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Brief Research Report

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# Patient-reported outcomes in cannabinoid hyperemesis syndrome patients treated in the emergency department: a pilot study

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**Objective** Abdominal pain is one of the most common emergency department (ED) complaints, with many patients experiencing recurrent episodes due to cannabinoid hyperemesis syndrome (CHS), a syndrome characterized by pain and vomiting in the setting of chronic cannabis use. This pilot study aimed to demonstrate the ability to enroll patients with CHS, characterize patient-reported outcomes (PROs), and estimate 30-day revisit rates.

**Methods** This prospective observational study enrolled adult ED patients with CHS at an academic center and community affiliate. The inclusion required a prior diagnosis of CHS and ED clinician judgment that symptoms at time of enrollment were likely due to CHS. Exclusions included unstable clinical status or other high-risk conditions. Primary outcomes included characterization of symptoms, assessment of multiple domains of PROs, measurement of the use of both computed tomography (CT) scans and opioid analgesia, and frequency of 30-day ED return visits.

**Results** A total of 18 participants were enrolled (mean age, 34 years; 10 female patients, 55.6%). Automated chart reviews were completed for each outcome of interest at 30 days and at 12 months. Pain severity was high (mean triage pain score, 6.2±4.3) and prior CT imaging was noted in 13 patients (72.2%) in the past 5 years. Opioids were administered in four patients (22.2%), while the 29-Item Patient-Reported Outcome Measurement Information System (PROMIS-29) scores highlighted high risk of anxiety (mean T-score, 56.11±11.45) and how pain interfered with normal activities of living (mean T-score, 62.24±11.11). Return visits occurred in three patients (16.7%) within 30 days.

**Conclusion** ED patients with CHS show a significant burden on PROs and high 30-day revisit rates. Future studies should consider interventions that address PROs and reduce ED revisits.

**Keywords** Cannabinoid hyperemesis syndrome; Biopsychosocial factors; Pain severity; Emergency department revisits; Opioid use

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## Capsule Summary

**What is already known**

*Cannabinoid hyperemesis syndrome is an increasingly recognized cause of recurrent nausea, vomiting, and abdominal pain among chronic cannabis users and is associated with repeated emergency department visits. Although acute symptoms may be temporarily managed with antiemetics, antipsychotics, fluids, or adjunctive therapies, reduction or cessation of cannabis use remains the key strategy for preventing recurrence.*

**What is new in the current study**

*This pilot study demonstrated the feasibility of enrolling emergency department patients with cannabinoid hyperemesis syndrome and conducting electronic follow-up. The findings suggest a substantial burden on patient-reported outcomes and highlight challenges in symptom management, supporting the need for future studies to improve patient-centered outcomes and reduce emergency department revisits.*

## INTRODUCTION

Cannabinoid hyperemesis syndrome (CHS) is emerging as a critical public health issue due to the rapid increase in daily or near-daily (DND) cannabis use, which has grown 20-fold over the past three decades to an estimated 17.7 million Americans [1,2]. Correspondingly, the incidence of CHS has grown 150% annually for the past 10 years and continues to rise nationally as more jurisdictions have legalized cannabis [2]. CHS, characterized by episodes of unremitting nausea, cyclic vomiting, and severe abdominal pain, is the most common cannabis-related cause of emergency department (ED) visits in the United States [3]. Alarming increases in cases have been reported around the country in states as diverse as Oklahoma [4], Massachusetts [5], Colorado [6,7], and California [2,6] demonstrating that this syndrome has become widespread and nationalized. Multiple media outlets have highlighted the condition and the need for more research, including PBS Newshour [8], The New York Times [9], Slate [10], ScienceAlert [11], and Business Insider [12]. In the lay press, the condition may be described as "scromiting" or scream vomiting due to the extreme nature of the symptoms [10,12]. On social media, multiple CHS support groups have formed with thousands of members.

