

Prevalence and association of non-medical cannabis use with post-procedural healthcare utilisation in patients undergoing surgery or interventional procedures: a retrospective cohort study



Elena Ahrens,^{a,b,k} Luca J. Wachtendorf,^{a,b,c,k} Laetitia S. Chiarella,^{a,b,k} Sarah Ashrafian,^{a,b} Aiman Suleiman,^{a,b,d} Tim M. Tartler,^{a,b} Basit A. Azizi,^{a,b} Guanqing Chen,^{a,b} Amnon A. Berger,^a Denys Shay,^{a,b,e} Bijan Teja,^f Valerie Banner-Goodspeed,^{a,b} Haobo Ma,^a Matthias Eikermann,^{c,g} Kevin P. Hill,^{h,i} and Maximilian S. Schaefer^{a,b,j,*}



^aDepartment of Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

^bCenter for Anesthesia Research Excellence (CARE), Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

^cDepartment of Anesthesiology, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA

^dDepartment of Anesthesia, Intensive Care and Pain Medicine, Faculty of Medicine, University of Jordan, Amman, Jordan

^eDepartment of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA, USA

^fDepartment of Anesthesiology and Pain Medicine, University of Toronto, Toronto, ON, Canada

^gKlinik für Anästhesiologie und Intensivmedizin, Universität Duisburg-Essen, Essen, Germany

^hDivision of Addiction Psychiatry, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

ⁱDepartment of Psychiatry, Harvard Medical School, Boston, MA, USA

^jKlinik für Anästhesiologie, Universitätskliniken Düsseldorf, Düsseldorf, Germany

Summary

Background There is paucity of data regarding prevalence and key harms of non-medical cannabis use in surgical patients. We investigated whether cannabis use in patients undergoing surgery or interventional procedures patients was associated with a higher degree of post-procedural healthcare utilisation.

Methods 210,639 adults undergoing non-cardiac surgery between January 2008 and June 2020 at an academic healthcare network in Massachusetts, USA, were included. The primary exposure was use of cannabis, differentiated by reported ongoing non-medical use, self-identified during structured, preoperative nursing/physician interviews, or diagnosis of cannabis use disorder based on International Classification of Diseases, 9th/10th Revision, diagnostic codes. The main outcome measure was the requirement of advanced post-procedural healthcare utilisation (unplanned intensive care unit admission, hospital re-admission or non-home discharge).

Findings 16,211 patients (7.7%) were identified as cannabis users. The prevalence of cannabis use increased from 4.9% in 2008 to 14.3% by 2020 ($p < 0.001$). Patients who consumed cannabis had higher rates of psychiatric comorbidities (25.3 versus 16.8%; $p < 0.001$) and concomitant non-tobacco substance abuse (30.2 versus 7.0%; $p < 0.001$). Compared to non-users, patients with a diagnosis of cannabis use disorder had higher odds of requiring advanced post-procedural healthcare utilisation after adjusting for patient characteristics, concomitant substance use and socioeconomic factors (aOR [adjusted odds ratio] 1.16; 95% CI 1.02–1.32). By contrast, patients with ongoing non-medical cannabis use had lower odds of advanced post-procedural healthcare utilisation (aOR 0.87; 95% CI 0.81–0.92, compared to non-users).

Interpretation One in seven patients undergoing surgery or interventional procedures in 2020 reported cannabis consumption. Differential effects on post-procedural healthcare utilisation were observed between patients with non-medical cannabis use and cannabis use disorder.

Funding This work was supported by an unrestricted philanthropic grant from Jeff and Judy Buzen to Maximilian S. Schaefer.

eClinicalMedicine
2023;57: 101831
Published Online xxx
<https://doi.org/10.1016/j.eclinm.2023.101831>

*Corresponding author. Department of Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, 330 Brookline Avenue, Boston, 02215, MA, USA.

E-mail address: msschaefer@bidmc.harvard.edu (M.S. Schaefer).

^kContributed equally.

Copyright © 2023 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Keywords: Cannabis; Healthcare utilization; Cannabis abuse; Recreational drugs

Research in context

Evidence before this study

To determine the paucity of research an extensive literature research was performed on PubMed and MEDLINE using key words including cannabis, cannabinoids, marijuana, hospital length of stay, readmission, non-home discharge and postoperative complications. This search was conducted between October 2021 and March 2022, identifying 88 articles. We observed that there is paucity of data regarding prevalence and key harms of non-medical cannabis use in surgical patients. Previous studies were further restricted by identifying cannabis users based on a diagnosis of cannabis use disorder.

Added value of this study

The prevalence of cannabis use, identified from structured nursing or physician interviews increased 2.5-fold between 2008 and 2020. In adjusted analyses, cannabis use disorder was associated with higher odds of requiring advanced post-procedural healthcare utilisation, while patients that consumed cannabis for non-medical purposes were at lower risk.

Implications of all the available evidence

One in seven patients undergoing surgery or interventional procedures in 2020 consumed cannabis. Physicians should consider differential risks of requiring advanced post-procedural healthcare utilisation between non-medical users and patients with cannabis use disorder.

Introduction

Approximately 18% of the population in the United States of America (USA) reported having used cannabis at least once in 2019, including whole-plant cannabis or specific compounds derived from the cannabis plant such as cannabidiol, following an increasing trend over the last decade.^{1,2} Between 2016 and 2018, up to 22.2% of Massachusetts residents reported any prior cannabis use for recreational or medical purposes.^{2,3} These trends in Massachusetts and across the USA may have been fueled by legislative changes throughout multiple states, such as the legalisation of cannabinoids for medical purposes in 2012, and of cannabis for recreational purposes in 2016 in Massachusetts.⁴

In Canada, the prevalence of moderately-injured drivers with elevated tetrahydrocannabinol levels on presentation was more than doubled after the legalisation of recreational cannabis.^{5,6} There is limited data on the prevalence and potential harms of legislative changes on cannabis use in patients undergoing surgery.⁷ Previous studies in non-surgical populations reported that cannabis use is associated with an increased risk of psychiatric diseases,^{8–13} neuropsychological decline,^{14,15} along with adverse cardiovascular¹⁶ and cerebrovascular events.¹⁷ These findings suggest that patients with an ongoing cannabis use constitute a complex patient population, potentially requiring higher levels of healthcare.

