Adverse Health Effects of Marijuana Legalization

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Abstract

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BACKGROUND: Washington State has been at the forefront of modern-day marijuana legislation for over two decades. In November 1998, Washington State became one of the first states to legalize medical marijuana and, nearly 15 years later, Washington State became one of two states to legalize marijuana for recreational purposes. Such legislation was unprecedented not only in the United States but also internationally. There is much interest in the potential health impacts of such unique legislation and, to date, few studies have evaluated the health effects of both medical and recreational marijuana legalization in Washington State.

OBJECTIVES: The specific aims of this study were to: 1) evaluate the ability of *International Classification of Diseases, Clinical Modification (ICD-CM)* codes available in an administrative hospital discharge dataset to completely and accurately identify marijuana-related hospitalizations, 2) investigate the association of marijuana-related hospitalizations in Washington State with major marijuana policy changes, 3) measure the association of Washington Poison Center (WAPC) call volume regarding marijuana exposures with key changes in marijuana policy, and 4) describe marijuana exposures occurring among young children after retail sales of marijuana were established in Washington State.

METHODS: Data for these analyses were obtained from three sources: 1) Washington State Trauma Registry (WSTR), 2) Comprehensive Hospital Abstract Reporting System (CHARS), and 3) WAPC

toxiCALL records. For Aim 1, validity measures for marijuana-related diagnosis codes identified in CHARS were calculated using toxicology screening results available in WSTR as the gold standard for measuring marijuana involvement. For Aim 2, logistic regression was conducted to evaluate the association between experiencing a marijuana-related hospitalization and key changes in marijuana-related policies. For Aim 3, an interrupted time-series analysis was completed to assess changes in the volume of calls to the WAPC for marijuana exposures in relation to important marijuana policy changes. For Aim 4, WAPC records for all children <12 years of age who were reported to have had an exposure to marijuana in 2016 were reviewed to describe exposure details, clinical impacts of exposure, and identify potential avenues for prevention of pediatric exposures.

RESULTS: Marijuana-related *ICD-CM* diagnosis codes are highly specific for identifying marijuana-related hospitalizations, but likely lack sensitivity to detect all hospitalizations in which marijuana is an underlying or contributing factor to hospitalization. The odds of experiencing a marijuana-related hospitalization in Washington State and the volume of marijuana exposure calls to WAPC were both significantly associated with changes in marijuana policy, including the Ogden Memorandum (October 2009), legalization of marijuana for recreational purposes (November 2012), and retail sale of marijuana for recreational purposes (July 2014). The largest associations between marijuana policy changes and marijuana-related hospitalizations were observed among older adults (50+ years). Regarding calls to WAPC, the largest increases in the volume of reported marijuana exposures were observed among very young children (<5 years) and older adults (50+ years). Edible marijuana products were observed to be the largest contributor to reported marijuana exposures, especially among young children.

CONCLUSIONS: Liberalization of marijuana policies is associated with increases in adverse health effects, despite efforts to reduce unintentional exposures and adverse effects. The impacts of these policy changes are not evenly distributed across populations, with young children and older adults being disproportionately affected. To reduce the adverse impacts of marijuana policy changes on these populations, a multi-faceted approach including education and legislation will likely be required.

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Chapter 1: Validity Study

Assessment of *International Classification of Diseases, Clinical Modification (ICD-CM)* Codes for Identification of Marijuana-related Hospitalizations

Background

In the United States, physician assessments of patients are assigned alpha-numeric codes using the U.S. Public Health Service's *International Classification of Diseases, Clinical Modification* (*ICD-CM*). The original intent of diagnosis coding was to classify morbidity and mortality information for statistical purposes (1). *ICD-CM* is based on the World Health Organization's *International Classification of Diseases* (*ICD*) and is recommended for use in all clinical settings but is required for reporting diagnoses and diseases to the Centers for Medicare and Medicaid Services (1). Beyond classification, these codes are also used for research, administration, and are the basis on which healthcare reimbursements are calculated (2). *ICD-CM* diagnoses are readily available in healthcare administrative data and are often used to identify study subjects or evaluate outcomes in epidemiological studies (3). Rules are in place to control when and how *ICD-CM* codes are assigned (4, 5). Even so, *ICD-CM* codes vary in their specificity and their presence in a record is subject to a number of factors including extensiveness of medical histories or documentation and relevance to primary injury or illness (2). The presence or absence of codes in a record could be systematic (e.g., hospital policies), or random (e.g., coding errors). If diagnosis codes are used as the basis for identifying study subjects or outcomes in epidemiological studies, coding practices have the potential to impact study conclusions (2).

Unprecedented marijuana policy changes have been implemented in recent years in the United States. As of February 2019, 34 states and the District of Columbia have legalized marijuana to some degree; 10 states and the District of Columbia have legalized marijuana for recreational purposes, and 9 states have established a marijuana retail market (6). These changes come in the wake of intense debate about the potential positive and negative impacts of marijuana legalization. In particular, there is much concern regarding the potential acute and long-term health effects associated with these policy changes. Early assessments of the health impacts associated with legalization have used *ICD-CM* codes to identify marijuana-related hospitalizations (7-10), but it is unknown how reliably these codes do so.

Diagnosis codes may not be used consistently when marijuana is involved, and their presence may not indicate marijuana is an underlying or contributing cause of hospitalization. Instead assignment of a marijuana-related code may serve as an indicator for a patient's history of marijuana use. Additionally, legalization of marijuana in December 2012 may have impacted the willingness of patients to disclose use of marijuana, physician toxicology testing and coding practices, or physician history and documentation practices. All of these factors have the potential to influence the likelihood that a marijuana-related diagnosis code is ascribed to a patient's visit. Finally, the *ICD* coding standard in the

United States changed from *ICD-CM*, 9th edition (*ICD-9-CM*) to *ICD-CM*, 10th edition (*ICD-10-CM*) on October 1, 2015. *ICD-10-CM* introduced a completely new coding structure with approximately five times more codes than *ICD-9-CM* (11). Due to drastic differences between the two coding standards, any studies crossing the timespan of the coding transition should consider the potential impact of this transition (12).

The results of studies examining the health impacts of marijuana legalization have the potential to influence future marijuana-related policy making. Since factors external to marijuana intoxication or use may impact the presence or absence of codes, it is important to understand how well these codes relate to the clinical involvement of marijuana. This study sought to evaluate the validity of *ICD-CM* codes for identifying marijuana-related hospitalizations in a hospital discharge administrative dataset. The study also assessed whether the reliability of marijuana-related codes changed in accordance with changes in marijuana legislation or the transition from *ICD-9-CM* to *ICD-10-CM*.