CHS is a paradoxical syndrome because, historically, cannabis has been widely used for its antiemetic properties, especially in relation to chemotherapy-induced nausea. However, for some chronic DND users of cannabis, the drug becomes highly proemetic with symptoms that are minimally responsive to conventional antiemetics such as ondansetron but show some response to traditional antipsychotics such as haloperidol [13]. While parenteral medications may be used as rescue therapy and temporarily alleviate symptoms, the only known way to eliminate CHS and associated repeat ED visits is a reduction of cannabis use [3]. However, it is unknown whether complete cannabis abstinence is needed and for how long to achieve cure. Once affected, sufferers appear to remain in a sensitized state for an extended period that ranges from months to years [14].

The rising national incidence of CHS, especially in the wake of widespread cannabis legalization, underscores the urgent need for research into its pathophysiology, risk factors, and healthcare costs. Despite its prevalence, CHS remains poorly understood, with significant gaps in knowledge regarding who is at risk, the biological mechanisms driving the syndrome, and the cost to the individual and healthcare system. The objective of this pilot study was to demonstrate the ability to enroll patients with CHS, characterize patient-reported outcomes (PROs), and determine the feasibility of automated 30-day and 12-month chart reviews. This study served to lay the foundation for a future multicenter case-cohort study analyzing the risk factors for developing CHS.

## METHODS

### Ethics statement

This study was approved by the Institutional Review Board of George Washington University (No. NCR213728). Informed consent was obtained from all patients prior to enrollment.

### Study setting and design

This pilot study used a prospective observational approach to determine the feasibility of enrolling patients with CHS and conducting automated chart reviews at 30 days and 12 months, trial survey tools used to measure desired outcome variables, and characterize the target population of a proposed future multicenter case-cohort study. This study was conducted at an urban academic hospital with a community affiliate between April 2023 and November 2024 as a sub-investigation of an ongoing multicenter study exploring recurrent abdominal pain in the ED. The cohort of patients with CHS was a convenience sample enrolled by professional research staff who screened ED patients on weekdays from 9 AM to 7 PM and obtained informed consent.

### Study population

The inclusion required a prior diagnosis of CHS and ED clinician judgment that symptoms at the time of enrollment were most likely due to CHS. CHS was defined by Rome IV guidelines (Fig. 1) or prior established CHS diagnosis [15]. Adult patients (≥ 18 years old) were screened if they presented to the ED with a chief complaint of abdominal pain or gastrointestinal complaints and at least one similar episode in the past year. Patients were evaluated for CHS by the Rome IV criteria and were excluded if they were altered mentally, prisoner/ward of state, pregnant, non-English speaker, or did not meet all of following low-risk criteria: (1) stable vital signs; (2) age 18 to 65 years; (3) not pregnant; (4) no history or physical findings of acute abdominal pathology; (5) no acute trauma within the last 7 days; (6) no prior organ transplantation or immunosuppression; (7) no abdominal surgery within 30 days and/or active cancer; (8) no history of inflammatory bowel disease; (9) no previous bowel obstructions; and (10) no active severe psychiatric illnesses requiring urgent stabilization. The current study is a sub-investigation of a multisite trial exploring abdominal pain and ED revisits. The exclusion criteria outlined here are the current exclusion criteria for the multisite abdominal pain study and prevent enrollment of those who have a clear structural cause for their abdominal pain.