Little is known about healthcare utilisation in patients with cannabis use after surgery or interventional procedures, where cannabis use has important additional clinical implications. Previous studies suggested potential associations with anaesthetic drug use, postoperative analgesics and pain control, as well as

antiemetic requirements.^{18–20} In addition, previous studies in the perioperative setting were limited by identifying cannabis users through International Classification of Diseases, 9th or 10th Revision, Clinical Modification (ICD-9/10-CM) diagnostic codes of cannabis use disorders, thereby likely not reflecting “classic” non-medical cannabis users.^{16,17,21}

In this study, we hypothesised that patients with cannabis use have higher odds of requiring advanced levels of healthcare after surgery, including unplanned intensive care unit admission, readmission to the hospital, or discharge to a post-acute care facility. We hypothesised that this would differ between patients with reported ongoing non-medical use and patients with a cannabis use disorder. We also investigated whether legislative changes in Massachusetts were associated with an increased prevalence of cannabis use among patients undergoing surgery or interventional procedures.

Methods

Study design and population

In this hospital registry study, we analysed data from patients undergoing non-cardiac surgery between January 2008 and June 2020 at one academic teaching hospital, Beth Israel Deaconess Medical Center (BIDMC), in Boston, Massachusetts. De-identified data from hospital information management systems containing patient-, procedural-, and outcome-related data were included (Supplemental Document, [Section S1.1](#)).

Adult patients (aged ≥ 18 years) with available information from pre-admission or pre-procedural structured interviews before undergoing non-cardiac surgery

were included. Patients undergoing transplant surgery (these patients are routinely admitted to the intensive care unit after surgery with higher rates of procedure-related complications), patients with an American Society of Anesthesiologists (ASA) physical status classification of V or higher (these patients are not expected to survive without the procedure, or declared brain-dead), and patients with preoperative intensive care unit (ICU) admission (post-procedural admission to the ICU is part of our primary outcome definition) were excluded. Observations with missing information for potential confounding variables were excluded and the complete case method was used for the primary analysis. Further details are described in the Supplemental Document, [Section S1.2](#).

Ethics

This study was approved by the institutional review board at BIDMC (Committee on Clinical Investigations, protocol number: 2021P000946) with a waiver of informed consent.

Primary analysis

Reported ongoing non-medical cannabis use was identified from routine, structured interviews held either before hospital admission, or in-hospital before the procedure. These interviews, during which nurses ask for ongoing habits of drug use, but could also document a range and frequency of use, as well as past use in a comment, were designed based on and in accordance with the American Society of Perianesthesia Nursing (ASPAN) recommendations.²² Reported ongoing non-medical cannabis use was defined as self-reported use without a diagnosis of cannabis use disorder and without prescriptions for medical cannabinoids. Cannabis use disorder was identified through ICD-9/10-CM diagnostic codes (Supplemental Document, [Section S1.3](#) and [eTable 1](#)). The primary exposure variable was validated through chart review of an interdisciplinary study team, as described in detail in the Supplemental Document, [Section S1.3](#).

We first explored whether the prevalence of cannabis use in patients undergoing surgery increased after two major legislative changes in Massachusetts: First, the legalisation of cannabinoids for medical purposes in November 2012, and second, the legalisation of cannabis for recreational purposes in December 2016, using an interrupted time series analysis (ITSA) adjusted for potential changes in patient characteristics including demographics, socioeconomic variables and psychiatric disorders.

We then conducted the primary analysis to test the research hypothesis that cannabis use, differentiated into patients with a cannabis use disorder and patients with reported ongoing non-medical cannabis use, is associated with advanced post-procedural healthcare utilisation using multivariable logistic regression

analyses. Advanced post-procedural healthcare utilisation²³ was defined as a composite outcome consisting of non-home discharge (post-procedural discharge to a skilled nursing home or long-term care facility),^{24–27} 30-day hospital readmission,²⁸ or seven-day unplanned ICU admission.²⁹ Patients who died within the hospital stay of the index procedure were considered as having the outcome.²⁵ Patients who were identified as not living at home prior to their procedure were excluded from this analysis. For all comparisons, patients that self-identified as non-users were the reference group.

The *a priori* defined primary confounder model included patient baseline characteristics, multiple socioeconomic factors including estimated household income,^{25,27} preoperative factors, as well as pre-existing physical and psychiatric comorbidities, along with concomitant substance use disorders. We also adjusted the analysis for the year in which the procedure was performed, the type of anaesthesia (general anaesthesia or monitored anaesthesia care), duration of surgery, and the Charlson Comorbidity Index. Confounding variables that did not show a linear relationship with the outcome were categorised into quintiles or clinically relevant categories prior to inclusion in the confounder model. Details related to the primary analysis and detailed information on confounding variables are provided in the Supplemental Document, [Section S2](#).

Secondary and exploratory analyses

In secondary analyses, we investigated the association of a cannabis use disorder and reported ongoing non-medical cannabis use with the individual components of advanced post-procedural healthcare utilisation, respectively.

With an exploratory intent, we aimed to determine the association of cannabis use, differentiated into cannabis use disorder and reported ongoing non-medical cannabis use, with hospital length of stay as well as hospital discharge against medical advice.

In a subset of patients with available data on non-medical cannabis usage frequency, we investigated the association of reported ongoing non-medical cannabis use with our primary outcome based on self-disclosed pattern and frequency of consumption, including daily, weekly, and monthly use. We investigated missingness patterns for frequency of consumption to ensure that missing data on cannabis use frequency were distributed randomly within our cohort.

Lastly, we investigated the association of medical cannabinoid use, compared to no use and to reported ongoing non-medical cannabis use, with advanced post-procedural healthcare utilisation. Medical cannabinoid use was identified based on prescription charts derived from our hospital prescription database. Details on secondary and exploratory analyses are provided in the Supplemental Document, [Sections S3 and S4](#).