Methods

Study Design

For this reliability study, fifteen years (2002 – 2016) of records from the Comprehensive Hospital Abstract Reporting System, the Washington State hospital discharge dataset, were probabilistically matched to records from the Washington State Trauma Registry. The ability of cannabis-related discharge diagnosis codes to identify hospitalizations in which cannabis was an underlying or contributing cause of hospitalization was evaluated by calculating several validity measures (e.g., sensitivity, specificity, positive predictive value). These measures were calculated using toxicology screening results, derived from the trauma registry, as a gold standard indicator for the involvement of marijuana.

Data Collection

The Washington State Trauma Registry (WSTR) is maintained by the Washington State Department of Health. This registry, which was established in 1994, collects data on injuries meeting specific inclusion criteria from all 82 state-designated trauma centers located in Washington State (Washington Administrative Code (WAC) 246-976-420 and WAC 246-976-430) (13). The dataset includes data on toxicology screening tests, which are conducted upon physician request for approximately 20% of trauma registry patients (14). Each toxicology test, which may use blood or urine, includes a screen for the presence of marijuana. The cutoff value for a positive marijuana result may vary between labs and specimen used, but most urine tests have a cutoff of either 20 ng/mL or 50 ng/mL (15). The WSTR dataset does not indicate the specimen tested, the screening test run, nor the actual value detected; it only reports absolute detection of a substance (positive/negative). For the present study, the data administrator for the WSTR created a dataset including patient identifiers, patient demographics, hospitalization information, toxicology test results, diagnoses, and injury severity indices.

Washington State hospital discharge data are collected by the Washington State Department of Health through the Comprehensive Hospital Abstract Reporting System (CHARS). This administrative dataset contains information on all hospitalizations that have occurred in Washington State since 1987, with the exception of those that occurred at the Veterans Administration and Department of Defense hospitals. A dataset containing patient identifiers, patient demographics, hospitalization information, and diagnoses for all Washington State hospitalizations that occurred between January 2002 and December 2016 was obtained. Of note, prior to 2008, patient names were limited to the first two letters of first and last name and a maximum of 10 diagnosis codes. Datasets were expanded in 2008 to contain full patient names (first, last, middle initial), the last four digits of social security number, and up to 25 diagnosis codes.

Approval to use these datasets was obtained from the Washington State Institutional Review Boards (Study ID: D-021116-H).

Data Analysis

Patient identifiers (i.e., first and last names, middle initial, date of birth, last four digits of the social security number, zip code, sex) and visit information (i.e., hospital ID, date of admission, and hospital discharge date) were used to probabilistically link patient records from the WSTR and CHARS from 2002 through 2016 using LinkPlus software (Atlanta, GA). Linked records with a match value <7.5 were considered non-matches. All other linked records were manually reviewed to determine which linkages represented true matches.

Records were removed from the resulting linked dataset if no diagnosis or external cause codes were present in the CHARS record or if toxicology screen information was missing from the WSTR record. Any record with a toxicology test result positive for marijuana was tagged. Additionally, any records with a principal or secondary diagnosis indicating cannabis dependence (*ICD-9-CM* 304.3x, *ICD-10-CM* F12.2xx), non-dependent cannabis abuse (*ICD-9-CM* 305.2x, *ICD-10-CM* F12.1xx), cannabis use (*ICD-10-CM* F12.9xx), poisoning by cannabis (*ICD-10-CM* T40.7xxx), poisoning by psychodysleptics (*ICD-9-CM* 969.9, E854.1), or adverse effect of psychodysleptics used therapeutically (*ICD-9-CM* E939.6) were identified.

Diagnosis codes were grouped into three categories, including: any cannabis-specific code (304.3, 305.2, F12.xxx, or T40.7xxx), any psychodysleptic code (969.9, E854.1, or E939.6), or any cannabis-specific or psychodysleptic code. Psychodysleptic diagnosis codes could indicate involvement of a number of substances including marijuana, LSD, or magic mushrooms, but were included in the study for comprehensiveness since no specific *ICD-9-CM* code exists for poisoning events involving marijuana.

Treating toxicology test results recorded in WSTR as the gold standard for determining whether marijuana was a contributing factor to hospitalization, the sensitivity, specificity, positive predictive value, and negative predictive value for each individual diagnosis code and combination of diagnosis codes obtained from CHARS records was calculated. The

Kappa Statistic was calculated to determine concordance between CHARS diagnoses and the toxicology test results from WSTR. Additionally, the area under the Receiver Operating Characteristic curve was calculated to assess overall code performance. Sensitivity analyses were conducted to assess the potential impact of missing toxicology test results on validity had all missing test results been positive or negative. To determine whether additional, non-marijuana diagnosis codes reliably identify hospitalizations in which toxicology tests are positive for marijuana, the frequency of non-cannabis related diagnosis codes assigned to patients who were toxicology screen positive, but lacking a cannabis-related diagnosis code, were reviewed. Validity measures were calculated for the ten most frequently reported codes to assess whether additional codes, that are not obviously marijuana-related, should be included in subsequent analyses.

Since coding practices likely differ by facility, among different patient types and at different times, univariate logistic regression analyses were conducted to identify any association between these characteristics and concordance. Validity measures were recalculated among the subset expected to have the highest concordance by limiting the dataset to those records with at least one characteristic significantly associated with concordance.

Univariate logistic regression analyses were conducted to determine whether certain patient, injury or facility characteristics were associated with having a toxicology test or cannabis-related discharge diagnosis. The population that underwent toxicology screening or that had a cannabis-related discharge diagnosis was compared to the population that did not using chi-square tests (for categorical variables) and t-tests (for continuous variables) to determine whether results of the validity analysis can be extrapolated to the general study population. All statistical analyses were performed in Stata 14 (College Station, TX).

Results

From 2002 – 2016, there were 10,078,335 CHARS records. Hospital discharge records were matched against 375,827 records collected from the WSTR, resulting in 216,088 linked records. Fourteen records that were missing diagnoses, 5,781 records that were missing toxicology test information, and 35 records missing toxicology test result information (11 missing toxicology test results (positive/negative) and 24 recorded as toxicology positive but no drug was specified) were removed from the dataset resulting in 210,258 records (Figure 1).

Patients in the linked dataset were predominately male, over the age of 50, and white or non-Hispanic (Table 1). Almost three-quarters of patients originated form urban locations and all but 6% of patients were Washington residents. Very few of the linked patients were sourced from observation discharge records and almost all of the patients were treated at acute healthcare settings.