### Outcome measures

Participants were evaluated to assess pain severity, frequency of symptoms, and confidence in diagnosis. Pain severity was evaluated via the numerical pain rating scale at three separate time points during their time in the ED: during the primary triage vitals assessment, at the time of enrollment, and upon discharge from the ED. Additionally, patients were asked to categorize their CHS-related abdominal pain "at its worst" to account for the intermittent nature of CHS pain as patients may not be experiencing the worst level of pain during enrollment. Participants completed an electronic survey to evaluate symptomatology, self-reported comorbidities, and psychosocial risk factors. The survey included a self-report of the number of computed tomography (CT) scans (either at the enrolling hospital or outside facilities) the enrolled patient had received in the last 5 years. Participants were followed via a review of the electronic health record (EHR) to measure repeat ED visits. Other validated scoring tools were used to assess substance use risk (Alcohol, Smoking, and Substance Involvement Screening Test [ASSIST], a screening tool to identify potential substance use disorders developed by the World Health Organization), social determinants of health (Accountable Health Communities Health-Related Social Needs [AHC-HRSN], a screening tool developed by the Centers for Medicare and Medicaid Services to measure needs in predefined areas [homelessness, hunger, exposure to violence, etc.]), and health-related quality of life (29-Item Patient-Reported Outcomes Measurement Information System, PROMIS-29) [16–18]. PROMIS is a set of person-centered measures that evaluates physical, mental, and social health in adults and children. For most PROMIS instruments, a score of 50 is average in the United States general population with a standard deviation of 10. The higher the PROMIS T-score represents more of the concept.

**Must have the following** (for 3 mo prior with symptom onset ≥ 6 mo ago):
(1) Stereotypical episodic vomiting resembling cyclic vomiting syndrome in terms of onset, duration, and frequency
(2) Presentation after prolonged excessive cannabis use
(3) Relief of vomiting episodes by sustained cessation of cannabis use

**Fig. 1.** Rome IV diagnostic criteria for cannabinoid hyperemesis syndrome.

### EHR follow-up

Additional data on clinical outcomes, including ED management, ED disposition, ED diagnosis, and 30-day ED revisits, were collected through automated EHR reports. The primary International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) diagnosis code associated with this visit was also recorded.

### Statistical analysis

Descriptive statistics were used to summarize demographic, clinical, and patient-reported outcome data. Continuous variables, such as pain scores and PROMIS-29 T-scores, were reported as mean ± standard deviation, while categorical variables, including gender, race, and opioid administration, were presented as frequencies and percentages. All analyses were conducted using SAS ver. 9.4 (SAS Institute Inc), with a two-tailed significance threshold of $P < 0.05$.

## RESULTS

A total of 18 participants were included in the study, with a mean age of 34.0 ± 11.3 years. Gender distribution was predominantly female, with 10 participants (55.6%) identifying as women, and 8 participants (44.4%) as men. Participants reported high levels of pain severity with pain on multiple days. The mean triage pain score was 6.2 ± 4.3 and the mean pain score at time of enrollment was 6.2 ± 3.9 on a 10-point scale (Table 1). When asked about their understanding of their pain, 11 participants (61.1%)

**Table 1.** Descriptive characteristics of cannabinoid hyperemesis syndrome patients at index visit (n=18)

| Characteristic | Value |
|---|---|
| Age (yr) | 34.0 ± 11.3 |
| Sex | |
| Female | 10 (55.6) |
| Male | 8 (44.4) |
| Ethnicity | |
| Not Hispanic/Latino | 17 (94.4) |
| Prefer not to answer | 1 (5.6) |
| Medical history | |
| Hypertension | 4 (22.2) |
| Diabetes | 3 (16.7) |
| Depression | 4 (22.2) |
| Anxiety | 7 (38.9) |
| Other | 4 (22.2) |
| None | 8 (44.4) |
| Insurance status | |
| Medicaid | 13 (72.2) |
| Private | 1 (5.6) |
| Uninsured | 1 (5.6) |
| Other | 3 (16.7) |
| Pain score | |
| At time of triage | 6.2 ± 4.3 |
| At time of enrollment | 6.2 ± 3.9 |
| Prior to discharge | 2.9 ± 3.6 |
| Frequency of abdominal pain in the previous week | |
| 1 Day | 5 (27.8) |
| 2–6 Days | 7 (38.9) |
| Once a day | 1 (5.6) |
| More than once a day | 5 (27.8) |
| At worst, how bad would you rate your abdominal pain? | |
| Not bad at all | 1 (5.6) |
| A little bad | 2 (11.1) |
| Quite bad | 1 (5.6) |
| Very bad | 14 (77.8) |
| In the past 7 days, how much did your abdominal pain interfere with day-to-day activities? | |
| Not at all | 1 (5.6) |
| A little bit | 3 (16.7) |
| Somewhat | 2 (11.1) |
| Quite a bit | 1 (5.6) |
| Very much | 11 (61.1) |
| Have received at least one CT scan in the last 5 years for this type of abdominal pain | 13 (72.2) |
| No. of CT scans in the last 5 years | 4.2 ± 2.3 |
| Has a doctor been able to tell you the cause of your pain? | |
| No, I was never told | 4 (22.2) |
| Yes, and the cause is clear | 11 (61.1) |
| Yes, however, cause unclear | 2 (11.1) |
| I never went to a doctor | 1 (5.6) |
| In the past 3 months, how often did you have pain? | |
| Never | 2 (11.1) |
| Some days | 13 (72.2) |
| Most days | 2 (11.1) |
| Everyday | 1 (5.6) |
| In the past 3 months, how often did pain limit your life or work activities? | |
| Never | 2 (11.1) |
| Some days | 12 (66.7) |
| Most days | 2 (11.1) |
| Everyday | 2 (11.1) |

