GOOD EVIDENCE MATTERS

GEMs of the Week

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FPIN
Family Physicians Inquiries Network

Volume 6 Issue 43

The Heavy Reality: Weight Regain after Cessation of Weight Management Medications

Weight Regain after Cessation of Medication for Weight Management: Systematic Review and Meta-Analysis

West S, Scragg J, Aveyard P, et al. Weight Regain after Cessation of Medication for Weight Management: Systematic Review and Meta-analysis. *BMJ*. 2026;392:e085304. Published 2026 Jan 7. doi:10.1136/bmj-2025-085304

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KEY TAKEAWAY: Cessation of all weight loss medications increases weight regain compared to non-pharmacologic weight loss interventions or placebo in adults with overweight or obesity.

STUDY DESIGN: Systematic review and meta-analysis of 35 randomized controlled trials, one non-randomized trial, and one observational cohort study (N=9,341)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: Obesity is a chronic, relapsing condition that affects almost two billion adults worldwide and is associated with increased morbidity and premature mortality. While behavioral weight loss modifications remain the mainstay of treatment, pharmacologic options show great promise as an additional treatment recommendation. However, the long-term impact on health after stopping these medications is not fully characterized. This study assessed weight regain and changes in cardiometabolic markers after stopping weight management medications (WMMs).

PATIENTS: Adults with overweight or obesity

INTERVENTION: Pharmacological intervention currently or previously licensed for weight loss

CONTROL: Non-pharmacologic weight loss interventions or placebo

PRIMARY OUTCOME: Rate of weight regain after cessation of treatment

Secondary Outcome: Cardiometabolic markers

METHODS (BRIEF DESCRIPTION):

- Studies were selected to compare medical management with behavioral weight loss interventions in adults with a body mass index (BMI) >25 at intervention start by a systematic search of online peer-reviewed databases performed prior to February 2025.
- Previous behavioral weight management program studies included adults with overweight or obesity and required at least 12 months of follow-up from baseline.
- Medical interventions included all medications that are currently used or medications that were previously licensed for weight loss, with subgroup analysis between all weight loss medications, incretin mimetics specifically, or the newer incretin mimetics that include semaglutide and tirzepatide.
- Medical therapy was required to last for at least eight weeks, and follow-up was performed at least four weeks following cessation of the drug.
- Controls for these studies included no behavioral interventions or, in the case of medical management trials, any nonpharmacologic intervention, placebo, or no support.
- Weight loss medication interventions were conducted for a mean duration of 39 (range 11–176) weeks with follow-up surveillance at a mean of 32 (range 4–104) weeks. Only one study followed up with patients after one year.
- All data were assessed using three different models to extrapolate weight gain trajectories using linear progression of prior data to the point at which weight returned to baseline.
- Primary outcomes assessed the weight regain rate following cessation of the intervention.
- Secondary outcomes assessed the change in cardiometabolic parameters such as HbA1c, fasting glucose, systolic blood pressure (SBP), diastolic blood pressure (DBP), cholesterol, and triglycerides.

INTERVENTION (# IN THE GROUP): 6,322

COMPARISON (# IN THE GROUP): 3,019

FOLLOW-UP PERIOD: 12 months after cessation of intervention

RESULTS:

Primary Outcome –

- Cessation of all weight loss medications increased weight regain compared to no intervention (63 intervention arms, n=6,322; mean 0.4 kg/month; 95% CI, 0.3–0.5).
- Cessation of incretin mimetics increased weight regain compared to no intervention (32 intervention

arms, n=4,757; mean 0.5 kg/month; 95% CI, 0.4–0.7).
- Cessation of semaglutide and tirzepatide increased weight regain compared (10 intervention arms, n=1,776; mean 0.8 kg/month; 95% CI, 0.7–0.9).
- Weight gain projections following cessation of medical management showed an estimated return of weight by 1.4 years compared to control.

