Management of GI Issues Associated with GLP-1 Use

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Disclosures

Dr. Carmen Fong- I have no disclosures
Jessie Wong- I have no disclosures

Objectives

- GLP-1 receptor agonist (GLP-1 RA) overview
- Review exposure-dependent GI side effects
- Discuss prevention and treatment strategies

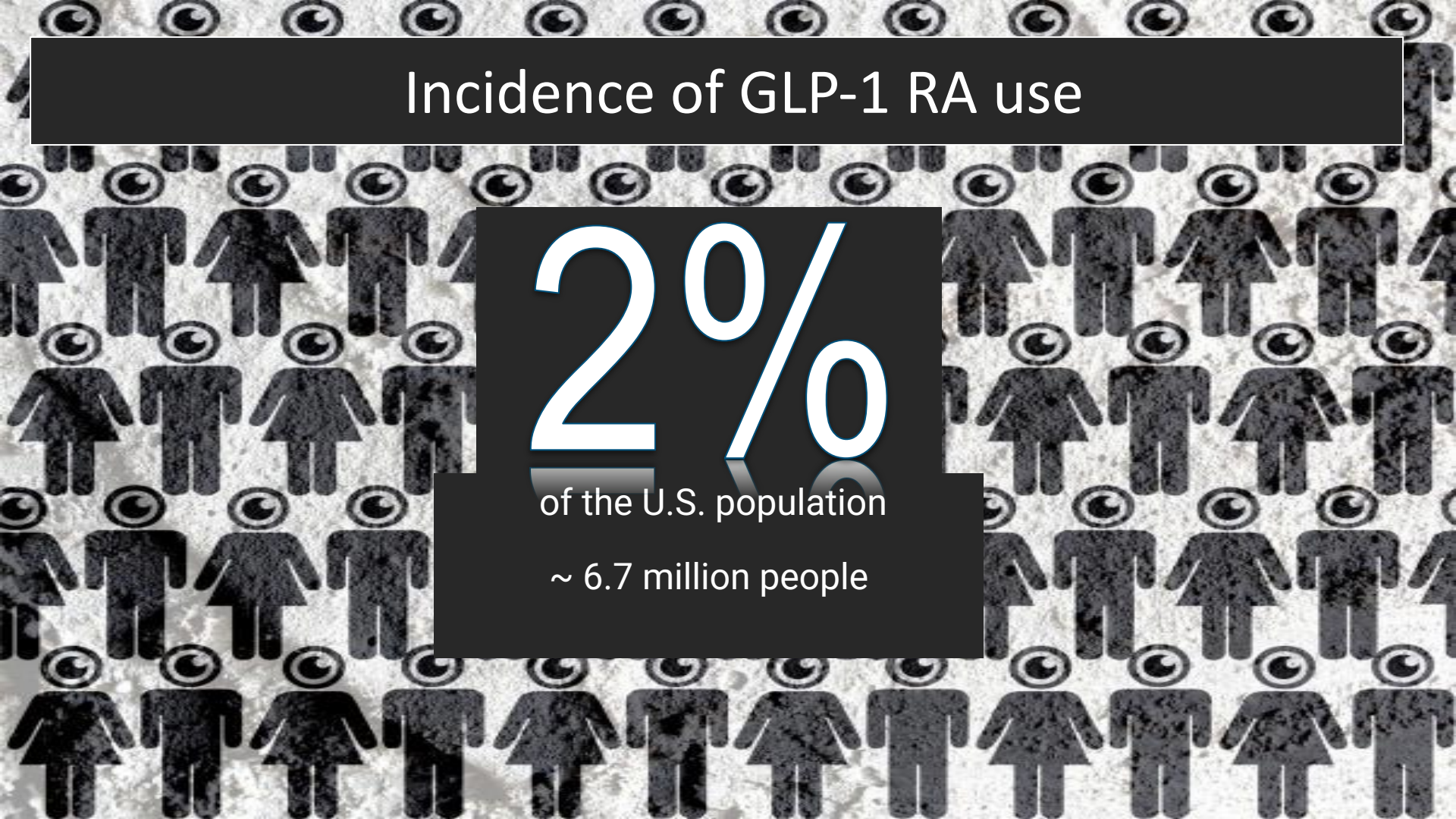
GLP-1 receptor agonist overview

GLP-1: A naturally-occurring peptide

Indications: T2D, obesity, CV risk reduction

Weight loss

Incidence of GLP-1 RA use



Mechanism of Action

- GLP-1 receptor stimulation
  - Increased insulin, decreased glucagon
  - Delayed gastric emptying
  - Increased satiety, decreased appetite

