Incidence and Predictors of Cannabis-Related Poisoning and Mental and Behavioral Disorders among Patients with Medical Cannabis Authorization: A Cohort Study

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ABSTRACT

Objective: As medical cannabis use increases in North America, establishing its safety profile is a priority. The objective of this study was to assess rates of emergency department (ED) visits and hospitalizations due to poisoning by cannabis, and cannabis-related mental health disorders among medically authorized cannabis patients in Ontario, Canada, between 2014 and 2017.

Methods: This is a retrospective cohort study of patients who received medical cannabis authorization in Ontario, Canada, using data collected in participating cannabis clinics. Outcomes included ED visit/hospitalization with a main diagnosis code for: cannabis/cannabinoid poisoning; and mental/behavioral disorders due to cannabis use. Cox proportional hazard regressions were utilized to analyze the data.

Results: From 29,153 patients who received medical authorization, 23,091 satisfied the inclusion criteria. During a median follow-up of 240 days, 14 patients visited the ED or were hospitalized for cannabis poisoning—with an incidence rate of 8.06 per 10,000 person-years (95% CI: 4.8–13.6). A total of 26 patients visited the ED or were hospitalized for mental and behavioral disorders due to cannabis use—with an incidence rate of 15.0 per 10,000 person-years (95% CI: 10.2–22.0). Predictors of cannabis-related mental and behavioral disorders include prior substance use disorders, other mental disorders, age, diabetes, and chronic obstructive pulmonary disease.

Conclusions: The results suggest that the incidence of cannabis poisoning or cannabis-related mental and behavioral disorders was low among patients who were authorized to use cannabis for medical care. Identified predictors can help to target patients with potential risk of the studied outcomes.

Abbreviations: COPD: chronic obstructive pulmonary disorder; CHF: congestive heart failure; CUD: cannabis use disorder; DAD: Discharge Abstract Database; ED: emergency department; ICD-19: International Classification of Diseases System—tenth revision; ICES: Institute for Clinical Evaluative Sciences; NAIRS: National Ambulatory Care Reporting System; OHIP: Ontario Health Insurance Plan

Introduction

The increasing use of cannabis and cannabis-based products either for medical purposes with or without medical authorization, or for purely recreational use raises safety concerns for patients and public health (Sahlem et al., 2018; Wilkinson et al., 2016). Potential increases in the prevalence of cannabis intoxication, cannabis withdrawal symptoms, and cannabis use disorder (CUD), are safety issues raised in discussions about the potential therapeutic benefits of cannabis for medical use (Budney et al., 2019). While cannabis intoxication and withdrawal symptoms are acute effects, CUD is defined as a longer-term mental health condition resulting from the chronic use of cannabis (Ksir & Hart, 2016; Loflin et al., 2020; Patel, 2020).

Cannabis poisoning was responsible for 16,884 admissions to emergency departments (EDs) in the United States in 2016, representing 0.014% of total ED visits for individuals ages 12 and older (Salas-Wright et al., 2019). Recent data collected from the Alberta National Ambulatory Care Reporting System in Canada (Yeung et al., 2020) showed that cannabis-related ED visits and cannabis-related calls to poison control centers increased, after the legalization of non-medical cannabis use in 2018. A US study using a nationwide inpatient sample showed that the prevalence of hospitalizations for cannabis abuse and dependence increased...
from 2002 (0.52%) to 2011 (1.34%) (Charilaou et al., 2017). However, these studies showing an increased risk of cannabis use disorders mainly involved recreational cannabis users. Several studies have shown that recreational and medical cannabis users are different populations. Indeed, data suggest that, compared to medical cannabis users, recreational cannabis users tend to be younger (Goulet-Stock et al.); be more likely to use alcohol (Gunn et al., 2019; Loflin et al., 2017), or to be diagnosed with alcohol use disorders (Mannes et al., 2018; Roy-Byrne et al., 2015; Subbaraman & Kerr, 2018); or with drug use disorders (Goulet-Stock et al., 2017; Roy-Byrne et al., 2015). They are also more likely to use cannabis less frequently (Sznitman, 2017); have fewer medical problems (Roy-Byrne et al., 2015); and have fewer psychiatric comorbidities (Turna et al., 2020). Thus, extrapolation of the evidence from recreational cannabis users to medical cannabis users could be strongly biased. In one of the rare studies that included only medical cannabis users and assessed problematic cannabis use during a 12-month follow-up (n = 265), cannabis misuse (for example taking more cannabis than prescribed) and addiction behavior (assessed with the 20-item Addiction Behavior Checklist) were observed among 26% and 9% of study participants, respectively (Ware et al., 2018).

