Micronutrient Status During GLP-1 Receptor Agonist Treatment for Obesity: A Dose-Response, Weight-Loss-Mediated Analysis

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obesityweek® NOV 14-17, 2026 WASHINGTON, DC | THE OBESITY SOCIETY

Background

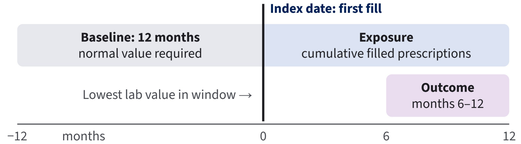
- GLP-1 receptor agonists (GLP-1RAs) produce substantial weight loss, but appetite suppression and gastrointestinal effects may reduce nutrient intake.
- Deficiencies have been reported mainly in type 2 diabetes; evidence in adults with obesity **without diabetes** is lacking.
- Whether nutrient changes reflect the drug itself or the weight loss it produces has not been formally tested.

Objective

To assess the dose-response association between cumulative filled prescriptions of liraglutide or semaglutide and incident nutritional deficiencies in adults with obesity, and whether it is mediated by weight loss.

Methods

Retrospective cohort in Clalit Health Services, Israel's largest integrated payer–provider (electronic health records).



- **Population:** adults ≥18 y, BMI ≥30 kg/m², starting liraglutide (Jul 2019–Apr 2024) or semaglutide (Jan–Feb 2025). Excluded: bariatric surgery, cancer, diabetes, liver, renal or celiac disease, alcohol-related disorder, pregnancy.
- **Outcomes:** deficiency (sex-specific ranges) of vitamin B12, ferritin, transferrin, iron, calcium, total protein, vitamin D, among those normal at baseline; continuous levels secondary.
- **Analysis:** logistic and linear regression per drug, adjusted for age, sex, baseline BMI and SES; regression-based mediation by % BMI change from baseline.

Study population

21,005 adults with obesity and without diabetes, with baseline and follow-up labs

● Liraglutide

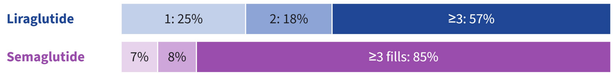
77,230	→	60,309	→	16,053
initiated treatment		eligible (16,921 excluded)		analytic cohort

◆ Semaglutide

29,758	→	21,743	→	4,952
initiated treatment		eligible (8,015 excluded)		analytic cohort

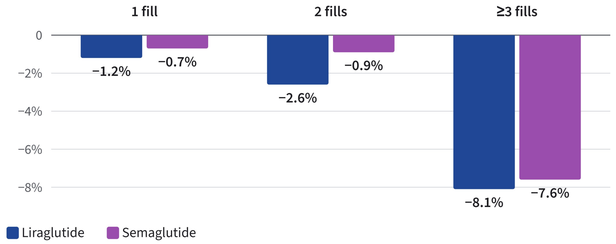
Analytic cohorts: patients with laboratory values in both the baseline and follow-up periods.

Filled prescriptions during exposure

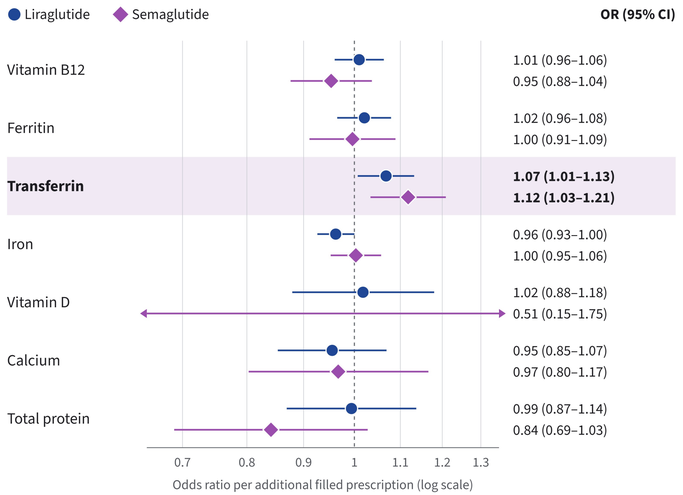


More fills, more weight loss

Mean % change in BMI from baseline, by number of filled prescriptions (both p<0.001)



Deficiency risk: a dose-response for transferrin only

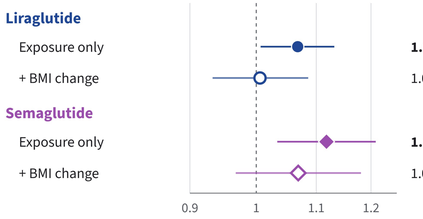


Logistic regression adjusted for age, sex, baseline BMI and SES. Transferrin p = 0.028 (liraglutide) and p = 0.005 (semaglutide); all others p > 0.05. Arrows: CI extends beyond axis.

Incident deficiency, months 6–12

Nutrient	Lira. at risk	Lira. deficient, n (%)	Sema. at risk	Sema. deficient, n (%)
Vitamin B12	2,721	230 (8.5)	948	60 (6.3)
Ferritin	2,375	220 (9.3)	888	61 (6.9)
Transferrin	**1,495**	**197 (13.2)**	**581**	**89 (15.3)**
Iron	2,308	584 (25.3)	803	203 (25.3)
Vitamin D	1,913	30 (1.6)	716	1 (0.1)
Calcium	11,601	56 (0.5)	3,686	14 (0.4)
Total protein	11,390	32 (0.3)	3,551	13 (0.4)

Weight loss fully explains the transferrin signal



Greater BMI reduction was associated with transferrin deficiency (OR 0.93 and 0.95 per 1% BMI change; both p ≤ 0.002). Adding it to the model moved the exposure effect to the null.

Continuous biomarker levels

- Small shifts per fill (e.g. transferrin −0.9 and −1.5 mg/dL; vitamin D, calcium and ferritin slightly higher), all within the normal range.
- BMI change fully or partially mediated these shifts.

Conclusions

- Cumulative GLP-1RA exposure was **not associated with clinically meaningful deficiency** for 6 of 7 nutrients.
- Transferrin deficiency rose 7% (liraglutide) and 12% (semaglutide) per fill, **fully mediated by BMI change**.
- Nutrient changes reflect weight loss, not an independent drug effect. Monitor nutrition in patients with substantial weight loss.

Selected references: Butsch WS et al. Obes Pillars 2025;15:100186 · Almandoz JP et al. Obesity 2024;32:1613-31 · Mozaffarian D et al. Obesity 2025;33:1475-503.

Disclosures: O.R., D.D. and G.L.: grants from the Israel Science Foundation outside this work. D.D.: grants, personal fees and nonfinancial support from Novo Nordisk and Eli Lilly; personal fees from Boehringer Ingelheim. No study funding.

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