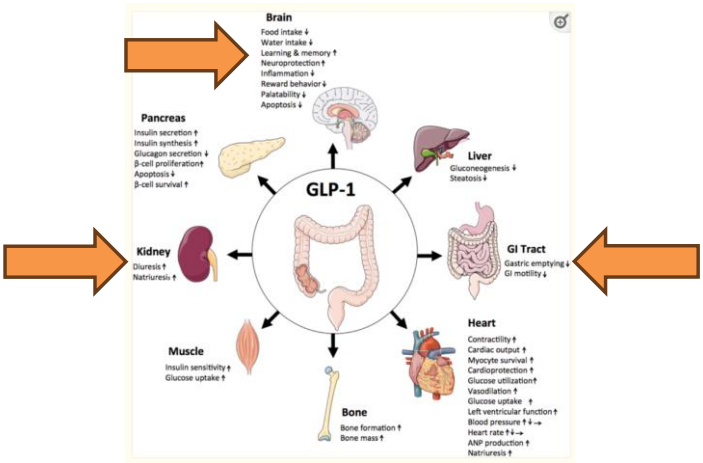
GLP-1 Actions



Müller TD, Finan B, Bloom SR, et al. Glucagon-like peptide 1 (GLP-1). *Mol Metab*. 2019;30:72-130. doi:10.1016/j.molmet.2019.09.010

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GIP

- Glucose-dependent insulinotropic peptide
- K-cells of the bowel
- Receptors throughout body and brain
- Inc Insulin, Dec Bone Resorption
- T1/2 = 5 min; DPP-4 metabolism

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Cost Concerns

- **Ozempic: France $83; Australia, $89/month**
- **US: Ozempic $996/mo, Wegovy ~$1,300/mo (OOP)**
- **Average Time w/ Private Payor = 3.5 years**
- **Medicare Part D (2006)**
  - **Illegal for Medicare Part D to cover AOM**

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What's the Deal with Compounding?

Hims, Ro, HenryMed etc.

- **Compounding:** combining, mixing, or altering ingredients to create a medication for an individual patient.
- FDA does not review any compounded medications
- 503A & 503 B of Food, Drugs, & Cosmetic Act allows compounding pharmacy to produce drugs on FDA shortage list

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Drug Shortages

https://www.fda.gov/drugs/drug-safety-and-availability/drug-shortages

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Evaluating Compounding Pharmacies

1. State Licensed & Inspected
2. Compliant with USP Standards
3. Accredited with PCAB or ACHC
4. Follows GMP
5. Compliant with Compounding Quality Act
6. Compliant with DQSA
7. Adverse Event Reporting system

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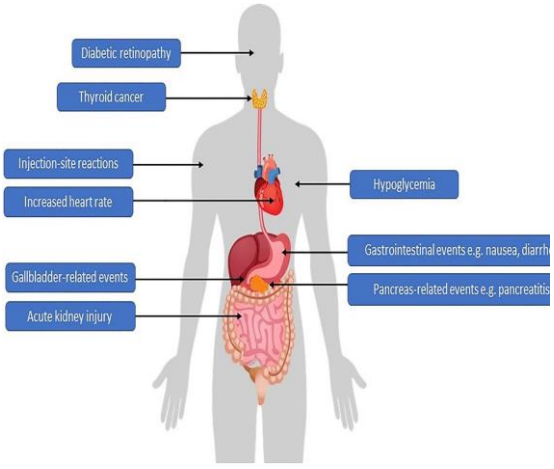
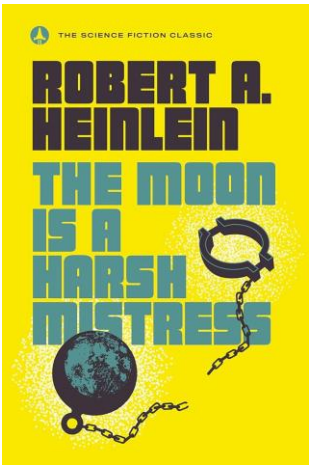
Concerns for Safety





Smits, M. M., & Van Raalte, D. H. (2021). Safety of Semaglutide. *Frontiers in endocrinology*, *12*, 645563. https://doi.org/10.3389/fendo.2021.645563