Approved Doses

- 0.25 mg to 2.4 mg weekly titration (Wegovy)
- 0.5 to 1.0 mg weekly (Ozempic for T2D)
- Maintenance: 2.4 mg for obesity, 1.0 mg for T2D

Dose Escalation Schedule

- 0.25 mg x 4 weeks
- 0.5 mg x 4 weeks
- 1.0 mg x 4 weeks
- 1.7 mg x 4 weeks
- 2.4 mg maintenance

GI Side Effects Overview

- Nausea
- Vomiting
- Diarrhea
- Constipation

Exposure-Response Modeling

- GI AEs increase with dose/exposure
- Most prominent: nausea and vomiting

STEP Trials – GI AE Rates

- Nausea: 43.9% vs 16.1% (placebo)
- Diarrhea: 29.7% vs 15.9%
- Vomiting: 24.5% vs 6.3%
- Constipation: 24.2% vs 11.1%

GI AEs in T2D Doses

- 0.5 mg: lower GI AE rates
- 1.0 mg: modest increase
- Dose-dependent increase confirmed in SUSTAIN trials

Dose-Exposure-AE Relationship

- GI AEs rise with semaglutide plasma levels
- Exposure-response curve flattens beyond 1.7–2.4 mg

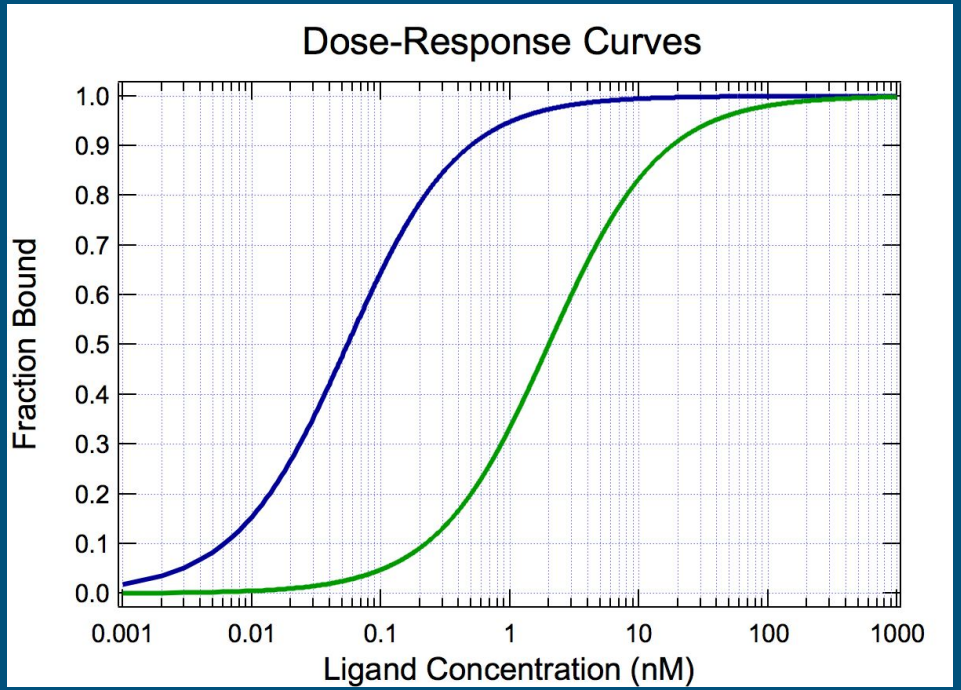


Table – Dose vs GI AE Summary

- 0.25 mg – Low AEs
- 0.5 mg – Nausea ~15%, Diarrhea ~10%, Constipation ~5%
- 1.0 mg – Nausea ~25%, Diarrhea ~15%
- 2.4 mg – Nausea 43.9%, Diarrhea 29.7%, Constipation 24.2%

Phase 2 Dose-Ranging Trials

- Higher doses (up to 16 mg/week) under study
- GI tolerability is a dose-limiting factor

4.3% quit

Constipation in STEP Trials

- ~24% on 2.4 mg vs 11% on placebo
- Underreported in prior GLP-1 literature

Vomiting Profile by Dose

- Not linear: jumps sharply >1.7 mg
- Plateau effect at 2.4 mg

Real-World vs Trial Data

- Real-world rates often lower
- Selection bias in RCTs vs real-world patients

Treatment Discontinuation

- ~4.3% discontinue due to GI AEs
- Most patients tolerate with proper titration

Start Low Strategy

- Adherence depends on GI tolerability
- Use lowest effective dose and titrate gradually

Dose Hold Strategy

- Hold titration if symptoms emerge
- Maintain current dose 2–4 more weeks

Managing GI AEs

- Hydration
- Soluble fiber
- Magnesium supplement
- PEG 3350 PRN
- Consider dose
- Check other medications with similar side effects

Nutrition Strategies for Common GLP-1 GI Symptoms

- Anticipate GI effects during titration and higher doses.
- Start with diet + hydration first; add meds as needed; escalate red flags.

