Does GLP intervention demonstrate superior outcomes compared to standard treatment protocols for cannabis cessation in patients with cannabis hyperemesis syndrome?

No studies have examined GLP intervention compared to standard treatment for cannabis cessation in patients with cannabis hyperemesis syndrome.

Abstract

No evidence is currently available to address whether GLP intervention demonstrates superior outcomes compared to standard treatment protocols for cannabis cessation in patients with cannabis hyperemesis syndrome. The single identified study examining GLP-1 receptor agonist intervention in relation to cannabis-related outcomes did not include patients with cannabis hyperemesis syndrome and instead focused on cannabis use disorder in patients with obesity and type 2 diabetes. The study did not provide specific cannabis cessation or CHS symptom outcomes, did not compare against standard CHS treatment protocols, and did not provide safety data specific to CHS patients. Therefore, the comparative effectiveness of GLP intervention versus standard treatment for cannabis cessation in CHS patients remains unknown and requires dedicated research in this specific clinical population.

Paper search

We performed a semantic search using the query "Does GLP intervention demonstrate superior outcomes compared to standard treatment protocols for cannabis cessation in patients with cannabis hyperemesis syndrome?" across over 138 million academic papers from the Elicit search engine, which includes all of Semantic Scholar and OpenAlex.

We retrieved the 50 papers most relevant to the query.

Screening

We screened in sources based on their abstracts that met these criteria:

- **Target Population**: Does the study include patients diagnosed with cannabis hyperemesis syndrome using clearly defined diagnostic criteria?
- **Intervention Type**: Does the study evaluate GLP (glucagon-like peptide) receptor agonist interventions?
- **Primary Outcomes**: Does the study measure cannabis cessation outcomes (such as complete cessation, reduction in use, or abstinence rates)?
- **Comparison Group**: Does the study include a comparison group receiving standard treatment protocols for cannabis cessation?
- **Study Design**: Is the study design one of the following: randomized controlled trial, controlled clinical trial, cohort study, case-control study, systematic review, or meta-analysis?
- **Participant Age**: Does the study involve adult participants (≥18 years of age)?
- **Comparative Design**: Is the study design something other than a case report or case series without comparison groups?
- **Intervention Isolation**: Is it possible to isolate the effects of the GLP intervention (i.e., is the GLP intervention NOT combined with other experimental treatments that would make it impossible to determine GLP-specific effects)?
- **Study Focus**: Does the study focus on cannabis cessation outcomes rather than solely on acute symptom management?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Data extraction

We asked a large language model to extract each data column below from each paper. We gave the model the extraction instructions shown below for each column.

- **Study Design & CHS Population**:

  Extract study design (RCT, cohort, case-control, etc.) and confirm that the study population includes patients with cannabis hyperemesis syndrome (CHS). If the study includes mixed populations, specify what proportion had CHS and whether CHS-specific results are reported separately. Note any diagnostic criteria used for CHS.

- **GLP Intervention Details**:

  Extract complete details about the GLP intervention used for cannabis cessation in CHS patients, including:

- Specific GLP drug name (semaglutide, liraglutide, etc.)
- Dosage and dosing schedule
- Duration of treatment
- Route of administration
- Any dose escalation protocols
- Concomitant treatments allowed

- **Standard Treatment Comparator**:

  Extract details about what constituted the 'standard treatment protocols' used as the comparison group for cannabis cessation in CHS patients, including:

- Specific medications used (e.g., ondansetron, haloperidol, supportive care)
- Dosages and treatment protocols
- Duration of standard treatment
- Any behavioral interventions included
- Whether this represents true standard of care for CHS

- **Cannabis Cessation Outcomes**:

  Extract all cannabis cessation and CHS symptom outcomes measured in both GLP and standard treatment groups, including:

- How cannabis cessation was defined and measured
- Cannabis use frequency/quantity changes
- Time to cessation
- Sustained abstinence rates and duration
- CHS symptom resolution (nausea, vomiting, abdominal pain)
- Emergency department visits for CHS
- Quality of life measures
- Follow-up duration for outcomes

- **Comparative Effectiveness Results**:

  Extract direct statistical comparisons between GLP intervention and standard treatment for cannabis cessation in CHS patients, including:

- Primary endpoint results with effect sizes
- Hazard ratios, relative risks, or mean differences with confidence intervals
- P-values for statistical significance
- Number needed to treat (if calculable)
- Subgroup analyses relevant to CHS patients
- Time-to-event analyses if reported

- **Patient Characteristics**:

  Extract baseline characteristics of CHS patients in both treatment groups, including:

- Age and gender distribution
- Duration of cannabis use before CHS diagnosis
- Severity/frequency of CHS episodes
- Previous cessation attempts and methods tried
- Comorbidities (especially psychiatric and gastrointestinal)
- Cannabis use patterns (daily use, THC potency, etc.)
- Concomitant substance use

- **Safety & Adverse Events**:

  Extract safety data comparing GLP intervention to standard treatment in CHS patients, including:

- Discontinuation rates due to adverse events
- Serious adverse events in each group
- Common side effects and their frequencies
- GLP-specific side effects (nausea, gastrointestinal issues)
- Drug interactions or contraindications
- Any safety concerns specific to CHS population

- **Study Quality & Limitations**:

  Extract factors affecting the interpretation and generalizability of results for GLP vs standard treatment in CHS patients, including:

- Randomization and blinding methods (if applicable)
- Sample size calculations and power
- Loss to follow-up rates
- Potential confounding factors
- Selection bias concerns
- Generalizability limitations
- Funding sources and conflicts of interest
- Authors' stated limitations

Results

Characteristics of Included Studies

The search identified one study examining GLP-1 receptor agonist intervention in relation to cannabis-related outcomes. However, this study did not address the specified research question regarding cannabis hyperemesis syn-

drome (CHS).