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Case #1

44yo F p/w to UC with n/v/d x 5d

- 1 wk ago doubled dose of compounded "weight loss medication"
- States she's taking "80 now"

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Semaglutide Dosing

- Ozempic: 0.25, 0.5, 1.0, 2.0 mg
- Wegovy: 2.4mg
  - Subcutaneous, Weekly
- Compounded: Variable
  - Dose = Units on insulin syringe
    - 100 units = 0.1mL
    - **Concentration: mg/mL**

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Tirzepatide Dosing

- Mounjaro: 2.5, 5, 7.5, 10, 12.5, 15mg
- Zepbound: Same
  - Subcutaneous, Weekly
- Compounded: Variable
  - Dose = Units on insulin syringe

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Universal Tips for GLP-1 Issues in UC

✓ **Evaluate if taking correctly/as prescribed**

✓ **<u>Stop the Medication</u>**

✓ Remember: **Side Effects are Dx of Exclusion**

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Common Side Effects

- Abdominal Pain/Early Satiety/Bloating
- GERD
- Nausea/Vomiting
- Constipation
- Diarrhea
- Injection Site Reactions

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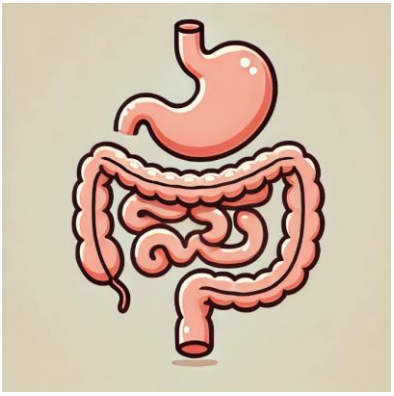
GI Side Effects

Side effect of GLP-1 is diagnosis of exclusion

- Side Effects are Dose Dependent
- Decrease Over Time (i.e., tachyphylaxis)
- Prioritize Behavioral > Pharmacologic Tx
- Slightly more severe with Semaglutide



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Nausea & Vomiting

- Nausea 17-22%
- Vomiting 8%

- Management:
  - **Hold Medication & Ensure adequate hydration**
  - Behavioral: smaller portions, less greasy
  - Pharmacotherapy: ondansetron, metoclopramide

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Constipation

- Constipation 5.5%

- Management:
  - **Ensure adequate hydration & Hold Medication**
  - **Review other meds (e.g. opioid, ondansetron)**
  - Behavioral: increase fruits, veg, water, physical activity
  - Pharmacotherapy: PEG PRN, Occasional Senna

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Diarrhea

- Diarrhea 7.5%
- Management:
  - **Ensure adequate hydration & Hold Medication**
  - Behavioral: avoid fruits other osmotic foods, coffee, nicotine. Do not reduce water/fluids.
  - Pharmacotherapy: Psyllium, occasional loperamide

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Case #2

48yo M w/ DM2, obesity, HTN, HL p/w retrosternal non-exertional chest pain. Tight and burning. Started new “diabetes med”

- Meds: Metoprolol, Lisinopril, Statin, Semaglutide

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Work-Up & Differential?

Side Effect from GLP1 is a Dx of Exclusion

DDx: PE, ACS, cholecystitis, pancreatitis, PUD, etc.

- EKG, PERC? HEAR?, CXR?
- GI Cocktail?

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GERD

- Dyspepsia/Reflux 8%
- Should improve with weight loss
- **Management:**
  - Hold Medication & Address **PDE-5i** use?
  - Behavioral: small portions, avoid spicy foods, avoid laying down after eating
  - **Pharmacotherapy:**
    - Maalox (AlMgOH, simethicone) if constipated
    - $CaCO_3$ if diarrhea
    - H_2Ra (famotidine) prn
    - Rarely limited course PPI

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Case #3

64yo F w/ DM2, obesity, h/o bariatric surgery p/w upper abdominal pain & vomiting

- Meds: Metformin, Statin, Semaglutide

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Work-Up & Differential?

Side Effect from GLP1 is a Dx of Exclusion

DDx: Internal hernia, bowel obstruction, chole, pancreatitis, ACS etc.