Secondary Outcome –

- In patients taking WMMs HbA1c increased after treatment cessation (14 studies; n=not available; 0.05 mmol/mol per month; 95% CI, 0.0.3–0.08).
- In patients taking WMMs, fasting glucose increased compared to after treatment cessation (21 studies, n=not available; 0.06 mmol/mol per month; 95% CI, 0.03–0.08).
- In patients taking WMMs, SBP increased after treatment cessation (15 studies, n=not available; 0.5 mmHg per month; 95% CI, 0.3–0.7).
- In patients taking WMMs, DBP increased after treatment cessation (15 studies, n=not available; 0.2 mmHg per month; 95% CI, 0.1–0.3).
- In patients taking WMMs, total cholesterol concentration increased after treatment cessation (14 studies, n=not available; 0.05 mmol/L per month; 95% CI, 0.03–0.07).
- In patients taking WMMs, triglyceride concentration increased after treatment cessation (14 studies, n=not available; 0.03 mmol/L per month; 95% CI, 0.01–0.04).
- All cardiovascular parameters were projected to return to baseline levels by 1.4 years following cessation of medical management.

LIMITATIONS:

- Data for newer weight loss medications were less prevalent. As these medications become more common, more studies are needed on their impact on sustained weight loss.
- Weight gain projections were made with linear trajectories, which may not accurately reflect actual weight gain.

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The opinions and assertions contained herein are those of the author and are not to be construed as official or as reflecting the views of the US Army Medical Department, the Army at large, or the Department of Defense.

Avoid the Mess: Ondansetron in Children with Gastroenteritis

Multidose Ondansetron after Emergency Visits in Children with Gastroenteritis

Freedman SB, Williamson-Urquhart S, Plint AC, et al. Multidose Ondansetron after Emergency Visits in Children with Gastroenteritis. *N Engl J Med*. 2025;393(3):255-266. doi:10.1056/NEJMoa2503596

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KEY TAKEAWAY: Providing multidose ondansetron after an emergency department (ED) visit is superior to placebo in reducing moderate-to-severe gastroenteritis in children with acute gastroenteritis-associated vomiting.

STUDY DESIGN: Double-blind, placebo-controlled, randomized superiority trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Ondansetron reduces vomiting in children with acute gastroenteritis when administered in the ED. It is commonly prescribed at discharge, but evidence supporting multidose use after discharge is limited. This trial evaluated whether providing multidose ondansetron after discharge from the ED to children with acute gastroenteritis would reduce disease severity.

PATIENTS: Children with acute gastroenteritis-associated vomiting

INTERVENTION: Multidose ondansetron

CONTROL: Placebo

PRIMARY OUTCOME: Moderate-to-severe gastroenteritis

Secondary Outcome: Presence, duration, and number of vomiting episodes, unscheduled health care visits, administration of intravenous (IV) fluids

METHODS (BRIEF DESCRIPTION):

- A double-blind, randomized, placebo-controlled, superiority trial was conducted giving multidose ondansetron to children with acute gastroenteritis-associated vomiting in six different EDs in Canada.
- Eligible patients were children from six months to <18 years old with acute gastroenteritis, at least three vomiting episodes during the preceding 24 hours, symptom onset within 72 hours, vomiting within six hours before enrollment, and receipt of ondansetron during the ED visit.
- Patients who presented with hematemesis, bilious vomiting, long QT syndrome, ventricular arrhythmia, use of QT-prolonging medication, or allergy to ondansetron were excluded from the trial.
- Patients' baseline characteristics included a median age of 48 months, weight of 16 kg, and 51% female.
- Caregivers were given six doses of oral ondansetron solution (4 mg/5mL; 0.15 mg/kg per dose, maximum 8 mg), or matching placebo, to administer for recurrent episodes of emesis, no more frequently than every eight hours during the first 48 hours after enrollment.
- A repeat dose could be provided if vomiting recurred within 15 minutes after solution administration.
- The primary analysis was assessed by calculating the severity of gastroenteritis using the modified Vesikari scale. Score ranges from 0–20; a score of ≥9 indicates severe disease.
- Patients were followed for seven days after enrollment.
- Caregivers completed follow-up surveys at 24 hours, 48 hours, and day seven after enrollment.
- The secondary outcomes included the presence of vomiting, duration from enrollment to the final vomiting episode within 48 hours, and unscheduled health care visits and receipt of IV fluids within seven days.