Four thousand eight hundred and thirty-two (2.3%) linked records had one or more cannabis-related diagnosis code. Toxicology testing was conducted in 49,745 (24%) of linked records. Of these, 9,806 (19.7%) tested positive for

cannabis (Table 2). Records with cannabis abuse (305.2 or F12.1xx), cannabis use (F12.9xx), or cannabis dependence (304.3 or F12.2xx) codes accounted for 98% of marijuana-related hospitalizations identified (Tables 3 and 4). Sensitivity, kappa, and the area under the receiver operating characteristic curve (ROC) were relatively low when evaluating all marijuana-related diagnosis codes combined, but specificity and positive/negative predictive values were quite high (Table 5).

Evaluating each cannabis-related *ICD-9-CM* diagnosis code individually and in combination, the combination of all cannabis or psychodysleptic codes performed marginally better than the cannabis-specific codes (305.2 and 304.3) or cannabis abuse (305.2) alone (Table 6). Similarly, evaluating all cannabis-related *ICD-10-CM* codes in combination provided the best overall validity (Table 7). Validity measures did not improve appreciably when limiting to the first five or ten diagnosis codes (Appendix A: Tables 1 - 4).

Sensitivity analyses to assess the impact of the 35 records missing a toxicology test result indicated that the results of these tests could mildly improve or degrade the observed validity measures (Appendix A: Tables 5 - 8).

The most common non-marijuana *ICD-9-CM* and *ICD-10-CM* codes identified among discordant pairs (Tox +/ICD -) were tobacco use disorder (305.1) and nicotine dependence, cigarettes, uncomplicated (F17.210) respectively. On their own, these codes had higher sensitivity than cannabis-related codes (29 and 31 vs. 20.7), but specificity was poorer (83.7 and 81.2 vs. 98.2) (Appendix A: Tables 9 and 10). When combined with the cannabis codes, they improved sensitivity substantially and ROC area marginally, but this came at a fairly significant cost to positive predictive value and, to a smaller degree, specificity. Combining the top ten diagnosis codes with cannabis codes resulted in specificity and positivity predictive values that were too low to be useful.

Several factors were significantly associated with improving or degrading concordance (Appendix A: Table 11). Public and urban hospitals were significantly associated with concordance. Patients most likely to be concordant were older adults, females, and Asian or Hawaiian/Pacific Islanders. Several injury types significantly improve concordance, including: falls, drowning, suffocation, bicycling, being a pedestrian, machinery-related, motor vehicle-related, transport-related, and other. Patients with more severe injuries (e.g., longer stay, discharged to a skilled nursing facility, transferred, or died) were more likely to be concordant. Patients who were admitted on the weekend or who lacked insurance (either public or private) were less likely to be concordant. Additionally, as marijuana policies have relaxed, concordance also degraded. Validity measures were recalculated after limiting to records with at least one factor significantly associated with concordance, but they were not appreciably improved above the validity measures calculated using all records (Appendix A: Table 12).

Nearly every factor evaluated was significantly associated with the likelihood of having a toxicology test done (Appendix A: Table 13). Patients seen at large, urban, or private facilities in western Washington were significantly more

likely to be tested. Of note, young and middle-aged adults were significantly more likely to have a toxicology test done than children or older adults. Males were more than twice as likely to be tested as females (OR = 2.2, p<0.0001). White, Asian, and Hispanic patients were least likely to be tested compared to patients reported to be Non-Hispanic, Black, Native American, Pacific Islander, or Other race. Injury type was significantly associated with the likelihood of being tested. Patients that were tested also had a significantly higher mean injury severity score (14.7 vs. 9.5) and were more likely to be transferred.

Patients who tested positive for marijuana and received a marijuana-related diagnosis code were more likely to be treated at smaller, rural, private, independent facilities or at a hospital located in Eastern Washington (Appendix A: Table 14).

The sensitivity of marijuana-related codes has improved since 2002 (Table 8). During the era of medical marijuana legalization (Jan 2002 – Nov 2012) sensitivity was 17.9 compared to 28.4 when retail marijuana stores were open (Jul 2014 – Dec 2016). The impact of the Ogden Memorandum was also evaluated by calculating validity measures for hospital discharges prior to November 2009 and those between November 2009 – November 2012, but it did not have a major impact on validity measures (results not shown).

Discussion

Coded diagnoses available in administrative datasets are widely used for research, and previous studies have used them to identify marijuana-related hospitalizations in order to measure the impact of liberalizing marijuana policies (7-10). As a result, it is important to assess how well *ICD-CM* codes can reliably identify hospitalizations in which marijuana use may have been an underlying or contributing factor and to determine whether there are factors that influence their ability to identify this outcome of interest.

To obtain a gold standard for evaluation of *ICD-CM* codes, hospital discharge records were linked to those from the Washington State Trauma Registry (WSTR) in order to obtain toxicology screening information. The final linked dataset included 57% of all WSTR records. There are several explanations for why WSTR records may not link to a hospital discharge record. One reason is that patients treated in the emergency department for a trauma are often subsequently transferred to another facility for hospitalization. These scenarios typically generate two records in WSTR, and only the records from the resulting hospitalization were kept in the linked dataset. Additionally, WSTR records may relate to patients who were dead upon arrival to a hospital or that died in the emergency department, prior to being admitted for hospital care. In such situations, no corresponding hospital discharge record would be expected to exist. A very small proportion (2%) of all hospital discharge records were linked to WSTR, but this was anticipated as traumas represent the minority of hospitalizations. Comparing total counts of CHARS and WSTR records, the number of WSTR

records was less than 4% the total number of CHARS records. Finally, patient identifiers collected by CHARS improved substantially after 2008, which likely increased the probability of linkage among hospital discharges that occurred after 2008.

This study revealed that toxicology testing and marijuana-related diagnosis codes are relatively rare in hospitalized patients. Only a quarter of hospitalizations in the linked dataset underwent toxicology testing, with only 20% of those (~5% of the linked dataset) testing positive for marijuana. Cannabis-related diagnoses were also rare, with just over 2% of hospitalizations in the linked dataset having a marijuana-related diagnosis code. Cannabis-related diagnosis codes overall had low sensitivity, but very high specificity. As a result, counts of marijuana-related visits identified using *ICD* codes are prone to be underestimated, but of those visits that are identified, the patient was very likely to have used marijuana. Jouanjus, Leymarie, Tubery and Lapeyre-Mestre (16) came to similar conclusions after conducting extensive chart reviews of records containing marijuana-related codes. Another capture-recapture study reported that hospital discharge summaries provide incomplete identification of hospitalizations involving illicit drugs (including cannabis) when compared to healthcare provider reports of drug abuse and dependence and a toxicology laboratory database (17).