Different factors may also predispose some individuals to cannabis poisoning and use disorders (Charilaou et al., 2017; Pinto et al., 2019; Ware et al., 2018). These include psychiatric comorbidities (Lucatch et al., 2018; Patel et al., 2019); concomitant use of other substances such as heroin, benzodiazepines and cocaine (Loflin et al., 2020); and prior substance use disorders (Dervaux, 2018; Ware et al., 2018). A study showed that individuals who sought emergency medical care for cannabis poisoning (no distinction between medical and recreational cannabis users) were more likely to be young, male, uninsured, experience economic hardship, reside in urban centers, and experience mental health disorders as compared to individuals admitted for other causes (Brezing & Levin, 2018).

However, little is known about factors that predict cannabis-induced intoxication and CUD amongst patients who use cannabis for medical purposes only, i.e., those who are legally authorized by their care providers to use cannabis to treat specific health conditions. Therefore, this study aimed to assess the incidence rates of ED visits or hospitalization due to (1) poisoning by cannabis and (2) mental and behavioral disorders due to use of cannabis among patients who were medically authorized to use cannabis in Ontario, Canada, between 2014 and 2017. Secondly, we assessed factors that are associated with these outcomes.

Methods

Study design

This is a retrospective longitudinal study conducted among a cohort of patients who received an authorization to use cannabis for treating different health conditions in Ontario, Canada. Patients’ follow-up started from their specific date of cannabis authorization.

Study population

This study included all patients aged ≥18 years authorized to access medical cannabis from a group of cannabis clinics in Ontario, Canada between April 24, 2014 and March 31, 2017. The cohort has been described in previous papers (Eurich et al., 2019, 2020). Briefly, in the study period (2014–2017), patients seeking cannabis for medical use in Canada were required to obtain physician approval and administrative authorization from Health Canada. Thus, all patients in our cannabis cohort were legally allowed to use cannabis for medical purposes. These patients were referred to the cannabis clinics by other physicians or self-referred. Patients who were not eligible for universal health insurance via the Ontario Health Insurance Plan (OHIP), provided to all people meeting Ontario residency requirements, and those with invalid or duplicate residency identifiers were excluded.

Data source

The cannabis cohort was selected using data collected in the cannabis clinics. Clinic data was linked to the Ontario administrative health data to assess the study outcomes and potential predictors. As described previously, the Institute for Clinical Evaluative Sciences (ICES) provided the health administrative data. These data include individual data files for each beneficiary, inpatient records, physician billings (inpatient and outpatient physician services) and prescription drug claims. The Ontario Health Insurance Plan (OHIP) contains information on physician services, including diagnostic codes. The Discharge Abstract Database (DAD) and the National Ambulatory Care Reporting System (NACRS) contain all data on hospitalizations and emergency department visits, respectively. For each emergency visit or hospitalization, up to 25 possible diagnoses were registered according to the International Classification of Diseases system—tenth Revision (ICD-10). Of these entries, only one indicates the most reliable diagnosis or the main diagnosis. The administrative databases were linked using the unique and encrypted patient health insurance number and covered the period of April 24, 2012 to March 31, 2017.

Ethics

Ethics approval was obtained for the study from the University of Alberta Health Research Ethics board (PRO 00083651), Veritas Research Ethics Board in Ontario (16111-13:21:103-01-2017), and the CHU de Quebec-Université Laval Research Ethics board ((#CER: 2022-5999).