INTERVENTION (# IN THE GROUP): 517

COMPARISON (# IN THE GROUP): 512

FOLLOW-UP PERIOD: Seven days

RESULTS:

Primary Outcome –

- Ondansetron reduced moderate to severe gastroenteritis-associated emesis after seven days compared to placebo (unadjusted risk difference –7.4; 95% CI, –11 to –3.7).

Secondary Outcome –

- Ondansetron reduced the number of vomiting episodes within 48 hours compared to placebo (adjusted rate ratio [aRR] 0.76; 95% CI, 0.67–0.87).
- There was no significant difference in the presence, duration, and number of vomiting episodes within seven days, unscheduled health care visits, and

administration of IV fluids between ondansetron and placebo.

LIMITATIONS:

- Recall bias following the loss of daily follow-up from days 3–7 and using a summarized single survey
- Careful interpretation is needed when using the modified Vesikari scale since it combines ≥2 outcomes into one.
- The primary outcome used the composite modified Vesikari scale; therefore, the significant overall result does not demonstrate that every individual component improved independently.
- The trial was conducted at six Canadian pediatric EDs, which may limit generalizability to settings with different IV rehydration and ondansetron-prescribing practices.

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Beyond Blood Sugar: Mapping the Broad Benefits and Risks of GLP-1 Receptor Agonists

Mapping the Effectiveness and Risks of GLP-1 Receptor Agonists

Xie Y, Choi T, Al-Aly Z. Mapping the effectiveness and risks of GLP-1 receptor agonists. *Nat Med*. 2025;31(3):951-962. doi:10.1038/s41591-024-03412-w

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KEY TAKEAWAY: Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) significantly reduce the risk of alcohol use disorders (AUDs), heart failure (HF), and pneumonia but increase the risk of nausea, vomiting, and gastroesophageal reflux disease (GERD) compared to usual care in adults with type 2 diabetes mellitus (T2DM).

STUDY DESIGN: Retrospective cohort study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: GLP-1RAs are increasingly used for T2DM and obesity due to their cardiovascular, renal, and weight loss benefits. While compared to other diabetic drugs, their comprehensive risks and benefits across multiple health outcomes had not been fully mapped. This study aimed to systematically evaluate the effectiveness and risks of GLP-1 RAs across 175 health outcomes compared to other antihyperglycemics and usual care.

PATIENTS: Adults with T2DM

INTERVENTION: GLP-1 RAs

CONTROL: Usual care

PRIMARY OUTCOME: Effectiveness of GLP-1 RAs

Secondary Outcome: Risks of GLP-1 RAs

METHODS (BRIEF DESCRIPTION):

- Study used cohort data derived from the U.S. Department of Veterans Affairs from 2017–2023.
- Participants had a mean age of 66 years, 93% were male, and 73% were White.
- Inclusion criteria included all patients with T2DM and use of GLP-1 RA between October 2017 and December 2023.
- The cohort compared GLP-1 RA users with sulfonylurea, DPP4 inhibitor, and SGLT2 inhibitor users, and usual care.
- There were 175 health outcomes across 12 diagnostic categories evaluated.
- The primary outcome assessed the effectiveness of GLP-1 RAs on AUD, stimulant use disorders, anemia, HF, pulmonary hypertension, myocardial infarction (MI), ischemic stroke, chronic obstructive pulmonary disease (COPD), pleural effusion (PE), pneumonitis, and liver cancer.
- The secondary outcomes assessed GLP-1 RAs on the risk of hypotension, GERD, hemorrhoids, nausea/vomiting, abdominal pain, nephrolithiasis, interstitial nephritis, and pancreatitis.
- Study performed weighted analyses using inverse probability weighting with Benjamini-Hochberg correction for multiple testing.