There are several cannabis-related diagnosis codes that may potentially be used when marijuana is the underlying or contributing cause of hospitalization. Assessment of individual cannabis-related codes alone and in combination revealed that the combination of all cannabis-related codes provided the highest sensitivity with the best performance, or nearly so, for all other validity measures. As a result, this study suggests it is not advisable to identify marijuana-related events using any single cannabis or psychodysleptic diagnosis code.

Coding guidance dictates that each hospitalization should be assigned a single principal diagnosis, which is defined by the Uniform Hospital Discharge Data Set as “that condition established after study to be chiefly responsible for occasioning the admission of the patient to the hospital for care (4).” Additional diagnoses, often referred to as “secondary diagnoses”, may be included for any conditions that coexist at the time of admission, that develop subsequently, that affect the treatment received, or that affect the length of stay (4). Aside from guidance on how to sequence certain *ICD-10-CM* codes that must be coupled together, the sequencing of secondary diagnoses is not dictated (4, 5). Even so, some studies using administrative datasets (e.g. Wang, Hall, Vigil, Banerji, Monte and VanDyke (10)), will identify an outcome using only the principal diagnosis or a limited number of secondary diagnosis codes, presumably on the premise that higher ranked codes may be most relevant to the reason for hospitalization. As a result of these practices, the impact of limiting diagnosis codes was assessed. Recalculation of validity measures using the first five or ten codes was found to reduce sensitivity drastically without marked improvement in other validity measures. Limiting to principal diagnosis may provide optimal identification of an outcome of interest in certain scenarios (18), but such an approach was immaterial to this study since only one record had a primary diagnosis code that was marijuana-related.

Since coding practices, and the codes themselves, are subject to change over time, it is critical to assess whether reliability of diagnosis codes varies accordingly. Upon initial review, the change to *ICD-10-CM* appeared to be associated with an increase in sensitivity of marijuana-related diagnosis codes, but when validity measures were calculated according to the timeframes relevant to marijuana policy, increased sensitivity was actually detected in hospital discharge records collected between December 2012 and June 2014, when marijuana use and possession, but not sales, was legal in Washington State and prior to the transition to *ICD-10-CM*. These measures remained relatively stable through December 2016, during which time both retail sale of marijuana began and the transition to *ICD-10-CM* occurred. Since the change to *ICD-10-CM* did not occur until late 2015 but sensitivity increased as early as December 2012, it seems that patient openness with providers, modified history taking practices, improved documentation, or hospital policies, rather than the change in coding standards, had the largest impact on the validity of marijuana-related diagnosis codes. This hypothesis is supported by the observation that specificity of marijuana-related codes decreased after marijuana possession and use was legalized, which may be an indication of increased reporting and coding of cannabis involvement, even if cannabis use is not actually an underlying or contributing cause of hospitalization. These findings are not unique to this study, as Myers, Leung, Shaheen and Li (3) have also reported minimal impact of the change to *ICD-10* on the validity of acetaminophen overdose codes.

A sensitivity analysis was conducted to assess the impact of another significant event in marijuana policy: the issuance of the "Ogden Memo", a memorandum released in October 2009 by the U.S. Deputy Attorney General directing United States Attorneys not to get involved in enforcement of federal marijuana laws if individuals were compliant with the laws states had enacted regarding medical marijuana. While the release of this memorandum has been credited with the proliferation of medical marijuana (9, 10), it appeared to have little impact on validity of cannabis-related codes when comparing hospitalizations from October 2009 – November 2012 to those that occurred prior to October 2009. In summary, researchers evaluating datasets involving administrative healthcare records collected both before and after marijuana legalization should be aware that the validity of marijuana-related diagnoses may change in tandem with landmark policy changes, but that the transition to *ICD-10-CM* coding standards will likely have little impact.

The sensitivity of cannabis-related codes was low. As a result, other, non-cannabis codes, were explored for their ability to reliably identify a marijuana-related hospitalization. The highest ranked non-cannabis diagnosis codes were all related to nicotine use or dependence. While these codes did improve capture of marijuana-related hospitalizations, the positive predictive value dropped far below what it was when cannabis-related codes were used alone. These additional codes may be useful if one's goal is to find as many potential marijuana-related hospitalizations as possible (e.g., for further review or follow-up). Otherwise, it would not be advisable to include other codes for identifying marijuana-related hospitalizations specifically.

As a result of the low concordance between cannabis-related codes and positive toxicology test result, the factors which were the biggest contributors to improving or degrading concordance were explored. A number of factors appeared to be significantly associated with concordance, but when the validity measures were recalculated among subgroups where concordance was the highest, they were not meaningfully improved. Even though the performance of marijuana-related codes could not be optimized by limiting to records with certain patient or visit characteristics, the resistance of the validity measures to changes in the underlying population indicates that cannabis-related code performance will be relatively unchanged regardless of the population in which they are used to identify cannabis-related events.

Nearly 80% of patients who tested positive for cannabis lacked a marijuana-related diagnosis code. One possible explanation for this discrepancy is that marijuana exposure may not have been considered clinically relevant and thus not recorded as a diagnosis (4). The inconsistency of toxicology test results and marijuana-related diagnosis codes does raise concerns regarding whether patients who received a cannabis-related diagnosis somehow differed from those who did not. In this study, patients who tested positive for marijuana and had a marijuana-related diagnosis code did not differ from those that did not, in terms of age, sex, race, or ethnicity. Injury and visit characteristics also did not differ appreciably between patients with and without cannabis-related diagnosis codes. There was some indication of differences in coding practices based on facility characteristics, which has been observed by others evaluating marijuana-related diagnosis codes (19). These analyses indicate that, among those who test positive for marijuana, there does not appear to be any systematic difference between the patients who receive a cannabis-related diagnosis code and those who do not. Even so, caution should be taken when comparing data obtained from different facilities, as results may be influenced by differences in coding practices at these facilities.