Outcomes

Two distinct outcomes were assessed: (1) ED visit or hospitalization with a main diagnosis code for cannabis/cannabinoid poisoning (ICD-10 T40.7) and (2) ED visit or hospitalization with a main diagnosis code for mental or behavioral disorders due to the use of cannabis (ICD-10 F12).
Potential predictors

Three groups of variables were assessed as potential predictors, which included sociodemographic variables, comorbidities, and previous drug poisoning or substance use disorders. Sociodemographic variables included age at index date, sex, the nearest census-based neighborhood income quintile and the area of residence (rural vs. urban). Selected morbidities based on previous studies (Charilaou et al., 2017; Salas-Wright et al., 2019; Ware et al., 2018) included diabetes, congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD), asthma, cancer, chronic kidney disease, liver disorders, musculoskeletal issues, pain, neurologic disorders, fatigue, and metabolic disease. These variables were defined using ICD-9 codes (based on physician claim data) and ICD-10 codes (based on ambulatory care data and discharge abstract data). Prior drug poisonings or substance use disorders were defined as ED visit or hospitalization with codes specific to drug poisoning or mental and behavioral disorders. These included poisoning by: (1) narcotics and hallucinogens, (2) anesthetics and therapeutic gas, (3) hypno-sedative drugs, (4) other psychoactive drugs, and (5) alcohol as well as mental and behavioral disorders due to (1) psychoactive drug/substance, (2) alcohol, (3) tobacco/nicotine, and (4) other mental and behavioral disorders (See the Appendix for more details).

Statistical analysis

Descriptive statistics were used to assess the characteristics of the study sample (mean and standard deviation or median for continuous variables; numbers and proportions for categorical variables). Incidence rates per 10,000 person-years with 95% confidence intervals (95% CI) were calculated for the study outcomes.

To assess potential predictors of each of the study outcomes, we first assessed the correlation (Spearman correlation) between the potential predictors. Next, we conducted univariate Cox proportional hazard regression between each potential predictor and the outcomes, including the assessment of the models’ assumptions. Next, variables that were associated at a $p$-value of 0.20 in univariate analysis were all included in a multivariate model. This first step was considered to reduce the dimensionality of the data to be included in the multivariate model considering the small number of events for each outcome. We then used a backward selection to retain the variables associated at a $p$-value < 0.10 in the final model. However, variables associated at a $p$-value < 0.05 were considered as statistically significant.

For these analyses (i.e., predictors identification), we extended the definition of the two study outcomes by considering both the primary and secondary reasons for ED visit or hospitalization (ICD-10 diagnosis codes) to increase the number of events and maximize the statistical power. The number of events based on solely the primary ICD-10 diagnosis codes was small (14 and 26 for cannabis poisoning and CUD, respectively). The analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

From 29,153 patients who received medical authorization to use cannabis, 23,091 satisfied the inclusion criteria (Figure 1). The majority of them were aged 31 to 60 years and 53% were male (Table 1). The most prevalent

![Figure 1. Selection of study population](image-url)
morbidities were respectively musculoskeletal disorders (48.87%), asthma (23.51%), neurological disorders (21.82%) and metabolic diseases (21.52%) (Table 1).

For the first outcome, during a median follow-up of 240 days and a total of 17,353.8 person-years, 14 patients visited the ED or were hospitalized for cannabis poisoning, giving an incidence rate of 8.06 per 10,000 person-years patients (95% CI: 4.8–13.6) (Table 2). For the second outcome, a total of 26 patients visited the ED or were hospitalized for mental and behavioral disorders due to cannabis use for a total of 17,354.2 person-years, which gave an incidence rate of 15.0 per 10,000 person-years (95% CI: 10.2–22.0) (Table 2).

Table 1. Characteristics of the study population.