- EKG
- Upright AXR? RUQ U/S?
- Labs?

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Gastroparesis

- GLP1-RAs delay gastric emptying
  - Relevance for ASA NPO guidelines?
    - Emergent Procedures/ED Sedation
  - Irreversible in certain cases?
- Relevant for delayed absorption of PO medications – OCP? AED? AC? PRN?

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Case #3

25yo w/ MDD, OCD, anxiety, obesity p/w partner concerned "Ozempic made her suicidal"

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Suicidal Ideation

- July 2023 - European Medicines Agency (EMA) states concern over anecdotal cases of increased suicidal thinking in ~150 DM2 pts on SG

Association of semaglutide with risk of suicidal ideation in a real-world cohort

William Wang, Nora D. Volkow, Nathan A. Berger, Pamela B. Davis, David C. Kaelber & Rong Xu

Nature Medicine **30**, 168–176 (2024) | Cite this article

- Jan 2024 – NIH-funded study – 200,000pts
  - HR for Suicidal ideation = 0.27 and recurrent Suicidal ideation = 0.44

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Case #4

- 76yo M w/ DM2, HTN, tobacco use, obesity p/w 3 hours of sudden, painless vision loss in OS
  - Meds: Insulin, Statin, ACEi, BB, Semaglutide
- DDx?

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Ocular Complications

June 2020
Volume 61, Issue 7

FREE
ARVO Annual Meeting Abstract | June 2020

Food and Drug Administration Adverse Event Reports of Diabetic Retinopathy, Macular Edema and Blurred Vision Associated with GLP-1 Receptor Agonist Use

Grace Xiao; Albert Li

- Rebound DM Retinopathy
- Late-Stage DM Retinopathy
- Macular Edema
- Open Angle Glaucoma
- NAION

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Non-Arteritic Ischemic Optic Neuropathy (NAION)

- FAERS (2018-20) – 140 cases of ocular complications in patients on SG
- 47 cases of “blurred vision”

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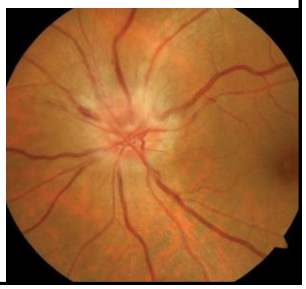
Non-Arteritic Ischemic Optic Neuropathy (NAION)

- Sudden, painless, monocular vision loss
- Recovery Rare - 1/3 vision <20/200
- 15% Risk to Contralateral eye
- Known risk factors:
  - DM, smoking, HTN etc.
  - Sleep apnea, small optic disc
- **PDE-5 Medications?**



Mollan SP. Semaglutide and Nonarteritic Anterior Ischemic Optic Neuropathy. *JAMA Ophthalmol.* Published online July 03, 2024. doi:10.1001/jamaophthalmol.2024.2514

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Non-Arteritic Ischemic Optic Neuropathy (NAION)

PDE-5 Inhibitors and NAION

Wayne J.G. Hellstrom, MD, FACS; Muammer Kendirci, MD

DISCLOSURES | August 04, 2005

0 Share Add to Email Alerts

In response to a small number of postmarketing reports of vision loss in men taking type 5 phosphodiesterase (PDE-5) inhibitors, the US Food and Drug Administration (FDA) has issued a news release to advise healthcare providers of the potential risk. FDA has received 43 reports of varying degrees of vision loss, including blindness, among users of these drugs -- 38 cases in men using sildenafil, 4 in men using tadalafil, and 1 case in a man using vardenafil. Most of these cases of vision loss were due to nonarteritic anterior ischemic optic neuropathy (NAION). The loss of vision in some cases has been irreversible.