Many previous studies have been conducted to evaluate the performance of various *ICD* codes derived from administrative datasets (3, 20-23), but there are few studies that have evaluated marijuana-related diagnosis codes. Marx, Chen, Askenazi and Albanese (19) attempted to identify marijuana-related emergency department visits at three hospitals in Colorado during 2016 and 2017. The authors used a variety of methods (e.g., *ICD* codes, free-text terms) to identify potential records of interest and conducted chart reviews of the resulting records to determine which records truly involved an acute adverse effect of marijuana. As in this study, the most commonly identified marijuana-related codes were cannabis use (*ICD-9-CM* 305.2, *ICD-10-CM* F12.9) or cannabis abuse (*ICD-10-CM* F12.1) while other marijuana-related codes were rare. Marx, Chen, Askenazi and Albanese (19) determined the positive predictive value (PPV) of marijuana-related *ICD-10* codes to be 60%, with codes for poisoning by cannabis (T40.7) and cannabis abuse (F12.1) both being significantly associated with true acute adverse effects of marijuana (19). This estimate is lower than the 68% PPV estimated for the same *ICD-10-CM* codes used in the current study. Interestingly, the hospital in which marijuana-related codes had the lowest PPV had a practice of including a marijuana-related code anytime a patient tested positive for

marijuana, regardless of the reason for the emergency department visit. This suggests that a positive toxicology screen cannot be directly correlated with a marijuana exposure that precipitates the need for hospitalization. Monte, Shelton, Mills, Saben, Hopkinson, Sonn, Devivo, Chang, Fox, Brevik, Williamson and Abbott (24) also conducted a chart review from a single emergency department in Colorado containing marijuana-related ICD codes between 2012 and 2016. In their study, approximately 26% of records identified were considered to be at least partially attributable to cannabis.

A third study, whose primary aim was to describe and quantify adverse events related to cannabis use, completed chart reviews of records identified in an administrative dataset using cannabis-related *ICD-10* codes to determine plausibility of cannabis being causally related to the hospitalization (16). Cannabis-related disorder codes (*ICD-10* F12), corresponded to an 88% PPV of cannabis being involved, based on review of medical record review and toxicology screening and a 76% PPV of cannabis being at least possibly causally-related to hospitalization (16). These findings are in the range of PPVs identified for cannabis-disorder codes in the current study. Of those records that were not confirmed to be marijuana-related, in-depth review of medical charts revealed lack of information regarding involvement of cannabis or cited another reason for hospitalization other than cannabis exposure. Of note, Jouanjus, Leymarie, Tubery and Lapeyre-Mestre (16) did not evaluate records with poisoning, adverse effects or underdosing (*ICD-10* T40.7) codes but did consider records containing a code indicating involvement of multiple drugs (*ICD-10* F19). F19 codes corresponded to a 20% and 11% PPV of cannabis being involved or cannabis being causally related to hospitalization. There were 136 records in the present study with a code for polysubstance involvement, 110 of which did not also have a diagnosis code specific to cannabis. Sensitivity analyses indicate that alone, F19 codes had limited ability to detect marijuana-related hospitalizations, but false positives were also infrequent. When F19 codes were bundled with other marijuana-related diagnosis codes, validity measures for identifying marijuana-related hospitalizations are essentially unchanged. This indicates that F19 codes are not likely to hugely improve accurate capture of marijuana-related hospitalizations.

Limitations

There are several limitations to consider in this study. While *ICD* codes are widely used for research, there are many opportunities for measurement error when relying on *ICD* codes to identify an outcome (2). For instance, codes may be used to indicate a history of marijuana use, rather than an acute intoxication with marijuana, and thus overestimate the outcome (25). Approximately 2% of patients with a toxicology test result negative for marijuana received a marijuana-related diagnosis code. This could be a result of coding error (e.g., use of a cannabis-related code for synthetic cannabinoid such as spice) or possibly an example of the code being included as a result of prior marijuana use documented in the medical history rather than acute intoxication. Conversely, codes for marijuana use may be omitted from the patient's record if the patient was not tested, the patient did not mention use of marijuana or was not asked about marijuana use, or marijuana usage was considered irrelevant to the patient's need for hospitalization (16). Lack of coding

for marijuana involvement would lead to an underestimate of the outcome. Additionally, coding practices may change over time with changes in staffing or hospital policies. In this study, legalization of marijuana did appear to have an impact on coding practices. Researchers should be aware of such external factors that may influence coding practices.

The minority of patients underwent toxicology screening. Clinicians may choose not to do toxicology screening if toxicology screening results would not have changed the course of care, the patient did not exhibit signs of intoxication, or the substance to which a patient was exposed is already known. Additionally, toxicology screening information was missing for a small proportion of linked records. It is unknown whether those patients underwent screening, and, if so, their result. If toxicology screening had been done in the full population, the validity measures may have changed. Sensitivity analyses were conducted to assess the potential influence of records missing toxicology results. While the sensitivity analyses indicated that there could be some impact of the missing information, the overall conclusions of the validity assessment would have remained the same.

Toxicology screens were used as the gold standard indicator for cannabis being an underlying or contributing cause of hospitalization. Unfortunately, a positive toxicology screen does not definitively indicate that a person is currently under the influence of cannabis. The urine toxicology test detects 11-nor-delta-9-tetrahydrocannabinol-9-carboxylic acid (9-carboxy-THC) and other metabolites of THC, which may take days to weeks to clear from a person's system, long after the acute effects of cannabis have worn off. The length of time these metabolites will be detected varies based on duration and frequency of exposure to cannabis. In addition, other substances may cause false positive or false negative toxicology test results (26) and urine toxicology test results cannot be directly correlated to the degree of exposure or level of impairment. In fact, Marx, Chen, Askenazi and Albanese (19) reported that marijuana-related *ICD* codes only had a PPV of 39% for acute adverse effects of marijuana at a hospital whose practice it was to include a marijuana-related *ICD* code whenever a toxicology screen was positive for marijuana, whereas hospitals that did not have this practice had PPVs of 86% and 84%. Additionally, toxicology screens may vary in their detection capabilities. Urine drug tests typically use one of two cutoff levels (e.g., 20 ng/mL or 50 ng/mL) for determining presence of cannabinoids (15). These cutoffs may vary between laboratories and may have varied with time. These factors may have limited the ability to isolate codes that identify acute cannabis intoxications that were actually contributory to being hospitalized as opposed to recording a history of cannabis use.

Finally, the study population was limited to people who were hospitalized for a trauma condition since the trauma registry collects toxicology testing information, which provided the basis on which this validation was conducted. As a result, it is unknown how marijuana-related diagnosis codes may perform in a full set of hospitalization records that contains a mixture of both illnesses and injuries. Many patients in the study population may have been intoxicated or intoxication may have led to their injury, but hospitalizations resulting from intoxication alone are under-represented or

missing from the study dataset entirely. It is expected that the sensitivity would be improved in a more general patient population as the dataset would contain more patients for whom intoxication may be the primary reason for seeking care and not an incidental factor.