Values are presented as mean±standard deviation or number (%).

reported being informed of the cause by a provider, while 2 (11.1%) indicated they were told but did not understand. Meanwhile, 4 participants (22.2%) stated they were never informed of the cause; and 1 participant (5.6%) reported never seeking medical attention for their pain. Prior CT imaging was also noted, with 13 (72.2%) having received at least one CT scan in the past 5 years. Of the 18 participants who completed PROMIS-29 tool assessment, the mean T-score for physical function was 50.20 ± 10.99, indicating average physical functioning in the sample. Anxiety levels were elevated, with a mean T-score of 56.11 ± 11.45, suggesting significant psychological distress. Table 2 presents the baseline PROMIS-29, ASSIST, and AHC-HRSN assessment scores, and Table 3 summarizes the clinical outcomes at the index visit, 30-day follow-up, and 12-month follow-up, including the frequency of ED return visits within 30 days. The ASSIST score risk categories used to interpret the substance-use assessment are shown in Table 4. Of the participants, 15 (83.3%) did not return to the ED during the follow-up period, while 2 participants (11.1%) returned once, and 1 participant (5.6%) returned four times. For each mean value reported, all participants were represented and there were no missing data values.

**Table 2.** Baseline PROMIS-29, ASSIST, and AHC-HRSN scores (n=18)

| Assessment | Score |
|---|---|
| PROMIS-29 | |
| Physical function | 50.20 ± 10.99 |
| Anxiety | 56.11 ± 11.45 |
| Depression | 51.90 ± 10.87 |
| Fatigue | 59.50 ± 11.08 |
| Sleep disturbance | 53.66 ± 8.54 |
| Ability to participate in social activities | 54.39 ± 11.37 |
| Pain interference | 62.24 ± 11.11 |
| ASSIST | |
| Cannabis | 15.75 ± 7.04 |
| Tobacco | 13.40 ± 6.85 |
| Alcohol | 8.33 ± 6.78 |
| Cocaine | 2 ± 0 |
| AHC-HRSN | |
| May face financial stress | 6 (33.3) |
| Has an employment need | 6 (33.3) |
| Needs family and community support | 3 (16.7) |
| May have unmet education needs | 2 (11.1) |
| May have a social need related to physical activity | 11 (61.1) |
| Has a housing need | 2 (11.1) |
| At risk for food insecurity | 4 (22.2) |
| Has transportation needs | 1 (5.6) |
| Interpersonal safety score | 4.63 ± 1.80 |

Values are presented as mean±standard deviation or number (%).
PROMIS-29, 29-Item Patient-Reported Outcomes Measurement Information System; ASSIST, Alcohol, Smoking, and Substance Involvement Screening Test; AHC-HRSN, Accountable Health Communities Health-Related Social Needs.