References: Wharton 2023; AGA 2024; FDA 2023

Nausea & Early Satiety (Delayed Gastric Emptying)

- Small, frequent meals; slow eating pace
- Bland food, low-fat meals; avoid spicy, greasy foods
- Use room-temperature or cool foods to reduce odor-triggered nausea
- Encourage hydration between meals
- Optional: ginger, peppermint, or antiemetics if needed

References: Wharton 2023; AGA 2024; FDA 2023

Constipation

- New 2025 data: avg. fiber ≈ 14.5 g/day; whole grains ≈ 0.7 svgs/day; refined grains ≈ 4.2 svgs/day (Johnson et al., 2025)
- Gradual fiber increase (goal: 20–25 g/day) with emphasis on soluble fiber
- Ensure hydration of at least 1.5–2 L/day
- Encourage gentle movement and a consistent bowel routine
- Introduce osmotic laxatives like PEG/Miralax if needed

References: Wharton 2023; AGA 2024; Johnson 2025

Diarrhea

- Replenish fluids and electrolytes (broth, diluted juice)
- During flares: choose low-fat, low-FODMAP foods
- Reintroduce soluble fiber (e.g., banana, oatmeal) to improve stool form
- Assess lactose or fat malabsorption as potential triggers

References: AGA 2024; Lin 2023

Bloating & Delayed Gastric Emptying

- Small, frequent meals; avoid lying down post-meal
- Limit carbonated beverages and fermentable foods temporarily
- Light movement after meals
- If symptoms mimic gastroparesis, collaborate with prescribers for dose or medication evaluation

References: AGA 2024; Wharton 2023; Rubino 2022

Protein & Macronutrient Guidance

- Target 1.2–2.0 g/kg/day of protein (adjusted body weight) to protect lean mass
- Only ~43% of GLP-1 users consume ≥ 1.2 g/kg/day
- Shift calories toward fiber-rich carbs and lean proteins; reduce saturated fat and refined grains
- Avg. sodium intake ~ 3,164 mg/day — encourage flavor strategies to reduce added salt
- Prioritize labs: vitamin D, B12, iron/ferritin for deficiency monitoring

References: Johnson 2025; Lin 2023; Butsch 2025

Nutrient Intake Study: Methods & Sample

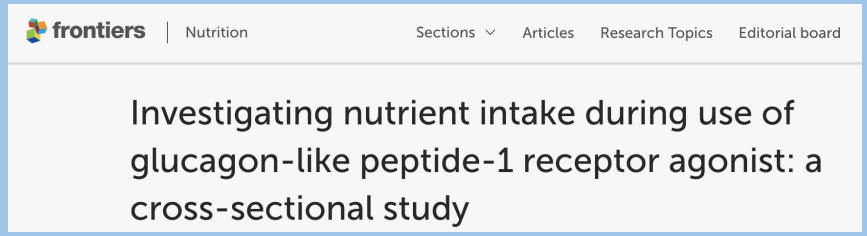
Objective:
Assess whether adults on GLP-1 receptor agonist therapy meet Dietary Reference Intakes (DRIs) using 3-day food logs and dietary questionnaires.

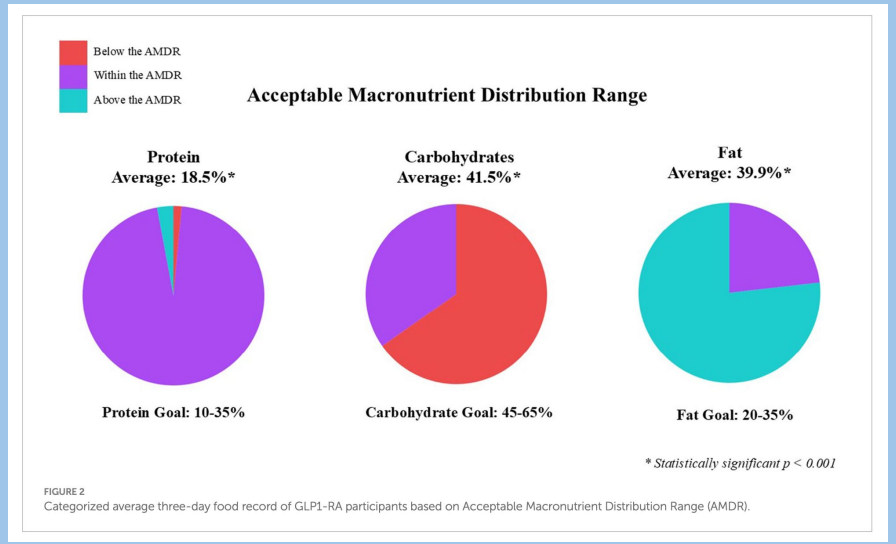
Sample:

- **N = 69 adults** on GLP-1 RAs ≥1 month
- Participants: completed **online demographic surveys** + **3-day food records**
- **Food group analysis**: self-reported MyPlate servings vs. actual intake
- Nutrient intake compared to DRI using 95% CI and Bonferroni correction ($p \leq 0.00156$)

Caloric & Macronutrient Intake:

- **1,748 kcal/day average**
- **Protein:** Adequate % kcals, but only **43% met ≥1.2 g/kg/day** (lean mass risk)
  Protein servings met target *only when measured in servings, not g/kg body weight*.
- **Fat:** 40% of kcals – high in saturated fat
- **Carbohydrates:** Below DRI range; added sugars low (11.5 g/day)





References: Johnson 2025 et el

Key Findings & Clinical Nutrition Implications

Micronutrient Gaps:

- Intake **below DRI** for: fiber, calcium, iron, magnesium, potassium
- Deficient in: **vitamins A, C, D, E, K**, and **choline**
- **~99% below DRI** for vitamin D and potassium

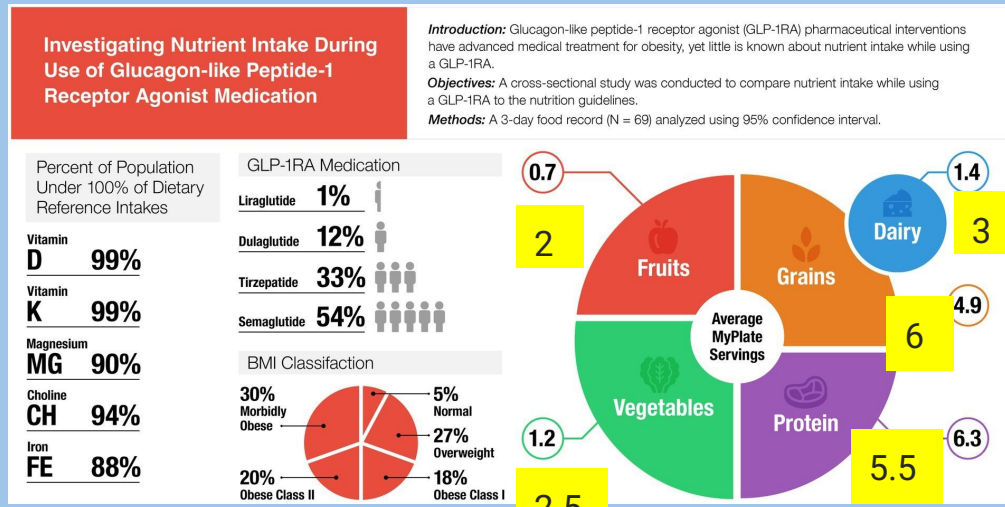
Food Group Patterns:

- Failed to meet **MyPlate servings** for fruit, vegetables, dairy, grains
- **Whole grains low** (0.7 servings/day)
- **Refined grains high** (4.2 servings/day)

Clinical Insights:

- Adequate intake of B vitamins, selenium, zinc
- Rapid weight loss + low protein intake = **risk of lean mass loss**
- **Low referral to dietitians** despite large dietary gaps

RDI is based on a 2000 calorie diet. Yellow are the DRI per serving.



Conclusion:

Most GLP-1 users fall short of nutrient and protein needs, indicating a crucial need for individualized, evidence-based medical nutrition therapy (MNT) and interdisciplinary follow-up during GLP-1 treatment.

• Only 20% were referred to a dietitian despite significant intake deficits. Incorporating a dietitian into GLP-1 care is essential to ensure nutritional adequacy, preserve lean mass, and support long-term treatment success.

References:

Johnson 2025 et el

What else? Higher-Dose Trials

- GI AEs increase but may plateau
- Still under investigation (8–16 mg/week)

What else? Oral vs SC Differences

- Oral semaglutide: similar GI AEs
- Patient education essential

Label Updates – Ileus

- FDA added ileus warning (2023)
- Educate on red flags (vomiting, severe pain)

Clinical Summary

- GI AEs are dose- and exposure-related
- Manage through slow titration and supportive care

Patient Education

- GI effects are expected and transient
- Reinforce adherence and side effect plan
- Peak side effects during titration, not maintenance

Clinical Action Items

- Use: titration calendar
- Provide: diet/bowel/activity plan
- Reassure: symptoms are transient
- Manage: other medications
- Investigate: prolonged symptoms

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QUESTIONS

Thank You for listening!

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