Source: MedScape, 2005

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Risk of Nonarteritic Anterior Ischemic Optic Neuropathy in Patients Prescribed Semaglutide

Jimena Tatiana Hathaway, MD, MPH[1,2,3]; Madhura P. Shah, BS[2,3]; David B. Hathaway, MD[4]; et al

» Author Affiliations | Article Information

JAMA Ophthalmol. Published online July 3, 2024. doi:10.1001/jamaophthalmol.2024.2296

the non-GLP-1 RA antidiabetes cohort. The cumulative incidence of NAION for the semaglutide and non-GLP-1 RA cohorts over 36 months was 8.9% (95% CI, 4.5%-13.1%) and 1.8% (95% CI, 0%-3.5%), respectively. A Cox proportional hazards regression model showed higher risk of NAION for patients receiving semaglutide (hazard ratio [HR], 4.28; 95% CI, 1.62-11.29); *P* <.001). In the population of patients who were overweight or obese, 20 NAION events occurred in the prescribed semaglutide cohort vs 3 in the non-GLP-1 RA cohort. The cumulative incidence of NAION for the semaglutide vs non-GLP-1 RA cohorts over 36 months was 6.7% (95% CI, 3.6%-9.7%) and 0.8% (95% CI, 0%-1.8%), respectively. A Cox proportional hazards

Mollan SP. Semaglutide and Nonarteritic Anterior Ischemic Optic Neuropathy. *JAMA Ophthalmol.* Published online July 03, 2024. doi:10.1001/jamaophthalmol.2024.2514

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Visual Complications

- Possible – probable a/w SG & LG (?TZ)
- Likely higher risk in riskier pts (htn, dm etc.)
- Stop medication!
- FDA warning may be coming…

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Case #5

38yo F w/ DM2, HTN, obesity p/w upper abdominal pain & vomiting w/ eating

- Meds: Metformin, Insulin, Statin, Semaglutide

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Work-Up & Differential?

- EKG?
- Upright AXR? RUQ U/S?
- Urine HCG?
- Labs?

Side Effect from GLP1-RA is a Diagnosis of Exclusion

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Gallstone Disease

High	61 962	54	1.56 (1.36-1.78)	0	.99	.006
Low	16 952	33	0.99 (0.74-1.33)	0	.67	
Duration, wk						
≤26	13 401	24	0.79 (0.48-1.31)	0	.97	.03
>26	90 417	53	1.40 (1.26-1.56)	0	.64	
Indication[c]						
Weight loss	11 282	13	2.29 (1.64-3.18)	0	.85	<.001
T2D/other	92 090	63	1.27 (1.14-1.43)	0	.94	

***did not include tirzepatide*

- GLP-1 → Dec GB emptying
- Weight Loss → Inc Gallstones
- 76 RCTs, 100,000+ pts
  - High Dose: +56%
  - Duration >26 wks: +40%
  - Weight Loss: +129%

He L, Wang J, Ping F, et al. Association of Glucagon-Like Peptide-1 Receptor Agonist Use With Risk of Gallbladder and Biliary Diseases: A Systematic Review and Meta-analysis of Randomized Clinical Trials. *JAMA Intern Med*. 2022;182(5):513-519.

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Liver : Beyond Gallstones

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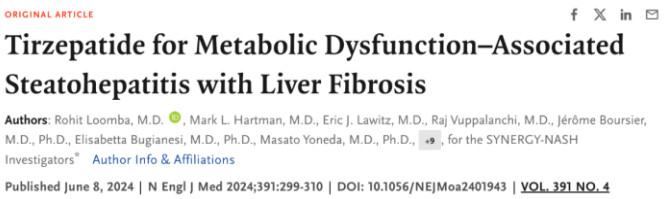
NASH/NAFLD

- NAFLD – 25% prevalence worldwide
- NASH - #1 cause of liver failure/txplt
- No FDA approved medication for NASH



ORIGINAL ARTICLE

Tirzepatide for Metabolic Dysfunction–Associated Steatohepatitis with Liver Fibrosis

Authors: Rohit Loomba, M.D., Mark L. Hartman, M.D., Eric J. Lawitz, M.D., Raj Vuppalanchi, M.D., Jérôme Boursier, M.D., Ph.D., Elisabetta Bugianesi, M.D., Ph.D., Masato Yoneda, M.D., Ph.D., +9, for the SYNERGY-NASH Investigators* Author Info & Affiliations

Published June 8, 2024 | N Engl J Med 2024;391:299-310 | DOI: 10.1056/NEJMoa2401943 | VOL. 391 NO. 4

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Case #5

- 54yo M w/ DM2, obesity, HL p/w upper abd & back pain and vomiting after eating for past 2 days.
  - Meds: Tirzepatide, Metformin, SGLT-2, Statin
- DDx?