| Characteristics                        | Total sample (n = 23,091) | n (%)   |
|----------------------------------------|---------------------------|---------|
| Age, years                             |                           |         |
| <21                                    | 143                       | (0.62)  |
| 21–30                                  | 2214                      | (9.59)  |
| 31–40                                  | 4153                      | (17.99) |
| 41–50                                  | 4665                      | (20.20) |
| 51–60                                  | 6011                      | (26.03) |
| 61–70                                  | 3736                      | (16.18) |
| 71–80                                  | 1541                      | (6.67)  |
| >80                                    | 628                       | (2.72)  |
| Sex                                    |                           |         |
| Female                                 | 10,835                    | (46.92) |
| Male                                   | 12,256                    | (53.08) |
| Nearest census based neighborhood income quintile |               |         |
| 1                                      | 5083                      | (22.01) |
| 2                                      | 4766                      | (20.64) |
| 3                                      | 4438                      | (19.22) |
| 4                                      | 4619                      | (20.00) |
| 5                                      | 4185                      | (18.12) |
| Rural                                  | 2317                      | (10.03) |
| Morbidities                            |                           |         |
| Asthma                                 | 5428                      | (23.51) |
| Cancer                                 | 3215                      | (13.92) |
| Congestive heart failure               | 705                       | (3.05)  |
| Chronic obstructive pulmonary disease  | 4059                      | (17.58) |
| Diabetes                               | 3733                      | (16.17) |
| Fatigue                                | 1282                      | (5.55)  |
| Metabolic disease                      | 4970                      | (21.52) |
| Musculoskeletal disorders              | 11,288                    | (48.88) |
| Neurological disorders                 | 5038                      | (21.82) |
| Pain                                   | 2012                      | (8.71)  |
| Chronic kidney disease                 | 522                       | (2.26)  |
| Liver disorders                        | 721                       | (3.12)  |
| Prior ED visit or hospitalization due to poisoning by: | |         |
| narcotics and hallucinogens            | 98                        | (0.42)  |
| Hypno-sedative drugs                   | 91                        | (0.39)  |
| Other psychoactive drugs               | 57                        | (0.25)  |
| Prior ED visit or hospitalization for mental and behavioral disorder due to: | |         |
| Psychoactive drugs/substances          | 255                       | (1.10)  |
| Alcohol                                | 177                       | (0.77)  |
| Other behavioral and mental disorders   | 1304                      | (5.65)  |

Discussion

This study shows that rates of ED visits or hospitalizations for poisoning by cannabis (total events = 14) and cannabis-related mental and behavioral disorders (total events = 26) were low among patients with medical cannabis authorization. One predictor was identified for cannabis poisoning (i.e., prior poisoning by narcotics or hallucinogens). For cannabis-related mental and behavioral ED visits and hospitalizations, seven predictors were identified, including prior poisoning by other psychoactive drugs (antidepressants and other); mental and behavioral disorders due to psychoactive drugs, or alcohol use; other mental and behavioral disorders; younger age; diabetes; and COPD.

Our observation of small rates of ED visits and hospitalization for cannabis poisoning and CUDs among this large cohort of medical cannabis users helps address concerns regarding increasing use of medical cannabis. However, for CUD, the small rate could also be explained by the relative short length of follow-up which might not

Table 2. Incidence rates of emergency department (ED) visits or hospitalization for poisoning by cannabis and cannabis use disorders among patients with medical cannabis authorization.

|                             | Outcome 1: Cannabis poisoning | Outcome 1: Cannabis poisoning (extended definition) | Outcome 2: Cannabis-related mental and behavioral disorders | Outcome 2: Cannabis-related mental and behavioral disorders (extended definition) |
|-----------------------------|-------------------------------|-----------------------------------------------|-----------------------------------------------------|-----------------------------------------------|
| Total events                | 14                            | 18                                            | 26                                                   | 82                                            |
| Total person-years          | 17,353.8                      | 17,355.35                                     | 17,354.2                                             | 17,318.36                                     |
| Incidence rates per 10,000 | 8.06 (4.8–13.6)               | 10.37 (6.33–16.46)                            | 15.0 (10.2–22.0)                                     | 47.35 (38.15–58.76)                           |
| person-years (95%CI)        |                               |                                               |                                                      |                                               |

*Incidence rates of emergency department visits or hospitalization (including primary and secondary diagnosis codes).*
allow sufficient time to observe onset and diagnosis among those patients. Studies with people who use medical cannabis that have a longer follow-up period are needed to fully address this question. Very few studies have assessed the rates of cannabis poisoning and CUDs among medical cannabis patients (Gage et al., 2016). Available data are mostly based on recreational cannabis users or a mix of both recreational and medical cannabis users (Blanco et al., 2016; Pinto et al., 2019) with no possibility to distinguish rates for medical cannabis users only.