**Table 3.** Outcomes of cannabinoid hyperemesis syndrome patients at index visit, 30 days, and 12 months (n=18)

| Outcome | Value |
|---|---|
| Received any opiate drugs while in the ED | 4 (22.2) |
| Received any antipsychotic drugs while in the ED | 12 (66.7) |
| Received any antiemetic drugs while in the ED | 14 (77.8) |
| Received any acid suppression drugs while in the ED | 11 (61.1) |
| Received any IV fluids while in the ED | 16 (88.9) |
| Had an order placed for a CT scan of the abdomen/pelvis prior to the admission order placement if admitted | 4 (22.2) |
| Received an ultrasound scan of the abdomen/pelvis in the ED prior to the admission order placement if admitted | 4 (22.2) |
| ED disposition (n = 17) | |
| Home | 9 (52.9) |
| Admission (inpatient and observation) | 7 (41.2) |
| Against medical advice or elopement | 1 (5.9) |
| The patient was sent home with any opiate drugs prescriptions regardless of if they were admitted or discharged | 0 (0) |
| No. of return ED visits within 30 days of the index visit | 0.35 ± 0.97 |
| No. of abdominal/pelvic CT scans within 12 mo following the index visit | 0.11 ± 0.32 |
| No. of hospital admissions within 12 mo following the index visit | 0.17 ± 0.51 |
| Opiate analgesia prescriptions within 12 mo following the index visit | 0 (0) |
| No. of ED visits within 12 mo following the index visit | 1.11 ± 2.37 |

Values are presented as number (%) or mean±standard deviation.
ED, emergency department; IV, intravenous; CT, computed tomography.

**Table 4.** ASSIST scoring and interpretation guidelines

| Risk level | ASSIST score | |
|---|---|---|
| | Alcohol | All other substances |
| Lower risk | 0–10 | 0–3 |
| Moderate risk | 11–26 | 4–26 |
| High risk | ≥ 27 | ≥ 27 |

ASSIST, Alcohol, Smoking, and Substance Involvement Screening Test.

## DISCUSSION

CHS has been shown to be a debilitating condition characterized by serial episodes of unremitting vomiting, abdominal pain, severe dehydration, electrolyte abnormalities, renal failure and even death [19]. In a survey of ED patients who smoked cannabis 20 or more days per month, almost one-third suffered from CHS, and the incidence of CHS has nearly doubled after state legalization of cannabis [20,21]. Patients suffer additional economic burden due to repeat ED visits, multiple hospital admissions, and repeated laboratory and imaging tests [22]. Prior research suggested that approximately 60% of patients seen in the ED for CHS have a return visit for similar symptoms within 6 months. Potential variables associated with CHS include demographic factors (age, sex, race/ethnicity) [23], social determinants of health [24], cannabis use including age of initiation, frequency of use, cannabis product features (delivery method, dominant cannabinoids, and dose) [25,26], stress [27,28], and psychiatric comorbidities [29–31].

CHS is thought to result from complex dysregulation of the endocannabinoid system (ECS), involving both central and peripheral mechanisms [32]. Chronic, heavy cannabis use may lead to overstimulation and subsequent desensitization or downregulation of cannabinoid receptors, particularly CB1, which are highly expressed in the central nervous system and gastrointestinal (GI) tract [33]. This dysregulation can paradoxically disrupt normal processes of nausea control, motility, and gastric emptying, contributing to the hallmark symptoms of CHS [25,27]. Additionally, dysfunction of the hypothalamus, a region rich in CB1 receptors involved in thermoregulation, may explain the characteristic relief of symptoms with hot showers, potentially through modulation of transient receptor potential vanilloid 1 (TRPV1) channels [34]. Cannabinoid-induced alterations in TRPV1 activity may further exacerbate nausea and vomiting while creating a feedback loop of symptom relief through heat exposure [35]. Other contributing factors include GI dysmotility, autonomic dysfunction, and hypothalamic-pituitary-adrenal axis disruption, which collectively impair stress and emesis regulation. Genetic predispositions, including variations in genes such as *CNR1*, *CNR2*, and *TRPV1*, as well as altered cannabinoid metabolism, may also increase susceptibility to CHS [36]. The slow clearance and accumulation of lipophilic cannabinoids and their metabolites may underlie the cyclical nature of symptoms. Psychological and behavioral factors, including stress and cannabis dependence, may further amplify the syndrome [27]. Together, these mechanisms create a multifaceted pathophysiology that requires further research to fully elucidate and address [32].