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Pancreatitis

- FDA mandated pancreatitis risk in package warnings for Ozempic & Wegovy
  - Mounjaro/Zepbound also have pancreatitis warning
- Evidence is mixed for increased risk of pancreatitis
- Gallstone risk may contribute to pancreatitis?

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Pancreatitis

- Small increase in cases in clinical trials
- SG - 2024 Meta-analysis – 21 studies, 35k pts: OR=0.7 vs placebo
- TZ – 2023 Meta-analysis – 9 studies; 10k pts: RR: 1.46 (95% CI 0.6– 3.6)

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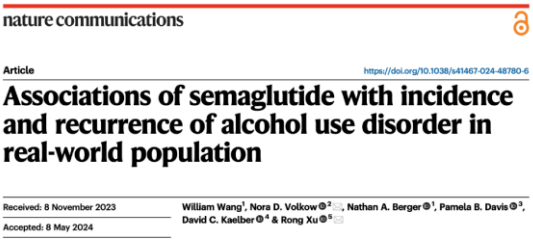
Pancreatitis – Mixed Results

- Could reduce incidence of pancreatitis overall by reducing EtOH use?
  **Delayed EtOH absorption?*



nature communications

Article https://doi.org/10.1038/s41467-024-48780-6

Associations of semaglutide with incidence and recurrence of alcohol use disorder in real-world population

Received: 8 November 2023
Accepted: 8 May 2024

William Wang[1], Nora D. Volkow[2], Nathan A. Berger[1], Pamela B. Davis[3], David C. Kaelber[4] & Rong Xu[5]

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Cancer

- Pancreatic
- Medullary Thyroid CA
- Other ?

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Pancreatic Cancer

- FAERS 2004-20 – RR 9.86

But…Obesity, DM are leading pancreatic CA risks

And…JAMA 2004-18 – HR 0.41

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Thyroid Cancer

- Liraglutide rodent studies
- FAERS 2004-20:
  - Medullary RR: 27.4
  - Papillary RR: 9.9

**5 yr survival: Medullary 90%; Papillary 98%*

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Competing Risks

- Patients w/ uncontrolled DM suffer many forms of early morbidity
  - Obesity/metabolic syndrome responsible for 20% of cancers
  - Insulin is an anabolic growth factor
  - Cancers take a long time to appear

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Case #6

- 72yo M w/ DM2, HTN, obesity p/w wife for confusion and anxiety. He's being treated for a UTI currently.
  - Meds: Losartan, TZ, metoprolol, cipro
  - DDx?
  - Tests?

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Hypoglycemia

- Rare with GLP-1 agents in isolation (or w/ only metformin and/or SGLT-2)
- Common with insulin, sulfonylureas
  - Hypoglycemia common w/ these meds in isolation
  - Consider Non-Antihyperglycemic drugs
    - e.g. ACEi, BB, Fluroquinolones
- Hold GLP-1, may need ED referral

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Case #6

- 72yo M w/ DM2, HTN, obesity p/w wife for increasing confusion, fatigue, malaise for 1 week.
  - Meds: Lisinopril, SG, metformin, metoprolol
  - DDx?
  - Tests?

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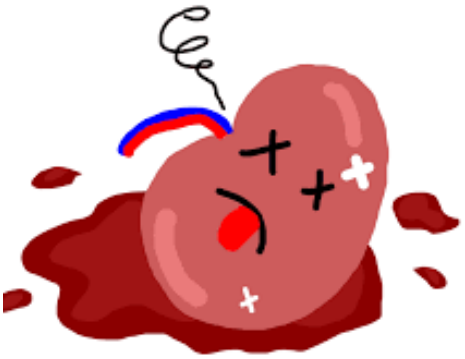
Kidney Injury

- Drug manufacturer warning of AKI only in setting of fluid losses from N/V/D
- Case reports of AIN (i.e., AKI w/o volume depletion)
- Low threshold to check UA & creatinine
- Regardless tx same: **stop the medication**



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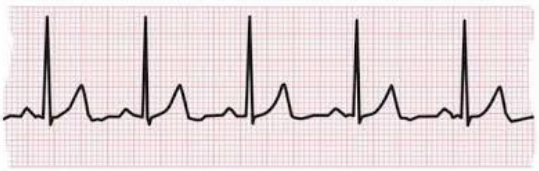
Case #7

- 50yo M w/ HTN, obesity p/w dizziness x 1 week. Passed out at work.
  - Meds: HCTZ/lisinopril, metoprolol, SG
  - DDx?
  - Tests?