Sensitivity analyses

To confirm the robustness of our findings, we performed multiple sensitivity analyses, including (1) multiple imputation of missing data for confounding variables; (2) inverse probability of treatment weighting (IPTW); and (3) additional adjustment for provider variability as a random effect. Further, we performed (4) effect modification analyses and (5) limited our definition of reported ongoing non-medical cannabis use to self-reported consumption within the last 30 days. In addition, we (6) assessed the potential impact of residual confounding by calculating the E-values for our primary analysis and (7) added additional markers of comorbidities, the Elixhauser Comorbidity Index³⁰ and a diagnosis of obsessive-compulsive disorder, to the model. Rationale, details and results are described in [Section S5](#) in the Supplemental Document.

Statistical analysis

Primary and secondary analyses were performed with *a priori* defined confounding factors, exposure and outcome measures, and pre-specified statistical methods. Exploratory and sensitivity analyses were conducted *post-hoc* after the main results became available. Multivariable logistic regression models were used to evaluate the relationships between cannabis use and advanced post-procedural healthcare utilisation. Adjusted odds ratios (aOR), adjusted risk differences (aARD) and 95% confidence intervals (CI) are presented for multivariable logistic regression models. Model calibration of the primary model was evaluated by a Hosmer–Lemeshow test and a reliability plot, which analysed the agreement between the observed and estimated outcomes. Model discrimination was evaluated through the concordance c-statistic, which was equivalent to the area under the receiver operating characteristic curve. Newey–West ordinary least-square regression ITSA was performed to investigate the association between the legalisation of cannabinoids for medical purposes in 2012, and of cannabis for recreational purposes in 2016 on the prevalence of cannabis use, based on the assumption that the legalisation event is expected to interrupt the trend subsequent to its introduction. For the ITSA, treatment effects are reported with 95% confidence intervals (CI). To assess potential autocorrelation, a Cumby–Huizinga test was applied, the optimal lag period was defined through Akaike’s information criterion, Schwarz’s Bayesian information criterion, and the Hannan and Quinn information criterion. Details are provided in the Supplemental Document, [Section S2.2eFigs. 1 and 2](#). Throughout all analyses, a two-sided alpha of <0.05 was considered statistically significant. Statistical analyses were performed using Stata (Version 16, StataCorp LLC, College Station, TX, USA) and R Statistical Software (Version 4.1.2., Foundation for Statistical Computing, Vienna, Austria).

Role of the funding source

This study was conducted with institutional funding. Therefore, no funders had a role in study design, data collection, data analyses, interpretation, or writing of the report.

Results

Patients and characteristics

A total of 276,656 patients were considered for inclusion. After the application of exclusion criteria and exclusion of patients with missing data, the final study cohort consisted of 210,639 patients ([Fig. 1](#)). 16,211 (7.7%) patients used cannabis prior to surgery, of which 14,045 (86.6%) were identified as non-medical cannabis users, and 2166 (13.4%) had a diagnosis of cannabis use disorder identified through ICD-9/10-CM diagnostic codes. Patients who self-identified as cannabis users were on average younger and more often male, more likely to suffer from psychiatric comorbidities including depression, anxiety and psychiatric as well as schizo-affective disorders ([Table 1](#)). Substance use disorders related to alcohol, cocaine, intravenous drugs, medications, and psychedelic drugs were more frequent in patients who used cannabis. Further details on patient demographics, socioeconomic factors, physical and psychiatric comorbidities, pre- and intraoperative factors, along with concomitant substance use disorders are provided in [Table 1](#).

At the beginning of the study period, in 2008, the prevalence of cannabis use was 4.9%, which over the course of the whole study period increased to 14.3% in 2020 ([Fig. 2](#)). After legalisation of inhalational cannabis for medical purposes, the prevalence of cannabis use

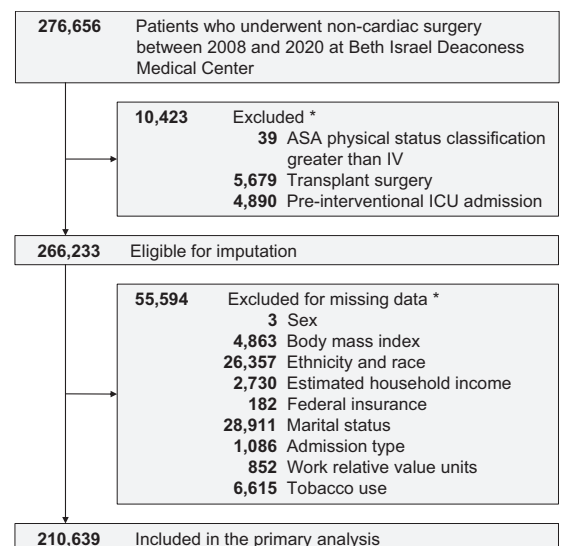


Fig. 1: Study flow diagram. ASA: American Society of Anesthesiologists; ICU: Intensive Care Unit.