Conclusions

This validity study assessed whether *ICD-9-CM and ICD-10-CM* codes obtained from an administrative hospital discharge dataset can be used to reliably identify cannabis-related hospitalizations. The results of this study indicate that use of *ICD* codes from administrative datasets to identify cannabis-related hospitalizations may not be ideal for describing the true count of marijuana-associated hospitalizations but may be useful for assessing trends in marijuana-related hospitalizations. Additionally, assuming there are no systematic differences between the hospitalizations that receive a cannabis-related diagnosis code and those that do not, datasets in which the outcome is identified using *ICD* codes may be suitable for describing populations experiencing a marijuana-related hospitalization or for evaluating risk factors associated with marijuana-related hospitalization. The results of this study provide future researchers with guidance on how to best use *ICD-CM* coded diagnoses for identifying marijuana-related hospitalizations, which will be of high priority as more states consider legalizing marijuana and researchers work to understand the public health impacts of these changes.

Figures

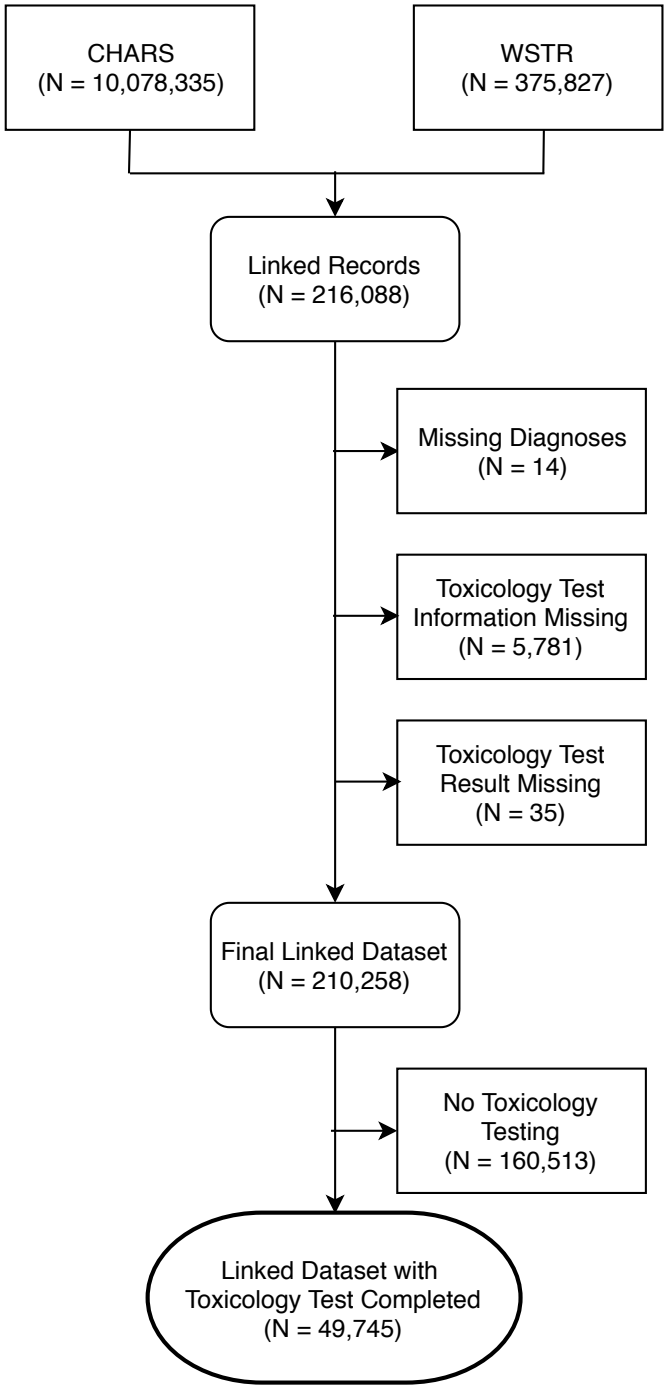

Figure 1. Creation of linked dataset for validity assessment.

Tables

Table 1. Patient and visit characteristics of linked dataset.

	No.	%
Age Category (In Years)		
0-11	15,617	7.4
12-17	10,951	5.2
18-20	7,776	3.7
21-30	23,516	11.2
31-50	41,921	19.9
50+	110,477	52.5
Sex		
Male	121,099	57.6
Race*		
White	101,043	48.1
Black	4,406	2.1
American Indian	2,492	1.2
Asian	3,127	1.5
Hawaiian/Pacific Islander	1,775	0.8
Other	368	0.2
Unknown	97,047	46.2
Ethnicity*		
Not Hispanic	103,637	49.3
Hispanic	6,976	3.3
Unknown	99,645	47.4
Patient Urbanicity		
Urban Core	152,925	72.7
Suburban	21,205	10.1
Large Rural	19,473	9.3
Small Town/Rural	15,672	7.5
Unknown	983	0.5
Washington Resident		
Yes	197,597	94.0
Washington Geography		
Eastern Washington	47,633	22.7
Western Washington	149,931	71.3
Non-Washington/Unknown	12,694	6.0
Weekend Admission		
Yes	68,498	32.6
Time of Admission*		
Morning (5am-11am)	17,671	8.4
Afternoon (11am-5pm)	32,836	15.6
Evening (5pm-11pm)	44,591	21.2
Late Night (11pm-5am)	31,400	14.9
Unknown	83,760	39.8
Insurance Type		
Public	102,758	48.9
Private	56,622	26.9
Self-Pay	16,262	7.7
Other/Unknown	34,616	16.5
Visit Type		
Inpatient	197,904	94.1
Observation*	12,354	5.9
Admission Type		
Emergency	154,131	73.3
Urgent	22,227	10.6
Elective	2,903	1.4
Trauma	30,693	14.6
Other/Unknown	304	0.1

Discharge Disposition		
Discharged	120,651	57.4
Admitted	56	0.0
Transferred to Hospital	3,885	1.8
Transferred to Other Care	74,310	35.3
Died	7,907	3.8
Other/Unknown	3,439	1.6
Care Setting		
Acute	209,634	99.7
Psychiatric	278	0.1
Other/Unspecified	346	0.2

*Information not collected until 2008

Table 2. Comparison of WSTR toxicology test results and CHARS diagnoses.

		WSTR Toxicology Results for Marijuana			
		Positive	Negative	Not tested	*Totals*
CHARS	Cannabis diagnosis	2,031 *True Positive* (Tox+/ICD+)	712 *False Positive* (Tox-/ICD+)	2,089 *Unknown Status*	4,832
	No cannabis diagnosis	7,775 *False Negative* (Tox+/ICD-)	39,227 *True Negative* (Tox-/ICD-)	158,424 *Unknown Status*	205,426
	Totals	9,806	39,939	160,513	210,258

Table 3. Count of marijuana-related *ICD-9-CM* diagnosis codes identified, by cannabis toxicology test result, discharged January 2002 – September 2015.