INTERVENTION (# IN THE GROUP): 215,970

COMPARISON (# IN THE GROUP):

- Sulfonylureas: 159,46
- DPP4 inhibitors: 117,989
- SGLT2 inhibitors: 258,614
- Non-GLP-1RA antihyperglycemics (usual care): 1,203,097

FOLLOW-UP PERIOD: Median 3.7 years

RESULTS:

Primary Outcome –

- GLP-1 RAs decreased the risk of AUDs compared to usual care (hazard ratio [HR] 0.89; 95% CI, 0.86–0.92).
- GLP-1 RAs decreased the risk of stimulant use disorders compared with usual care (HR 0.84; 95% CI, 0.78–0.91).
- GLP-1 RAs decreased the risk of anemia compared to usual care (HR 0.97; 95% CI, 0.95–0.99).
- GLP-1 RAs decreased the risk of HF compared to usual care (HR 0.89; 95% CI, 0.87–0.91).
- GLP-1 RAs decreased the risk of pulmonary hypertension compared to usual care (HR 0.82; 95% CI, 0.78–0.85).
- GLP-1 RAs decreased the risk of MI compared to usual care (HR 0.91; 95% CI, 0.87–0.94).
- GLP-1 RAs decreased the risk of ischemic stroke compared to usual care (HR 0.93; 95% CI, 0.90–0.96).
- GLP-1 RAs decreased the risk of COPD compared to usual care (HR 0.90; 95% CI, 0.87–0.92).
- GLP-1 RAs decreased the risk of PE compared to usual care (HR 0.86; 95% CI, 0.83–0.89).

- GLP-1 RAs decreased the risk of pneumonitis compared to usual care (HR 0.89; 95% CI, 0.86–0.92).
- GLP-1 RAs decreased the risk of liver cancer compared to usual care (HR 0.82; 95% CI, 0.75–0.89).
- Overall, GLP-1 RAs reduced the risk of 42 outcomes (24%) compared to usual care.

Secondary Outcome –

- GLP-1 RAs increased the risk of hypotension compared to usual care (HR 1.1; 95% CI, 1.04–1.1).
- GLP-1 RAs increased the risk of GERD compared to usual care (HR 1.1; 95% CI, 1.1–1.2).
- GLP-1 RAs increased the risk of hemorrhoids compared to usual care (HR 1.1; 95% CI, 1.06–1.1).
- GLP-1 RAs increased the risk of nausea and vomiting compared to usual care (HR 1.3; 95% CI, 1.3–1.3).
- GLP-1 RAs increased the risk of abdominal pain compared to usual care (HR 1.1; 95% CI, 1.1–1.1).
- GLP-1 RAs increased the risk of nephrolithiasis compared to usual care (HR 1.2; 95% CI, 1.1–1.2).
- GLP-1 RAs increased the risk of interstitial nephritis compared to usual care (HR 1.1; 95% CI, 1.03–1.1).
- GLP-1 RAs increased the risk of pancreatitis compared to usual care (HR 2.5; 95% CI, 2.0–3.0).
- Overall, GLP-1 RAs increased the risk of 19 outcomes (11%) compared to usual care.

LIMITATIONS:

- Observational design is limited in establishing causal inference.
- The study involved the older male veteran population predominantly, thus limiting generalizability.
- There is potential for residual confounding despite weight adjustments.
- The study did not compare within-class GLP-1 RA effects and may have missed weaker associations after multiple testing corrections were made.

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SGB, An Underutilized Intervention in the Treatment of PTSD, Post-20-Year War on Terrorism

Effectiveness of Combined Cognitive Processing Therapy with Stellate Ganglion Block: An Open-Label Randomized Wait-List Clinical Trial

Bryan CJ, Lynch J, Bryan AO, et al. Effectiveness of Combined Cognitive Processing Therapy with Stellate Ganglion Block: An Open-Label Randomized Wait-List Clinical Trial. *Psychother Psychosom*. Published online December 15, 2025. doi:10.1159/000550014

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KEY TAKEAWAY: Stellate ganglion block (SGB) in combination with cognitive processing therapy (CPT) reduces symptom severity of post-traumatic stress disorder (PTSD) compared to CPT alone in the military patient population.

STUDY DESIGN: Open-label randomized wait-list trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: PTSD imposes a heavy burden of morbidity on military populations. Although massed-format CPT acts as a potent first-line treatment, incomplete recovery is common, necessitating research into augmentation strategies. SGB offers a promising adjunctive approach to mitigate physical and sympathetic reactivity associated with PTSD. This study aimed to assess if SGB before or after CPT provides a greater improvement in symptom control.