	No cannabis use n = 194,428 n (%)	Recreational cannabis use n = 14,045 n (%)	Cannabis use disorder n = 2166 n (%)	Maximum absolute standardised difference ^a	p-value ^b
Demographics					
Age, mean (SD), years	55 (15)	47 (15)	47 (14)	0.550	<0.001
Sex, female	114,839 (59.1)	5753 (41.0)	870 (40.2)	0.370	<0.001
BMI, mean (SD), kg/m ^{2c}	28.56 (6.84)	28.20 (6.70)	28.34 (7.11)	0.054	<0.001
Ethnicity and race				0.182	<0.001
White	141,988 (73.0)	10,683 (76.1)	1402 (64.7)		
Asian	9515 (4.9)	104 (0.7)	6 (0.3)		
Black	21,310 (11.0)	1879 (13.4)	510 (23.5)		
Hispanic	11,587 (6.0)	625 (4.4)	173 (8.0)		
Other	9800 (5.0)	722 (5.1)	74 (3.4)		
Two or more	228 (0.1)	32 (0.2)	1 (0.0)		
ASA physical status ^d				0.368	<0.001
I	22,812 (11.7)	1874 (13.3)	109 (5.0)		
II	100,454 (51.7)	7464 (53.1)	911 (42.1)		
III	66,902 (34.4)	4519 (32.2)	1072 (49.5)		
IV	4206 (2.2)	188 (1.3)	74 (3.4)		
Socioeconomic factors					
Federal insurance	57,749 (29.7)	3860 (27.5)	805 (37.2)	0.162	<0.001
Estimated household income, mean (SD), USD ^e	84,000 (64,000–110,000)	80,000 (58,000–97,000)	73,000 (55,000–94,000)	0.357	<0.001
Marital status ^f	14,609 (7.5)	1157 (8.2)	177 (8.2)	0.027	0.004
Preoperative characteristics					
Admission type				0.349	<0.001
Ambulatory	123,048 (63.3)	8919 (63.5)	1088 (50.2)		
Inpatient	56,263 (28.9)	4122 (29.3)	659 (30.4)		
Same-day admission	15,117 (7.8)	1004 (7.1)	419 (19.3)		
Preoperative opioids	35,885 (18.5)	3589 (25.6)	766 (35.4)	0.376	<0.001
Surgical service				0.035	<0.001
Colorectal	5709 (2.9)	606 (4.3)	111 (5.1)		
Dental, oral, ENT	6356 (3.3)	556 (4.0)	58 (2.7)		
Ophthalmology	10,409 (5.4)	262 (1.9)	60 (2.8)		
General surgery	24,900 (12.8)	1676 (11.9)	194 (9.0)		
Gastroenterology	8755 (4.5)	808 (5.8)	224 (10.3)		
Gynaecology	33,057 (17.0)	1861 (13.3)	267 (12.3)		
Neurology	7002 (3.6)	726 (5.2)	111 (5.1)		
Orthopaedics	41,160 (21.2)	3567 (25.4)	522 (24.1)		
Plastic surgery	12,257 (6.3)	1068 (7.6)	126 (5.8)		
Podiatry	5138 (2.6)	316 (2.2)	62 (2.9)		
Surgical oncology	8724 (4.5)	412 (2.9)	50 (2.3)		
Thoracic	9530 (4.9)	664 (4.7)	108 (5.0)		
Trauma	3106 (1.6)	207 (1.5)	76 (3.5)		
Urology	12,911 (6.6)	1038 (7.4)	114 (5.3)		
Vascular	5414 (2.8)	278 (2.0)	83 (3.8)		
Intraoperative characteristics					
General anaesthesia	127,981 (65.8)	9919 (70.6)	1446 (66.8)	0.103	<0.001
Monitored anaesthesia care	66,447 (34.2)	4126 (29.4)	720 (33.2)	0.103	<0.001
Duration of surgery, median (IQR), minutes	89 (50–152)	96 (53–161)	88 (48–156)	0.054	<0.001
Work RVU, mean (SD)	8.49 (4.96–15.37)	8.20 (4.78–15.37)	7.39 (4.43–15.53)	0.011	<0.001
Physical comorbidities					
Charlson comorbidity index	0 (0–2)	0 (0–2)	1 (0–4)	0.376	<0.001
Congestive heart failure	8329 (4.3)	371 (2.6)	128 (5.9)	0.091	<0.001
Atrial fibrillation	12,454 (6.4)	561 (4.0)	126 (5.8)	0.109	<0.001
Cancer	38,541 (19.8)	2378 (16.9)	428 (19.8)	0.075	<0.001
COPD	15,279 (7.9)	1097 (7.8)	343 (15.8)	0.249	<0.001

(Table 1 continues on next page)

	No cannabis use n = 194,428 n (%)	Recreational cannabis use n = 14,045 n (%)	Cannabis use disorder n = 2166 n (%)	Maximum absolute standardised difference ^a	p-value ^b
(Continued from previous page)					
Diabetes					
With end-organ damage	11,052 (5.7)	555 (4.0)	220 (10.2)	0.171	<0.001
Without end-organ damage	24,698 (12.7)	1237 (8.8)	373 (17.2)	0.135	<0.001
Chronic liver disease	1744 (0.9)	210 (1.5)	85 (3.9)	0.195	<0.001
Chronic kidney disease	9964 (5.1)	491 (3.5)	219 (10.1)	0.194	<0.001
Anaemia	51,220 (26.3)	3199 (22.8)	991 (45.8)	0.418	<0.001
Psychiatric comorbidities					
Anxiety	23,853 (12.3)	2394 (17.0)	812 (37.5)	0.600	<0.001
Depression	32,172 (16.5)	2982 (21.2)	1026 (47.4)	0.691	<0.001
Schizophrenia	655 (0.3)	62 (0.4)	32 (1.5)	0.120	<0.001
Psychosis	1844 (0.9)	138 (1.0)	100 (4.6)	0.224	<0.001
Schizoaffective disorder	538 (0.3)	65 (0.5)	32 (1.5)	0.127	<0.001
Concomitant substance use					
Alcohol	5876 (3.0)	1155 (8.2)	420 (19.4)	0.521	<0.001
Cocaine	3446 (1.8)	1680 (12.0)	480 (22.2)	0.629	<0.001
IVDA	6824 (3.5)	1530 (10.9)	617 (28.5)	0.703	<0.001
Medications	1699 (0.9)	405 (2.9)	203 (9.4)	0.384	<0.001
Psychedelics	855 (0.4)	341 (2.4)	99 (4.6)	0.255	<0.001
Tobacco	86,556 (44.5)	9597 (68.3)	1767 (81.6)	0.794	<0.001
Medical cannabinoids	2182 (1.1)	495 (3.5)	171 (7.9)	0.320	<0.001

ASA, American Society of Anesthesiologists; BMI: body mass index; COPD, chronic obstructive pulmonary disease; ENT, ear, nose and throat; IQR, interquartile range; IVDA, intravenous drug abuse; SD, standard deviation; USD, United States Dollar; Work RVU, work relative value units. ^aMaximum absolute standardised differences of potential confounding variables compared between groups. The standardised difference is calculated as the mean of a variable between two groups divided by an estimate of the standard deviation of that variable. Absolute standardised differences are the standardised differences as absolute values. The maximum absolute standardised difference across all pairwise comparisons of the exposure groups is presented. ^bP-values derived from ANOVA or Kruskal-Wallis tests for continuous variables, and Pearson's chi-square tests for binary and categorical variables. ^cCalculated as weight in kilograms divided by height in metres squared. ^dThe American Society of Anesthesiologists (ASA) physical status classification was used to evaluate a patient's physical state before undergoing anaesthesia or surgery. Current definitions include six categories (ASA I [healthy patient] to ASA VI [patient with brain death]). ^eEstimated household income was obtained based on zip code data and the median household income in an area was calculated. ^fMarital status of patients, identifying those living with a life partner.