The acute treatment of CHS focuses on symptom management and cessation of cannabis use. Immediate relief involves intravenous fluids to address dehydration and antiemetic medications such as ondansetron or promethazine, though their effectiveness can be variable [13]. Benzodiazepines may also help reduce anxiety and hyperemesis in some cases. Adjunctive therapies, including topical capsaicin cream applied to the abdomen or back and hot showers or baths, are commonly used to activate TRPV1 channels and provide temporary symptom relief [37]. For abdominal pain, nonopioid analgesics are preferred, as opioids can worsen nausea and motility issues [38]. The cornerstone of treatment is cannabis reduction or complete cessation, as symptoms typically resolve within days to weeks after stopping use [39]. Patient education is critical, emphasizing the connection between cannabis use and CHS symptoms, along with providing resources for managing cannabis dependence, such as behavioral support or

substance use treatment programs [40]. Long-term abstinence may be essential to prevent recurrence.

A limitation of the current study is that the cohort was enrolled at one hospital and community affiliate and the distribution of demographic variables such as ethnicity is skewed. This could have an effect on the generalizability of the results. Furthermore, the current study did not track whether enrolled participants were visiting alternate hospitals in the area for further care. Patients may have received additional CT scans and treatment following their enrollment that was not captured by the study. To avoid this limitation, future research should employ a regional dataset to capture all ED visits made by the enrolled individual. Despite the listed limitations, the current study demonstrates that enrolling CHS patients in the ED is feasible and that researchers can prospectively follow these patients to gain a better understanding of their pain and symptoms. This insight is essential for the planned case-cohort study, which aims to identify differences between DND cannabis users who develop CHS and those who do not.

Future research on CHS should focus on understanding its pathophysiology, risk factors, and optimal management strategies. Key areas include elucidating the role of endocannabinoid system dysregulation, TRPV1 channel interactions, and the neurobiological effects of chronic cannabis use. Investigating genetic and epigenetic factors, such as polymorphisms in ECS-related genes and changes in gene expression, may identify individuals at higher risk. Epidemiological studies are needed to clarify the prevalence of CHS and its association with cannabis use patterns, while biomarker development could improve diagnostic accuracy. Research on treatment strategies should evaluate the effectiveness of current therapies, explore novel pharmacological targets, and assess interventions for cannabis cessation. Long-term studies are essential to understand symptom recurrence, health outcomes, and the psychological impact of CHS. Public health research should examine the influence of cannabis legalization and high-potency products on CHS prevalence, alongside educational efforts to increase awareness. Finally, studies on the economic burden of CHS could inform cost-effective prevention and management approaches. Together, these efforts will enhance understanding and improve care for CHS patients.

### Conclusions

This pilot and automated EHR data pull feasibility study highlights specific challenges associated with symptom management in patients with CHS. The study demonstrates that it is feasible to obtain consent and enroll these patients in the ED and have high fidelity via electronic follow-up. Among participants with CHS in the study, the findings suggest a negative impact of the syndrome on PROs. Future research should investigate cannabis exposure and the biopsychosocial factors influencing both the development and severity of CHS to enhance therapeutic interactions and improve overall management.

## ARTICLE INFORMATION

### Author contributions

Conceptualization: ACM; Data curation: ACM; Formal analysis: all authors; Methodology: ACM; Writing–original draft: all authors; Writing–review & editing: all authors. All authors read and approved the final manuscript.

### Conflicts of interest

The authors have no conflicts of interest to declare.

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### Data availability

Data analyzed in this study are available from the corresponding author upon reasonable request.

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