Study	Full text retrieved?	Study design	Population	Primary focus	Sample size
William Wang et al., 2024	Yes	Retrospective cohort study	Patients with obesity (n=85,223) and type 2 diabetes (n=596,045)	Cannabis use disorder incidence and recurrence	681,268 total

The included study was a retrospective cohort study that did not include information on cannabis hyperemesis syndrome or its diagnostic criteria. The study population consisted of patients with obesity (mean age 51.3 years, 65.6% women) and patients with type 2 diabetes who were prescribed semaglutide or comparator medications. The study focused on cannabis use disorder (CUD) rather than cannabis hyperemesis syndrome, and did not provide specific cannabis cessation or CHS symptom outcomes.

Relevance to Research Question

The included study does not directly address the research question for several critical reasons:

Population mismatch: The study did not include patients with cannabis hyperemesis syndrome. Instead, the study population comprised patients with obesity and type 2 diabetes who had comorbidities including morbid obesity, T2D, and obesity-associated comorbidities, with lower prevalence of mental disorders and substance use disorders in the semaglutide cohort.

Intervention details: While the study examined semaglutide as the GLP-1RA intervention, it did not specify dosage and dosing schedule, route of administration, or any dose escalation protocols. The duration involved a 12-month follow-up period, but concomitant treatments were not explicitly detailed.

Comparator mismatch: The comparison groups consisted of non-GLP-1RA anti-obesity medications (bupropion, naltrexone, orlistat, topiramate, phentermine) and anti-diabetes medications (insulins, metformin, sulfonylureas, alpha glucosidase inhibitors, thiazolidinediones, DPP-4 inhibitors, SGLT2 inhibitors), rather than standard treatment protocols for cannabis hyperemesis syndrome. While behavioral interventions were mentioned, including tapering marijuana use, support for withdrawal symptoms, contingency management, cognitive-behavioral therapy, and motivational enhancement therapy, these were described in the context of cannabis use disorder management rather than CHS-specific treatment. The study did not specify dosages or detailed treatment protocols for these medications, and did not explicitly state whether these treatments represent the true standard of care for cannabis hyperemesis syndrome.

Outcome mismatch: The study did not provide specific cannabis cessation or CHS symptom outcomes. Instead, the study measured incident and recurrent CUD diagnoses through electronic health records rather than direct measures of cannabis cessation, frequency/quantity changes, time to cessation, sustained abstinence rates, CHS symptom resolution (nausea, vomiting, abdominal pain), emergency department visits for CHS, or quality of life measures.

Study Findings on Cannabis Use Disorder

Although not addressing the research question about CHS, the study reported the following findings regarding cannabis use disorder:

Population	Outcome	Semaglutide HR (95% CI)	Comparison group
Obesity (n=85,223)	Incident CUD	0.56 (0.42–0.75)	Non-GLP-1RA anti-obesity medications
Obesity (n=85,223)	Recurrent CUD	0.62 (0.46–0.84)	Non-GLP-1RA anti-obesity medications
Type 2 diabetes (n=596,045)	Incident CUD	0.40 (0.29–0.56)	Non-GLP-1RA anti-diabetes medications
Type 2 diabetes (n=596,045)	Recurrent CUD	0.66 (0.42–1.03)	Non-GLP-1RA anti-diabetes medications

Semaglutide was associated with lower risk for incident CUD (HR: 0.56, 95% CI: 0.42–0.75) and recurrent CUD (HR: 0.62, 95% CI: 0.46–0.84) in the obesity population. In the type 2 diabetes population, similar patterns were observed for incident CUD (HR: 0.40, 95% CI: 0.29–0.56) and recurrent CUD (HR: 0.66, 95% CI: 0.42–1.03). Subgroup analyses showed consistent reductions across gender, age group, and race, though specific subgroup results were not detailed. The number needed to treat was not calculable from the provided data. Time-to-event analyses were implied through Kaplan-Meier analysis, but specific results were not provided.

Study Quality and Limitations

The study was not applicable for assessing the research question due to its observational, non-randomized design. As a retrospective cohort study, it lacked randomization and blinding methods. Sample size calculations and power analyses were not mentioned, and loss to follow-up rates were not explicitly reported.

The study addressed potential confounding factors through propensity-score matching, but unmeasured confounders remained possible. Selection bias concerns were present due to reliance on electronic health record data from specific healthcare organizations. Generalizability was limited to patients with obesity or type 2 diabetes and constrained by reliance on EHR data. The study was funded by national institutes with no conflicts of interest declared. The authors explicitly stated limitations including the retrospective nature, potential biases, and limited follow-up time.

The study did not provide specific safety data or adverse event information related to semaglutide in CHS patients, as it did not focus on this population or measure these outcomes.

Summary

No studies were identified that directly examined GLP intervention compared to standard treatment protocols for cannabis cessation in patients with cannabis hyperemesis syndrome. The single included study investigated cannabis use disorder in patients with obesity and type 2 diabetes, representing a different clinical condition, population, and set of outcomes than specified in the research question. Therefore, no evidence-based conclusions can be drawn regarding the comparative effectiveness of GLP intervention versus standard treatment for cannabis cessation in CHS patients based on the available literature.

References

William Wang, Nora D. Volkow, Nathan A. Berger, P. Davis, D. Kaelber, and R. Xu. "Association of Semaglutide with Reduced Incidence and Relapse of Cannabis Use Disorder in Real-World Populations: A Retrospective Cohort Study." *Molecular Psychiatry*, 2024.