Table 1: Patient characteristics by cannabis use.

increased from 5.4% in 2012 to 8.0% by 2016 (absolute increase by 0.3% per quarter; 95% CI 0.1–0.4; p < 0.001). After legalisation for recreational purposes in 2016, this prevalence further increased to 14.3% in 2020 (absolute increase by 0.5% per quarter; 95% CI 0.3–0.7; p < 0.001) (Fig. 3).

Primary analysis

A total of 24,516 patients (11.8%) required advanced post-procedural healthcare utilisation after surgery, among which 1465 patients self-identified as non-medical cannabis users, 418 patients presented with cannabis use disorder, and 22,633 patients had no reported ongoing cannabis use. Compared to patients who did not use cannabis, patients with a diagnosis of cannabis use disorder had higher odds of requiring advanced post-procedural healthcare utilisation (OR 1.87; 95% CI 1.67–2.08), which remained present after adjustment for patient demographics, socioeconomic factors, comorbidities, concomitant substance abuse, and psychiatric disorders (aOR 1.16; 95% CI 1.02–1.32). By contrast, patients with reported ongoing non-medical cannabis use had lower odds of advanced

post-procedural healthcare utilisation (OR 0.88; 95% CI 0.84–0.94; aOR 0.87; 95% CI 0.81–0.92, compared to non-users, respectively). Details regarding characteristics and performance of the primary statistical model are presented in the Supplemental Document, Section S2.

Secondary and exploratory analyses

Among patients with a cannabis use disorder, we found higher odds of 30-day hospital readmission (aOR 1.36; 95% CI 1.19–1.56), but a cannabis use disorder was not associated with seven-day unplanned ICU admission (aOR 0.87; 95% CI 0.66–1.14), and non-home discharge (aOR 0.98; 95% CI 0.77–1.24), respectively, when compared to non-users. By contrast, there were lower odds of 30-day hospital readmission (aOR 0.88; 95% CI 0.81–0.94) and seven-day unplanned ICU admission (aOR 0.85; 95% CI 0.75–0.96) among non-medical cannabis users, respectively, while no association was observed between reported ongoing non-medical cannabis use and non-home discharge (aOR 0.90; 95% CI 0.80–1.02, compared to patients without cannabis use, respectively).

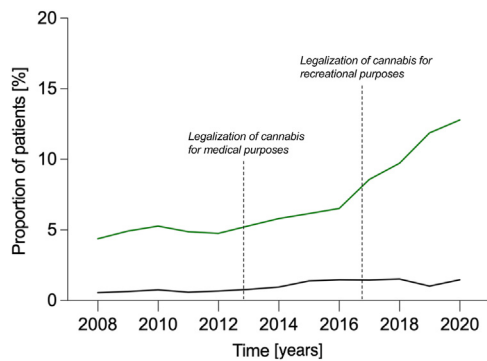


Fig. 2: Prevalence of cannabis use in patients undergoing surgery over time. The prevalence of non-medical cannabis use in patients undergoing surgery over time (years on the x-axis) is shown. The proportion of patients is displayed on the y-axis and is further stratified by the type of use for reported ongoing non-medical (green), and cannabis use disorder (grey). The legislative changes in Massachusetts are highlighted with a vertical dashed line. The reported ongoing non-medical use of cannabis has markedly increased over time, whereas the proportion of patients with cannabis use disorder has increased only marginally.

In adjusted analyses and compared to non-users, we observed an association between reported ongoing non-medical cannabis use and a shorter hospital length of stay (aARD -0.04 days; 95% CI -0.07 to 0.00 days). There was no association between cannabis use disorder

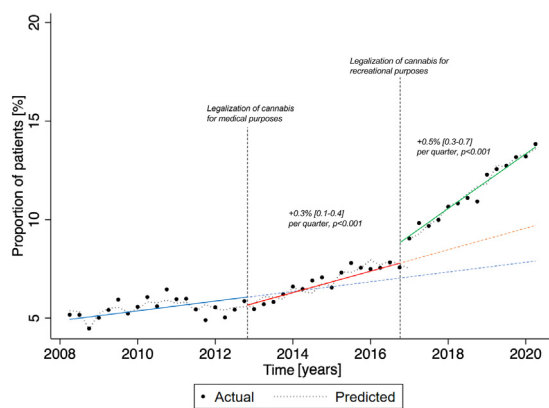


Fig. 3: Change in cannabis use over time in patients undergoing surgery in relation to two major legislative changes in Massachusetts. The results from interrupted time series analysis, adjusted for potential changes in patient demographics, socioeconomic variables, and schizoaffective disorders over time, are shown with the years on the x-axis and the proportion of patients using non-medical cannabis on the y-axis. After legalisation of cannabis for medical purposes, the prevalence of cannabis use increased from 5.4% in 2012 to 8.0% by 2016 (absolute increase by 0.3% per quarter; 95% CI $0.1-0.4$; $p < 0.001$). After legalisation for recreational purposes in 2016, this prevalence further increased to 14.3% in 2020 (absolute increase by 0.5% per quarter; 95% CI $0.3-0.7$; $p < 0.001$). A p -value < 0.05 was considered statistically significant.

and duration of hospitalisation (aARD -0.04 days; 95% CI -0.11 to 0.04 days), although patients with cannabis use disorder had higher odds to leave the hospital against medical advice, when compared to non-users (aOR 5.14; 95% CI 2.24–11.81).