Regarding the characteristics of patients that might have an increased risk of cannabis poisoning or CUDs, our results suggest that patients with history of drug poisoning or substance use disorder, and more generally patients with mental and behavioral disorders, should be regarded as patients with higher susceptibility. Consistent with previous data (Charilaou et al., 2017; Ware et al., 2018), our results suggest that these conditions should be systematically assessed among patients seeking medical cannabis. In fact, researchers have developed specific models that focus on the mechanism of CUD, drug addiction, and cannabis use—suggesting that chronic cannabis use may be associated with an increased risk of developing CUD (Zehra et al., 2018). This suggestion aligns with the recommendation by the Canadian Coalition for Seniors’ Mental Health (CCSMH) (Bertram et al., 2020), calling for proactive vigilance among clinicians to detect a history of CUD in patients seeking medical cannabis. The observation that younger medical cannabis users are at higher risk of CUDs is also observed in a previous US nationwide sample that showed that hospitalizations for CUDs were more prevalent among younger patients (Charilaou et al., 2017). In this US study, diabetes, COPD and CHF were also prevalent conditions among patients who were hospitalized for CUDs (Charilaou et al., 2017). Mental health disorders are highly prevalent among patients with diabetes (Garrett et al., 2014). Depression and anxiety are also highly prevalent in patients with COPD (Wang et al., 2021). As we observed in our data, mental health disorders were associated with CUD. This could therefore explain why diabetes and COPD were associated with cannabis use disorders in our data.

The primary strength of this study is that it is currently the largest (to our knowledge) Canadian population-based

### Table 3. Predictors of ED visit or hospitalization due to cannabis poisoning among patients with medical cannabis authorization in univariate analyses.

| Variables                              | HR    | 95%CI       | P-value |
|----------------------------------------|-------|-------------|---------|
| Sex (male vs. female)                  | 0.412 | 0.154–1.099 | 0.0764  |
| ED visit or hospitalization for poisoning by narcotics and hallucinogens | 15.75 | 2.089–118.776 | 0.0075  |
| other mental and behavioral disorders  | 3.20  | 0.93–11.06  | 0.0658  |

Note: Variables with p-value ≤ 0.10 were retained for inclusion in the multivariate model.

### Table 4. Predictors of ED visit or hospitalization due to cannabis poisoning among patients with medical cannabis authorization in multivariate analyses.

| Variables                              | Hazard Ratio | 95% CI       | p-value |
|----------------------------------------|--------------|--------------|---------|
| ED visit or hospitalization for poisoning by narcotics and hallucinogens | 15.19 | 2.01–114.66  | 0.0083  |
| Sex (male vs. female)                  | 0.42         | 0.16–1.11    | 0.0793  |

Note: Variables with p-value ≤ 0.10 were maintained in the final multivariate model.

### Table 5. Predictors of ED visit or hospitalization due to cannabis-related mental and behavioral disorders among patients with medical cannabis authorization in univariate analysis.

| Predictors                              | HR    | 95%CI       | p-value |
|-----------------------------------------|-------|-------------|---------|
| Age (years)                             |       |             |         |
| 41–60 vs. ≤40                          | 0.400 | 0.247–0.647 | 0.0002  |
| ≥61 vs. ≤40                            | 0.357 | 0.188–0.677 | 0.0016  |
| Sex (male vs. female)                  | 1.539 | 0.0979–2.421| 0.0619  |
| Nearest census based neighborhood income quintile |       |             |         |
| 2 vs. 1                                | 0.754 | 0.426–1.333 | 0.3310  |
| 3 vs. 1                                | 0.412 | 0.201–0.845 | 0.0156  |
| 4 vs. 1                                | 0.477 | 0.243–0.935 | 0.0310  |
| 5 vs. 1                                | 0.487 | 0.243–0.974 | 0.0419  |
| ED visit or hospitalization for poisoning by psychoactive drugs (ICD-10 T43) | 19.696 | 7.207–53.826 | <0.0001 |
| Mental and behavioral disorder due to psychoactive drugs | 11.701 | 5.855–23.383 | <0.0001 |
| Mental and behavioral disorder due to alcohol use | 13.643 | 6.572–28.321 | <0.0001 |
| Other mental and behavioral disorders  | 6.76  | 4.20–10.87  | <0.0001 |
| Liver disorders                         | 2.207 | 0.894–5.452 | 0.0862  |
| Cancer                                  | 0.290 | 0.092–0.920 | 0.0356  |
| Congestive heart failure                | 2.861 | 1.246–6.569 | 0.0132  |
| Diabetes                                | 2.138 | 1.321–3.462 | 0.0020  |
| Fatigue                                 | 1.868 | 0.901–3.873 | 0.0933  |
| Metabolic disease                       | 1.889 | 1.192–2.995 | 0.0068  |
| Pain                                    | 2.207 | 1.241–3.923 | 0.0070  |

Note: Variables with p-value ≤ 0.10 were retained for inclusion in the multivariate model.