Marijuana-related diagnosis code	**Toxicology Positive** N[a] (Row %)	**Toxicology Negative** N[a] (Row %)	**Not Tested** N[a] (Row %)	**Totals**[a]
Nondependent cannabis abuse (305.2)	1607 (45)	532 (15)	1401 (40)	3540
Cannabis dependence (304.3)	112 (46)	45 (18)	89 (36)	246
Poisoning by psychodysleptics (969.6)	36 (86)	4 (9)	2 (5)	42
Accidental poisoning by psychodysleptics (E854.1)	10 (71)	2 (14)	2 (14)	14
Adverse effects by psychodysleptics (E939.6)	1 (100)	0	0	1
No cannabis-related diagnosis code	7,025 (4)	36,374 (19)	142,577 (77)	185,976

[a] Column totals of record counts do not add to the total number of records since each record may have more than one marijuana-related diagnosis code.

Table 4. Count of marijuana-related *ICD-10-CM* diagnosis codes identified, by cannabis toxicology test result, discharged Oct 2015 – Dec 2016.

Marijuana-related diagnosis code(s)	**Toxicology Positive** N[a] (Row %)	**Toxicology Negative** N[a] (Row %)	**Not Tested** N[a] (Row %)	**Totals**[a]
Nondependent cannabis abuse (F12.1xx)	93 (45)	31 (15)	82 (40)	206
Cannabis dependence (F12.2xx)	6 (46)	0	7 (54)	13
Cannabis use (F12.9xx)	185 (23)	102 (13)	511 (64)	798
Poisoning by cannabis (T40.7X1x, T40.7X2x, T40.7X3x, T40.7X4x)	3 (75)	0	1 (25)	4
Adverse effects of cannabis (T40.7X5x)	1 (100)	0	0	1
Underdosing of cannabis (T40.7X6x)	0	0	0	0
No cannabis-related diagnosis code	750 (4)	2,853 (15)	15,844 (81)	19,447

[a] Column totals of record counts do not add to the total number of records since each record may have more than one marijuana-related diagnosis code.

Table 5. Validity measures for any marijuana-related diagnosis code.

Validity Measure

Sensitivity	20.7
Specificity	98.2
Positive Predictive Value (PPV)	74.0
Negative Predictive Value (NPV)	83.5
Kappa	0.26
ROC	0.59

Table 6. Validity measures of marijuana-related *ICD-9-CM* diagnosis codes of any rank.

Marijuana-related diagnosis code(s)	Kappa	Sensitivity	Specificity	PPV	NPV	ROC
Nondependent cannabis abuse (305.2)	0.24	18.33	98.56	75.13	83.57	0.58
Cannabis dependence (304.3)	0.02	1.28	99.88	71.34	81.00	0.51
Poisoning by psychodysleptics (969.6)	0.01	0.41	99.99	90.00	80.88	0.50
Accidental poisoning by psychodysleptics (E854.1)	0.002	0.11	99.99	83.33	80.84	0.50
Adverse effects by psychodysleptics (E939.6)	0.0002	0.01	100.0	100.0	80.82	0.50
Cannabis-specific code (305.2 or 304.3)	0.25	19.58	98.44	74.88	83.76	0.59
Psychodysleptic code (969.6, E854.1, E939.6)	0.01	0.42	99.99	90.24	80.88	0.50
Cannabis or psychodysleptic (305.2, 304.3, 969.6, E854.1, E939.6)	0.25	19.89	98.43	75.08	83.81	0.59

Table 7. Validity measures of marijuana-related *ICD-10-CM* diagnosis codes of any rank.

Marijuana-related diagnosis code(s)	Kappa	Sensitivity	Specificity	PPV	NPV	ROC
Nondependent cannabis abuse (F12.1xx)	0.11	8.97	98.96	75.00	75.79	0.54
Cannabis dependence (F12.2xx)	0.01	0.58	100.0	100.0	74.33	0.50
Cannabis use (F12.9xx)	0.19	17.84	96.58	64.46	77.19	0.57
Poisoning by cannabis (T40.7X1x, T40.7X2x, T40.7X3x, T40.7X4x)	0.004	0.29	100.0	100.0	74.28	0.50
Adverse effects of cannabis (T40.7X5x)	0.001	0.10	100.0	100.0	74.24	0.50
Underdosing of cannabis (T40.7X6x)	--	--	--	--	--	--
Any cannabis (F12, T40.7)	0.29	27.68	95.50	68.33	79.18	0.61

Table 8. Validity measures for any marijuana-related diagnosis code during each marijuana policy timeframe.

Policy	Kappa	Sensitivity	Specificity	PPV	NPV	ROC
Medical Marijuana (Jan 2002-Nov 2012)	0.24	17.9	98.8	77.0	84.0	0.58
Recreational Marijuana (Dec 2012-Jun 2014)	0.33	27.9	97.2	71.9	84.1	0.63
Retail Marijuana (Jul 2014-Dec 2016)	0.30	28.4	95.7	68.5	80.0	0.62
Recreational Marijuana (Dec 2012-Jun 2014) or Retail Marijuana (Jul 2014-Dec 2016)	0.31	28.2	96.2	69.5	81.5	0.62

Appendix A. Extended Results

Table 1. Validity measures of marijuana-related *ICD-9-CM* diagnosis codes ranked 1 – 5.

Marijuana-related diagnosis code(s)	Kappa	Sensitivity	Specificity	PPV	NPV	ROC
Nondependent cannabis abuse (305.2)	0.09	6.55	99.59	78.95	81.79	0.53
Cannabis dependence (304.3)	0.01	0.54	99.96	74.60	80.90	0.50
Poisoning by psychodysleptics (969.6)	0.003	0.17	99.99	88.24	80.85	0.50
Accidental poisoning by psychodysleptics (E854.1)	0.002	0.11	99.99	83.33	80.84	0.50
Adverse effects by psychodysleptics (E939.6)	0.0002	0.01	100.0	100.0	80.82	0.50
Cannabis-specific code (305.2 or 304.3)	0.10	7.08	99.54	78.61	81.87	0.53
Psychodysleptic code (969.6, E854.1, E939.6)	0.004	0.24	99.99	91.30	80.86	0.50
Cannabis or psychodysleptic (305.2, 304.3, 969.6, E854.1, E939.6)	0.10	7.32	99.54	78.97	81.90	0.53

Table 2. Validity measures of marijuana-related *ICD-9-CM* diagnosis codes ranked 1 – 10.