We found a frequency-dependent association of reported ongoing non-medical cannabis consumption with advanced post-procedural healthcare utilisation (aOR 0.81; 95% CI 0.70–0.94 for daily, aOR 0.78; 95% CI 0.66–0.92 for weekly, and aOR 0.73; 95% CI 0.57–0.94 for monthly cannabis use, compared to non-users, respectively).

Upon investigation of medical cannabis use, we observed that medical cannabinoid users had higher odds of requiring advanced post-procedural healthcare utilisation compared to non-users (aOR 1.24; 95% CI 1.11–1.38) and to non-medical cannabis users (aOR 1.43; 95% CI 1.26–1.62), respectively.

Sensitivity analyses

Our findings remained robust throughout multiple sensitivity analyses including (1) multiple imputation of missing data for confounding variables; (2) IPTW; (3) additional adjustment for the care-providing anaesthesiologists as a random effect in a multivariable mixed-effects regression model; as well as in (4) effect modification analyses by the patient's ASA physical status and the Charlson Comorbidity Index, respectively. Our results were further confirmed after (5) redefinition of reported ongoing non-medical cannabis use as self-reported consumption within the last 30 days, and (7) additional confounding adjustment. The E-values (6) for our primary analysis were 1.6 (point estimate) and 1.2 (confidence interval) for non-medical cannabis use, and 1.6 (point estimate) and 1.4 (confidence interval) for cannabis use disorder, implying that considerable unmeasured confounding would be needed to explain away the observed effect estimate.^{31,32} Details pertaining to the exploratory and sensitivity analyses are presented in the Supplemental Document, Sections S4 and S5, respectively.

Discussion

The prevalence of cannabis use in patients undergoing surgery or interventional procedures in Massachusetts almost tripled between 2008 and 2020. Cannabis users had a higher complexity of comorbidities including schizoaffective and concomitant substance use disorders. When differentiating between types of use, patients with a diagnosed cannabis use disorder more often required advanced levels of post-procedural healthcare utilisation which was not the case for “simple” self-identified non-medical cannabis users. These findings were robust in multiple sensitivity analyses.

Legislative changes in Massachusetts in 2012 and 2016 were associated with a strong increase in cannabis

use among patients undergoing surgery, even when adjusting for changes in underlying demographics, types of procedures, and other patient characteristics including socioeconomic factors. These findings indicate that a state- and nationwide trend in non-healthcare settings, along with non-surgical populations is reflected in patients undergoing surgery.^{2,3,7} In our study, the overall prevalence of cannabis use increased by an absolute value of 9.4% from 2008 to 2020, where every seventh patient was identified as cannabis user. This trend was primarily driven by a strong increase in the incidence of self-reported use in structured nursing and physician interviews.

This observed prevalence in more recent years exceeds numbers reported in other studies. While this might be related to nationwide differences in cannabis consumption, previous studies relied primarily on ICD-9/10-CM diagnostic codes to identify cannabis users.^{16,17,33} Although diagnostic codes may identify patients with significant cannabis consumption, they ignore more prevalent “simple” recreational cannabis use. Therefore, our study adds to previous reports, by estimating the prevalence of ongoing, self-reported non-medical cannabis use based on structured pre-admission and pre-procedural nursing and physician interviews. Compared to patients identified through ICD-9/10-CM diagnostic codes of a cannabis use disorder,^{17,33} this cohort represents a distinctively different patient population of more general non-medical users. Of note, the underlying structure of the interview questionnaire, which is integrated into the electronic healthcare record, did not change over the study period.

The use of cannabis has previously been linked to a higher incidence of perioperative acute myocardial infarction,^{17,34,35} but data regarding other peri- and postoperative complications, such as hospital length of stay, acute cerebrovascular events, and healthcare costs, remain equivocal.^{33,36} In our study, we found a higher level of post-procedural healthcare utilisation among patients with a cannabis use disorder, which reflects findings in non-surgical and surgical cohorts that primarily identified cannabis use based on ICD-9/10-CM diagnostic codes.^{16,17,21} Our adjusted analyses further indicate that cannabis use disorder does not only identify more complex patients, but by itself is associated with higher odds of healthcare utilisation independent of a variety of comorbidities, socioeconomic factors, and concomitant abuse of other substances. Differential findings in patients who self-identified as ongoing non-medical cannabis users without a diagnosis of use disorder strongly suggest that future studies need to differentiate these two patient populations. Findings based on the identification of cannabis use from ICD-9/10-CM diagnostic codes might not be applicable to most cannabis users.

Corroborating previous reports, we observed that patients using cannabis were more likely to present with

concomitant substance use disorders related to alcohol, nicotine and drugs including cocaine, intravenous drugs, psychedelics and opioids, which corroborates findings of previous studies.^{10–12,37–39}

There was further a higher prevalence of psychiatric disorders including anxiety and depression in patients consuming cannabis.^{10,38,40–42} As these comorbidities have been associated with increased complications including arrhythmias and sudden cardiac death after anaesthesia,^{43,44} a history of cannabis use disorder might serve as an indicator of potentially complicating factors for patients undergoing anaesthesia that in turn contribute to the requirement of higher level healthcare utilisation after surgery.

Our data help inform clinicians and policymakers that reflecting trends in the general population, cannabis use is very common among patients undergoing surgery or interventional procedures. Clinicians should take into consideration how different purposes of cannabis use might represent different patient populations, which may in turn translate into distinguished perioperative risk profiles. Our findings should inform future studies that aim to differentiate the role of cannabis use in perioperative medicine.