### Table 6. Predictors of ED visit or hospitalization due to cannabis-related mental and behavioral disorders among patients with medical cannabis authorization in multivariate analysis.

| Variables                              | Hazard Ratio | 95% Confidence Interval | p-value |
|----------------------------------------|--------------|-------------------------|---------|
| ED visit or hospitalization for Poisoning by other psychoactive drugs (ICD-10 T43) | 5.18 | 1.83–14.63 | 0.0019  |
| Mental and behavioral disorder due to psychoactive drugs | 3.03 | 1.33–6.87  | 0.0082  |
| Mental and behavioral disorder due to alcohol use | 4.27 | 1.83–9.98  | 0.008  |
| Other mental and behavioral disorders  | 3.88         | 2.32–6.51              | <0.0001 |
| Age 41–60 vs. ≤40                      | 0.33         | 0.19–0.58              | 0.0001  |
| Age > 60 vs. ≤40                      | 0.29         | 0.14–0.63              | 0.0016  |
| Cancer                                 | 0.37         | 0.12–1.21              | 0.0999  |
| Congestive heart failure               | 2.35         | 0.92–5.99              | 0.0730  |
| COPD                                   | 1.95         | 1.04–3.65              | 0.0376  |
| Diabetes                               | 2.63         | 1.54–4.47              | 0.0004  |

Note: Variables with p-value ≤ 0.10 were maintained in the final multivariate model.

*Include tricyclic and tetracyclic antidepressants, monoamine-oxidase-inhibitor antidepressants, butyrophenone and thioxanthene neuroleptics, and other (see the Appendix for complete list).
cohort study of medical cannabis authorized patients. It is also the only study that specifically studies the incidences rates and predictive factors of hospitalization from CUD/ cannabis poisoning in an adult population in Canada. However, our study is not without limitations. Firstly, our study was unable to capture CUD or cannabis intoxication cases that did not result in ED visit or hospitalization. As this was an observational study, potential spectrum bias is a concern since our cohort is based on patients who individually sought authorization for medical cannabis. Secondly, this population may not be representative of all individuals who are using cannabis for medical purposes as individuals who self-medicate with cannabis are not included in the study sample. Notably, our study cannot ensure cannabis products were consumed as authorized or if patients elected to use alternative agents than what was authorized. Thirdly, information on other prescribed medications was only available for a subset of the study population. Therefore, the concomitant use of other psychoactive drugs was not considered in the analysis. Lastly, it is important to note that diagnosis coding of ER visits and hospitalizations can often be unreliable and inaccurate as it is heavily provider-dependent. The validity of the used codes was not formally assessed.

Future research should specifically assess the patterns of cannabis use that are more likely to be associated with CUDs. This should include the types of cannabis products used, the concentration of active substances (cannabinoids), and routes of use. Validation of the accuracy of CUD diagnosis coding would also be useful for future research. Considering that cannabis is increasingly used either for medical or recreational purposes in many countries, healthcare professionals in those countries should consider assessing cannabis use during their patients’ consults. This could help prevent potential drug-cannabinoid interactions and may also help to early identify and intervene among patients at risk of problematic use of cannabis.

Conclusions

In all, this cohort study suggests that the incidence of cannabis poisoning or CUDs was low among patients who were authorized by healthcare providers to use cannabis for medical care. Important predictors were identified and should be considered during cannabis prescription for a better benefit-risk assessment. More particularly, the results suggest that patients with prior drug use disorders or mental and behavioral disorders should be regarded as at higher risk of CUDs.