PATIENTS: Military personnel with PTSD recruited between 2022–2024

INTERVENTION: SGB prior to or after CPT

CONTROL: Baseline reported symptoms

PRIMARY OUTCOME: PTSD symptom severity

Secondary Outcome: Depression, anxiety, somatic symptoms

METHODS (BRIEF DESCRIPTION):

- An open-label, randomized, wait-list clinical trial was conducted to evaluate the impact of combining SGB with massed CPT.
- The study included 86 military personnel and veterans with a diagnosis of PTSD, >18 years old, who had current or prior military service, spoke and understood English, were on stable medication for at least three months, and consented to the study.
- Participants were excluded if they had received SGB within a year prior, had a prior diagnosis of bipolar or psychiatric conditions, a diagnosis of severe traumatic brain injury (TBI), symptoms of substance abuse disorder in the past month, elevated suicidality requiring urgent evaluation or hospitalization, impaired mental status, or any other condition investigators thought could predispose the patients to negative outcomes.
- Participants eligible for intervention were randomized to receive SGB either before or after undergoing massed CPT.
- The effect of the intervention was compared to the symptom severity as measured at baseline, before SGB or CPT was performed.
- The primary outcome assessed was symptom severity of PTSD as measured by the PTSD Checklist for DSM-5 (PCL-5), a self-assessed 20-question survey of PTSD symptoms in the past week. Scores range from 0–80, with higher scores indicating higher severity of symptoms.
- The following were measured as the secondary outcomes:
  - Depression was measured using the Patient Health Questionnair-9 (PHQ-9), a nine-question self-assessed survey of depressive symptoms in the past two weeks. Scores range from 0–27, with higher scores indicating more severe symptoms
  - Anxiety was measured using the Generalized Anxiety Disorder-7 (GAD-7), a seven-question self-assessed survey of anxiety symptoms. Scores range from 0–21, with higher scores indicating higher levels of anxiety.
  - Somatic symptoms were measured using the Patient Health Questionnaire-15 (PHQ-15), a 15-question self-assessed survey of somatic/physical symptoms in the past two weeks. Scores range from 0–30, with higher scores indicating higher severity of somatic symptoms.
- The results were analyzed using linear mixed effects modeling of the specific outcome assessed with the covariance matrix selected by the smaller Bayesian Information Criterion values.
- The reliable change indices (RCIs) were calculated using the ratio of the difference between the

baseline and post-intervention scores compared to the standard error within that difference, with a score of >2.0 equating to a >95% confidence interval.

INTERVENTION (# IN THE GROUP):

- SGB-before-CPT: 42
- SGB-after-CPT: 44

COMPARISON (# IN THE GROUP): The same 86 patients

FOLLOW-UP PERIOD: Outcomes assessed in regular intervals for 52 weeks

RESULTS:

Primary Outcome –

- SGB-before-CPT significantly reduced symptoms of PTSD compared to baseline (F (12,724)=23; *p*<.001).
- SGB-after-CPT significantly reduced symptoms of PTSD compared to baseline (F (12,724)=21; *p*<.001).
- Reductions were faster in SGB-before-CPT, leveling off after two weeks, while the SGB-after-CPT intervention group decreased symptoms until week 14 before leveling off.

Secondary Outcome –

- SGB-before-CPT significantly reduced symptoms of depression compared to baseline (F (12,728)=14; *p*<.001).
- SGB-after-CPT significantly reduced symptoms of depression compared to baseline (F (12,728)=9.2; *p*<.001).
- SGB-before-CPT significantly reduced somatic symptoms compared to baseline (F (12,726)=7.1; *p*<.001).
- SGB-after-CPT significantly reduced somatic symptoms compared to baseline (F (12,726)=5.8; *p*<.001).
- SGB-before-CPT significantly reduced symptoms of anxiety compared to baseline (F (12,725)=13.9; *p*<.001).
- SGB-after-CPT significantly reduced symptoms of anxiety compared to baseline (F (12,725)=11; *p*<.001).
- Reductions were faster in SGB-before-CPT for all secondary endpoints, including depression, anxiety, and somatic symptoms.

LIMITATIONS:

- The study only includes US Military Personnel and veterans, limiting generalizability.
- This study did not differentiate between subtypes of PTSD and how these subtypes could impact treatment response.
- Optimal SGB dosing and patient selection criteria remain undetermined.

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