Limitations of our study arise from its retrospective design. Although the large cohort size allowed for an extensive confounder control and multiple sensitivity analyses confirmed the robustness of our results, residual confounding cannot be entirely excluded, as fundamental inter-group differences in patient characteristics need to be anticipated. Further, while we were able to control for a variety of demographics, socioeconomic factors, comorbidities and procedural characteristics, the selection of confounding variables was limited by the availability of electronically stored data. The data analysed in this study were collected in a limited geographical region in the USA, which may limit generalisability to other settings, especially with regards to temporal changes in the prevalence of self-reported cannabis use. While trends in our academic institution reflect underlying changes in the general population,¹ our findings should be verified in different scenarios, including non-academic institutions in- and outside of Massachusetts, to enhance the representativeness of our data. Further, while allowing control for many confounding factors as well as trends over time, interrupted time series analysis as used in our study carries inherent limitations in establishing causal inferences. Although unlikely, we cannot fully exclude that unmeasured confounding, or changes in willingness to report cannabis use over time contributed to our findings. In contrast to previous retrospective studies, we combined different data sources to include a variety of cannabis users consisting of self-identified cannabis use or diagnosed cannabis use disorder, and patients based on ICD-9/10-CM diagnostic codes involving cannabis use disorder. Our study may also contain reporting bias, as

patients might not disclose cannabis use during the interviews, resulting in exclusion of patients who would qualify for the diagnosis of active cannabis use.

In summary, the prevalence of cannabis use in patients undergoing surgery in Massachusetts markedly increased following legislative changes to every seventh patient being identified as cannabis user. A disorder of cannabis use identifies patients at risk of requiring higher levels of post-procedural healthcare including intensive care unit admission, readmission and non-home discharge, while a lower risk was observed among patients with ongoing non-medical cannabis use.

Contributors

All authors worked on conceptualisation, data acquisition, and interpretation of data. Formal analysis, investigation, and visualisation was performed by Elena Ahrens, Luca J. Wachtendorf, Laetitia S. Chiarella, and Sarah Ashrafian. Statistical consultation was provided by Guanqing Chen. All authors drafted the work or revised it critically for important intellectual content. All authors have read and approved the final version to be published. Maximilian S. Schaefer was responsible for supervision and methodology. All authors had full access to the data analysed in this study and agree to be accountable for all aspects of the work. Elena Ahrens, Luca J. Wachtendorf, and Laetitia S. Chiarella contributed equally. Elena Ahrens, Luca J. Wachtendorf, Laetitia S. Chiarella, Guanqing Chen, Sarah Ashrafian, Aiman Suleiman and Maximilian S. Schaefer accessed and verified the underlying data reported in the manuscript. Maximilian S. Schaefer is the guarantor of the study and takes full responsibility for the integrity of the data and the accuracy of the data analysis.

Data sharing statement

Due to the sensitive nature of the data collected for this study, requests to access additional documents and the dataset containing deidentified patient data from qualified researchers trained in human subject research and confidentiality with publication may be sent to Maximilian S. Schaefer at msschaefer@bidmc.harvard.edu.

Declaration of interests

Haobo Ma received a SEAd Grant from the Society for Education in Anesthesia not related to this manuscript. Matthias Eikermann has received unrestricted funds from philanthropic donors Jeffrey and Judy Buzen and grants from Merck & Co. not related to this study. He is an Associate Editor of the British Journal of Anaesthesia. Kevin Hill has served as a consultant to for Greenwich Biosciences and has received an honorarium from Wolters-Kluwer as an author. Maximilian S. Schaefer received funding for investigator-initiated studies from Merck & Co., which do not pertain to this manuscript. He is an associate editor for BMC Anesthesiology. Maximilian S. Schaefer received honoraria for presentations from Fisher & Paykel Healthcare and Mindray Medical International Limited. Maximilian S. Schaefer has received an unrestricted grant from Jeff and Judy Buzen. All other authors declare no competing interests.

Acknowledgements

We would like to thank Annika S. Witt, Sarah Y. Nabel, Tuyet Tran, and JoAnn Jordan for non-author contributions.

Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.eclinm.2023.101831>.