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Autonomic Changes

- Hypotension due to drug effects
  - Naturesis & Vasodilation
- Hypotension due to excessive anti-htn tx after weight loss
- Volume Depletion
- Hold GLP-1 & Reduce/hold anti-HTN

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Case #8

32yo F w/ hypothyroidism, obesity p/w insomnia and anxiety

Meds: Levothyroxine, metformin, tirzepatide

DDx?

Tests?

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Effects on Other Meds

- Thyroid Replacement is Weight Based
- Anticonvulsants Levels
- Anticoagulation & Oral Contraception Efficacy?

August 5, 2024

Tirzepatide-Induced Rapid Weight Loss-Related Thyrotoxicosis

Kagan E. Karakus, MD[1]; Viral N. Shah, MD[1]; Halis K. Akturk, MD[1]

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Muscle Mass Loss

- GLP-1 create weight loss by inducing caloric deficit (i.e., malnutrition)
  - Possible muscle wasting/sarcopenia
  - Concerns for osteoporosis in women
- Mitigated by increasing protein, resistance training
  - Protein RDA not optimal (0.36 g/lb/day)
  - Optimal protein intake (1g/lb/day)

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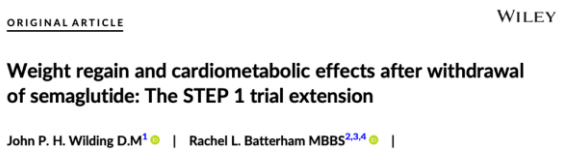
Weight Regain

- Discontinuation is Common
- 2/3 Regain Weight in 1yr after Stopping SG
- Metabolic Syndrome Returns (DM2, HTN)



ORIGINAL ARTICLE WILEY

Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension

John P. H. Wilding D.M[1] | Rachel L. Batterham MBBS[2,3,4] |

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Summary

- Obesity - chronic disease w/ few safe & effective tx & many adverse consequences
  - Metabolic Syndrome
  - Many types of Cancer
  - MSK, Dementia, Mental Health
- GLP-1RAs Generally Very Safe & Effective

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Summary

- GLP-1RA - Now 1st line option in DM
  - Long Half-Life – Usually SQ Weekly
- Beware Possible Dosing Errors if Compounded
- Medication Side Effect is **Dx of Exclusion**

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Summary

- No Evidence for Increased Suicide Risk
- Acute Vision Loss – Rare, Risk Slightly Increased
- Gallstone Disease – Common, Risk Greatest w/ Rapid Wt Loss
- Pancreatitis – Uncommon, Uncertain Risk, Consider Gallstone Dz
- Gastroparesis – Common, Important for Procedural/Surgical Planning

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Summary

- GI Side Effects are Most Common
  - Ensure Dosing Appropriate
  - Behavioral Interventions First
  - Hold Medication
  - Short Duration of Pharmacotherapy
- Changes in GI Motility & Wt Loss Effects on Other Meds (OCP, thyroid, AC, seizure meds)

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Summary

- Hypoglycemia – Rare w/ GLP-1RA alone
- Kidney Injury – Uncommon w/o N/V/D, AIN possible, low threshold to check Creatinine
- Hypotension – Common, Hold/Dec Anti-HTN medications
- Cancer? – TBD
- Muscle Loss/Osteoporosis – Common
- Weight Regain w/ Cessation – Common

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Summary of the Summary

- Hold the Medication
- Consider Alternate Diagnoses First
- Consider How Weight Loss and/or Altered GI Motility might affect other medications
- Treat Symptomatically

You're Ready!

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