Authors’ contributions

AZ, DTE, JRBD, JGH, EH designed the study and DTE and JRBD acquired the data. AZ analyzed the data. AZ, CL and JM drafted the manuscript. All other authors revised it critically for important intellectual content and approved the final version to be published. All authors are accountable for the work and integrity of the work. The corresponding author and guarantor accept full responsibility of the work and/or conduct of the study, had access to the data and controlled the decision to publish. AZ attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. AZ affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and if relevant) have been explained.

Ethics approval and consent to participate

All methods in this study were performed in accordance with the relevant guidelines and regulations as outlined in the Declaration of Helsinki and has been approved by an appropriate ethics committee. Ethics approval was obtained for the study from the University of Alberta Health Research Ethics board (PRO 00083651), Veritas Research Ethics Board in Ontario (16111-13:21:103-01-2017), and the CHU de Quebec-Université Laval Research Ethics Board (#CER: 2022-5999). Patients and the public were not involved in the design, conduct and reporting of this research project as it was not applicable to this project.

Cannabis use disorders and poisoning.

Incidence rates of emergency department visits or hospitalization (including primary and secondary diagnosis codes) for poisoning by cannabis and cannabis use disorders among patients with medical cannabis authorization.

| Outcome | Total events | Total person-years | Incidence rate/10,000 persons-years (95% CI) |
|---------|--------------|--------------------|--------------------------------------------|
| Cannabis poisoning (primary and secondary diagnosis codes) | 18 | 17,355.35 | 10.37 (6.53–16.46) |
| Cannabis-related mental and behavioral disorders (primary and secondary diagnosis codes) | 82 | 17,318.36 | 47.35 (38.15–58.76) |

Declaration of interest

JRBD is a former member on the board of directors of Aurora Cannabis Inc., which is a for-profit, company licensed for the cultivation and sale of medical cannabis. In the past, JGH has worked as a paid advisor and speaker for Canadian Cannabis Clinics, but currently has no ties with the CCCs. JRBD has a financial interest in Aurora Cannabis Inc. DTE, JRBD, and AZ (as a post-doctoral fellow) held a Mitacs Grant with Aurora as a partner. Mitacs is a national, not-for-profit organization that works with universities, private companies, and both federal and provincial governments, to build partnerships and administer research funding that supports industrial and social innovation in Canada. DTE and AZ do not have any past or present financial interest in the companies involved. CL, JM and EH have no conflicts of interest to declare. Moreover, the above mentioned entities, research funders and companies listed were not involved in any aspect of the design or write-up of the study and all analysis was performed independent from the funders and companies.

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Data availability statement

The dissemination of data results to study participants and or patient organizations in this research project is not possible/applicable as the data are de-identified. Being administrative health data, the data cannot be shared publicly. However, requests for the data can be sent to ICES. No special access privileges were granted to the authors.

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# Appendix: Definitions of study outcomes and potential predictors