References

- Centers for Disease Control and Prevention. Marijuana and public health. Published 2021 <https://www.cdc.gov/marijuana/data-statistics.htm>. Accessed August 25, 2022.
- National conference of state legislatures. State medical cannabis laws. Published 2022 <https://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx>. Accessed August 25, 2022.
- Substance abuse and mental health services administration. National survey of drug use and health (NSDUH) releases. <https://www.samhsa.gov/data/release/2018-national-survey-drug-use-and-health-nsduh-releases>; 2018. Accessed August 25, 2022.
- Substance abuse and mental health services administration. National survey of drug use and health (NSDUH) releases. <https://www.samhsa.gov/data/release/2020-national-survey-drug-use-and-health-nsduh-releases>; 2020. Accessed August 25, 2022.
- Brubacher JR, Chan H, Erdelyi S, Staples JA, Asbridge M, Mann RE. Cannabis legalization and detection of tetrahydrocannabinol in injured drivers. *N Engl J Med*. 2022;386:148–156.
- Cole TB, Saitz R. Cannabis and impaired driving. *JAMA*. 2020;324:2163.
- Fischer B, Lee A, O'Keefe-Markman C, Hall W. Initial indicators of the public health impacts of non-medical cannabis legalization in Canada. *eClinicalMedicine*. 2020;20:100294.
- Marconi A, Di Forti M, Lewis CM, Murray RM, Vassos E. Meta-analysis of the association between the level of cannabis use and risk of psychosis. *Schizophr Bull*. 2016;42:1262–1269.
- Hindley G, Beck K, Borgan F, et al. Psychiatric symptoms caused by cannabis constituents: a systematic review and meta-analysis. *Lancet Psychiatry*. 2020;7:344–353.
- Lucatch AM, Coles AS, Hill KP, George TP. Cannabis and mood disorders. *Curr Addict Rep*. 2018;5:336–345.
- Hill KP. Cannabis use and risk for substance use disorders and mood or anxiety disorders. *JAMA*. 2017;317:1070.
- Hill KP. Recreational cannabis legalisation: details will determine mental health effects. *Lancet Psychiatry*. 2016;3:798–799.
- Manseau MW, Goff DC. Cannabinoids and schizophrenia: risks and therapeutic potential. *Neurotherapeutics*. 2015;12:816–824.
- Meier MH, Caspi A, Ambler A, et al. Persistent cannabis users show neuropsychological decline from childhood to midlife. *Proc Natl Acad Sci U S A*. 2012;109:E2657–E2664.
- Lorenzetti V, Hoch E, Hall W. Adolescent cannabis use, cognition, brain health and educational outcomes: a review of the evidence. *Eur Neuropsychopharmacol*. 2020;36:169–180.
- Thomas G, Kloner RA, Rezkalla S. Adverse cardiovascular, cerebrovascular, and peripheral vascular effects of marijuana inhalation: what cardiologists need to know. *Am J Cardiol*. 2014;113:187–190.
- Rumalla K, Reddy AY, Mittal MK. Recreational marijuana use and acute ischemic stroke: a population-based analysis of hospitalized patients in the United States. *J Neurol Sci*. 2016;364:191–196.
- Lynn RSR, Galinkin JL. Cannabis, e-cigarettes and anesthesia. *Curr Opin Anaesthesiol*. 2020;33:318–326.
- Zhang BH, Saud H, Sengupta N, et al. Effect of preoperative cannabis use on perioperative outcomes: a retrospective cohort study. *Reg Anesth Pain Med*. 2021;46:650–655.
- Kraft B, Stromer W. The effects of cannabis and cannabinoids on anesthesia and analgesia during the perioperative period. *Schmerz*. 2020;34:314–318.
- Mittleman MA, Lewis RA, Maclure M, Sherwood JB, Muller JE. Triggering myocardial infarction by marijuana. *Circulation*. 2001;103:2805–2809.
- 2021-2022 perianesthesia nursing standards, practice recommendations and interpretive statements. Cherry Hill, New Jersey: American Society of PeriAnesthesia Nurses; 2020.
- Suleiman A, Munoz-Acuna R, Azimaraghi O, et al. The effects of sugammadex vs. neostigmine on postoperative respiratory complications and advanced healthcare utilisation: a multicentre retrospective cohort study. *Anaesthesia*. 2022. <https://doi.org/10.1111/anae.15940>. published online Dec 23.
- Gosling AF, Hammer M, Grabitz S, et al. Development of an instrument for preoperative prediction of adverse discharge in patients scheduled for cardiac surgery. *J Cardiothorac Vasc Anesth*. 2021;35:482–489.
- Schaefer MS, Hammer M, Platzbecker K, et al. What factors predict adverse discharge disposition in patients older than 60 Years undergoing lower-extremity surgery? The adverse discharge in older patients after lower-extremity surgery (ADELES) risk score. *Clin Orthop Relat Res*. 2021;479:546–547.
- Rostin P, Teja BJ, Friedrich S, et al. The association of early postoperative desaturation in the operating theatre with hospital discharge to a skilled nursing or long-term care facility. *Anaesthesia*. 2019;74:457–467.

- 27 Wachtendorf LJ, Azimaraghi O, Rangasamy V, et al. Preoperative treatment of severe diabetes mellitus and hypertension mitigates healthcare disparities and prevents adverse postoperative discharge to a nursing home. *Ann Surg.* 2022;276(3):e185–e191.
- 28 Wachtendorf LJ, Schaefer MS, Santer P, et al. Association between preoperative administration of gabapentinoids and 30-day hospital readmission: a retrospective hospital registry study. *J Clin Anesth.* 2021;73:110376.
- 29 Scheffenbichler FT, Teja B, Wongtangman K, et al. Effects of the level and duration of mobilization therapy in the surgical ICU on the loss of the ability to live independently: an international prospective cohort study. *Crit Care Med.* 2021;49:e247–e257.
- 30 Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care.* 1998;36:8–27.
- 31 VanderWeele TJ, Ding P. Sensitivity analysis in observational research: introducing the E-value. *Ann Intern Med.* 2017;167:268–274.
- 32 Mathur MB, Ding P, Riddell CA, VanderWeele TJ. Web site and R package for computing E-values. *Epidemiology.* 2018;29:e45–e47.
- 33 Goel A, McGuinness B, Jivraj NK, et al. Cannabis use disorder and perioperative outcomes in major elective surgeries: a retrospective cohort analysis. *Anesthesiology.* 2020;132:625–635.
- 34 Ladha KS, Mistry N, Wijeyesundera DN, et al. Recent cannabis use and myocardial infarction in young adults: a cross-sectional study. *CMAJ (Can Med Assoc J).* 2021;193:E1377–E1384.
- 35 Banerjee A, Gandhi AB, Antony I, et al. Role of cannabis in the incidence of myocardial infarction: a review. *Cureus.* 2020;12:e11097.
- 36 Swetlik C, Migdady I, Hasan LZ, Buletko AB, Price C, Cho S-M. Cannabis use and stroke: does a risk exist? *J Addict Med.* 2022;16:208–215.
- 37 Volkow ND, Swanson JM, Evins AE, et al. Effects of cannabis use on human behavior, including cognition, motivation, and psychosis: a review. *JAMA Psychiatry.* 2016;73:292–297.
- 38 Petrilli K, Ofori S, Hines L, Taylor G, Adams S, Freeman TP. Association of cannabis potency with mental ill health and addiction: a systematic review. *Lancet Psychiatry.* 2022;9:736–750.
- 39 Di Forti M, Quattrone D, Freeman TP, et al. The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): a multicentre case-control study. *Lancet Psychiatry.* 2019;6:427–436.
- 40 Blanco C, Hasin DS, Wall MM, et al. Cannabis use and risk of psychiatric disorders: prospective evidence from a US national longitudinal study. *JAMA Psychiatry.* 2016;73:388–395.
- 41 Moore THM, Zammit S, Lingford-Hughes A, et al. Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *Lancet.* 2007;370:319–328.
- 42 Lev-Ran S, Le Foll B, McKenzie K, George TP, Rehm J. Cannabis use and cannabis use disorders among individuals with mental illness. *Compr Psychiatry.* 2013;54:589–598.
- 43 Ghoneim MM, O'Hara MW. Depression and postoperative complications: an overview. *BMC Surg.* 2016;16:5.
- 44 Constance LSL, Lansing MG, Khor FK, Muniandy RK. Schizophrenia and anaesthesia. *BMJ Case Rep.* 2017;221659.