| Variables | ICD-9 codes | ICD-10 codes |
|-----------|-------------|--------------|
| **Outcomes** |  |  |
| Outcome 1: ED visit or hospitalization with a main diagnosis (primary diagnosis code) for poisoning by cannabis |  | T40.7 Poisoning by cannabis (derivatives) |
| Outcome 2: ED visit or hospitalization with a main diagnosis (primary diagnosis code) for mental and behavioral disorders due to use of cannabinoids |  | F12 Mental and behavioral disorders due to use of cannabinoids |
|  |  | F12.0 Acute intoxication |
|  |  | F12.2 Dependence syndrome |
|  |  | F12.3 Withdrawal state |
|  |  | F12.4 Withdrawal state with delirium |
|  |  | F12.5 Psychotic disorder |
|  |  | F12.6 Annesic syndrome |
|  |  | F12.7 Residual and late-onset psychotic disorder |
|  |  | F12.8 Other mental and behavioral disorders |
|  |  | F12.9 Unspecified mental and behavioral disorder |
| **Potential predictors (pre-index date)** |  |  |
| ED visit or hospitalization for poisoning by narcotics and hallucinogens | NA | T40 Poisoning by narcotics and hallucinogens |
|  |  | T40.0 Poisoning by opium |
|  |  | T40.1 Poisoning by heroin |
|  |  | T40.2 Poisoning by other opioids (includes: Codeine, Morphine) |
|  |  | T40.3 Poisoning by methadone |
|  |  | T40.4 Poisoning by other synthetic narcotics (includes: Pethidine) |
|  |  | T40.5 Poisoning by cocaine |
|  |  | T40.6 Poisoning by other and unspecified narcotics |
|  |  | T40.7 Poisoning by cannabis (derivatives) |
|  |  | T40.8 Poisoning by lysergide (LSD) |
|  |  | T40.9 Poisoning by other and unspecified (hallucinogens) (Includes: Mescaline, Psilocin, Psilocybine) |
| ED visit or hospitalization for poisoning by anesthetic and therapeutic gas | T41 | T41 Poisoning by anesthetics and therapeutic gases |
|  |  | T41.0 Poisoning by inhaled anesthetics |
|  |  | T41.1 Poisoning by intravenous anesthetics |
|  |  | T41.2 Poisoning by other and unspecified general anesthetics |
|  |  | T41.3 Poisoning by local anesthetics |
|  |  | T41.4 Poisoning by anesthetic, unspecified |
|  |  | T41.5 Poisoning by therapeutic gases (includes: Carbon dioxide, Oxygen) |
| ED visit or hospitalization for poisoning by antiepileptic, sedative-hypnotic and antiparkinsonism drugs | T42 | T42 Poisoning by antiepileptic, sedative-hypnotic and antiparkinsonism drugs |
|  |  | T42.0 Poisoning by hydantoin derivatives |
|  |  | T42.1 Poisoning by iminostilbenes |
|  |  | T42.2 Poisoning by succinimides and oxazolidinediones |
|  |  | T42.3 Poisoning by barbiturates |
|  |  | T42.4 Poisoning by benzodiazepines |
|  |  | T42.5 Poisoning by mixed antiepileptics, not elsewhere classified |
|  |  | T42.6 Poisoning by other antiepileptic and sedative-hypnotic drugs (includes: Methaqualone, Valproic acid) |
|  |  | T42.7 Poisoning by antiepileptic and sedative-hypnotic drugs, unspecified |
|  |  | T42.8 Poisoning by antiparkinsonism drugs and other central muscle-tone depressants (includes: Amantadine) |
| ED visit or hospitalization for poisoning by other psychoactive drugs | T43 | T43 Poisoning by psychoactive drugs, not elsewhere classified |
|  |  | T43.0 Poisoning by tricyclic and tetracyclic antidepressants |
|  |  | T43.1 Poisoning by monoamine-oxidase-inhibitor antidepressants |
|  |  | T43.2 Poisoning by other and unspecified antidepressants |
|  |  | T43.3 Poisoning by phenothiazine antipsychotics and neuroleptics |
|  |  | T43.4 Poisoning by butyrophenone and thioxanthene neuroleptics |
|  |  | T43.5 Poisoning by other and unspecified antipsychotics and neuroleptics |
|  |  | T43.6 Poisoning by psychostimulants with abuse potential |
|  |  | T43.8 Poisoning by other psychoactive drugs, not elsewhere classified |
|  |  | T43.9 Poisoning by psychoactive drug, unspecified |
| ED visit or hospitalization for poisoning by alcohol | T51 | T51 Alcohol related disorders |
| ED visit or hospitalization for mental and behavioral disorder due to psychoactive drugs or substance use |  | F11—Opiod related disorders |
|  |  | F12—Cannabis related disorders |
|  |  | F13—Sedative, hypnotic or anxiolytic related disorders |
|  |  | F14—Cocaine related disorders |
|  |  | F15—Other stimulant related disorders |
|  |  | F16—Hallucinogen related disorders |
|  |  | F18—Volatile solvents related disorders |
|  |  | F19—Other psychoactive substance related disorders |
| ED visit or hospitalization for mental and behavioral disorder due alcohol use |  | F10—Alcohol related disorders |
| ED visit or hospitalization for mental and behavioral disorder due tobacco/nicotine |  | F17—Nicotine related disorders |
| ED visit or hospitalization for other mental and behavioral disorders |  | F00-F09, F20-F99 |
| Chronic kidney disease | 585 | N18 |
| Liver disorders | 570, 571, 572, 573 | K70-K77, B15-B19 |