Marijuana-related diagnosis code(s)	Kappa	Sensitivity	Specificity	PPV	NPV	ROC
Nondependent cannabis abuse (305.2)	0.20	15.08	98.91	76.59	83.07	0.57
Cannabis dependence (304.3)	0.02	1.11	99.89	70.80	80.98	0.51
Poisoning by psychodysleptics (969.6)	0.005	0.34	99.99	88.24	80.87	0.50
Accidental poisoning by psychodysleptics (E854.1)	0.002	0.11	99.99	83.33	80.84	0.50
Adverse effects by psychodysleptics (E939.6)	0.0002	0.01	100.0	100.0	80.82	0.50
Cannabis-specific code (305.2 or 304.3)	0.21	16.18	98.80	76.17	83.24	0.57
Cannabis or psychodysleptic (305.2, 304.3, 969.6, E854.1, E939.6)	0.22	16.55	98.79	76.41	83.30	0.58

Table 3. Validity measures of marijuana-related *ICD-10-CM* diagnosis codes ranked 1 – 5.

Marijuana-related diagnosis code(s)	Kappa	Sensitivity	Specificity	PPV	NPV	ROC
Nondependent cannabis abuse (F12.1xx)	0.02	1.35	99.73	63.64	74.43	0.51
Cannabis dependence (F12.2xx)	0.003	0.19	100.0	100.0	74.26	0.50
Cannabis use (F12.9xx)	0.05	3.95	99.33	67.21	74.86	0.52
Poisoning by cannabis (T40.7X1x, T40.7X2x, T40.7X3x, T40.7X4x)	--	--	--	--	--	--
Adverse effects of cannabis (T40.7X5x)	--	--	--	--	--	--
Underdosing of cannabis (T40.7X6x)	--	--	--	--	--	--
Any cannabis (F12, T40.7)	0.07	5.50	99.06	67.06	75.11	0.52

Table 4. Validity measures of marijuana-related *ICD-10-CM* diagnosis codes ranked 1 – 10.

Marijuana-related diagnosis code(s)	Kappa	Sensitivity	Specificity	PPV	NPV	ROC
Nondependent cannabis abuse (F12.1xx)	0.06	5.11	99.33	72.60	75.09	0.52
Cannabis dependence (F12.2xx)	0.004	0.29	100.0	100.0	74.28	0.50
Cannabis use (F12.9xx)	0.13	11.48	98.19	68.79	76.16	0.55
Poisoning by cannabis (T40.7X1x, T40.7X2x, T40.7X3x, T40.7X4x)	0.001	0.10	100.0	100.0	74.24	0.50
Adverse effects of cannabis (T40.7X5x)	--	--	--	--	--	--
Underdosing of cannabis (T40.7X6x)	--	--	--	--	--	--
Any cannabis (F12, T40.7)	0.19	16.97	97.52	70.4	77.18	0.57

Table 5. Sensitivity analysis, all missing toxicology test results converted to positive: Validity measures of marijuana-related *ICD-9-CM* diagnosis codes of any rank.

Marijuana-related diagnosis code(s)	Kappa	Sensitivity	Specificity	PPV	NPV	ROC
Nondependent cannabis abuse (305.2)	0.15	12.2	98.56	75.89	75.17	0.55
Cannabis dependence (304.3)	0.01	0.82	99.88	71.52	73.08	0.50
Poisoning by psychodysleptics (969.6)	0.004	0.29	99.99	90.91	73.00	0.50
Accidental poisoning by psychodysleptics (E854.1)	0.001	0.09	99.99	86.67	72.96	0.50
Adverse effects by psychodysleptics (E939.6)	0.0001	0.01	100.0	100.0	72.94	0.50
Cannabis-specific code (305.2 or 304.3)	0.16	13.03	98.44	75.61	75.32	0.56
Psychodysleptic code (969.6, E854.1, E939.6)	0.004	0.31	99.99	91.30	73.00	0.50
Cannabis or psychodysleptic (305.2, 304.3, 969.6, E854.1, E939.6)	0.16	13.25	98.43	75.83	75.36	0.56

Table 6. Sensitivity analysis, all missing toxicology test results converted to negative: Validity measures of marijuana-related *ICD-9-CM* diagnosis codes of any rank.

Marijuana-related diagnosis code(s)	Kappa	Sensitivity	Specificity	PPV	NPV	ROC
Nondependent cannabis abuse (305.2)	0.24	18.33	98.57	72.81	85.22	0.58
Cannabis dependence (304.3)	0.02	1.28	99.89	70.89	82.86	0.51
Poisoning by psychodysleptics (969.6)	0.01	0.41	99.98	81.82	82.75	0.50
Accidental poisoning by psychodysleptics (E854.1)	0.002	0.11	99.99	66.67	82.71	0.50
Adverse effects by psychodysleptics (E939.6)	0.0002	0.01	100.0	100.0	82.69	0.50
Cannabis-specific code (305.2 or 304.3)	0.25	19.58	98.46	72.69	85.40	0.59
Psychodysleptic code (969.6, E854.1, E939.6)	0.01	0.42	99.98	80.43	82.75	0.50
Cannabis or psychodysleptic (305.2, 304.3, 969.6, E854.1, E939.6)	0.26	19.89	98.44	72.79	85.45	0.59

Table 7. Sensitivity analysis, all missing toxicology test results converted to positive: Validity measures of marijuana-related *ICD-10-CM* diagnosis codes of any rank.

Marijuana-related diagnosis code(s)	Kappa	Sensitivity	Specificity	PPV	NPV	ROC
Nondependent cannabis abuse (F12.1xx)	0.05	5.02	98.96	75.59	61.92	0.52
Cannabis dependence (F12.2xx)	0.004	0.31	100.0	100.0	61.03	0.50
Cannabis use (F12.9xx)	0.08	10.14	96.58	65.54	62.65	0.53
Poisoning by cannabis (T40.7X1x, T40.7X2x, T40.7X3x, T40.7X4x)	0.002	0.16	100.0	100.0	60.99	0.50
Adverse effects of cannabis (T40.7X5x)	0.001	0.05	100.0	100.0	60.96	0.50
Underdosing of cannabis (T40.7X6x)	--	--	--	--	--	--
Any cannabis (F12, T40.7)	0.13	15.63	95.55	69.21	63.87	0.56

Table 8. Sensitivity analysis, all missing toxicology test results converted to negative: Validity measures of marijuana-related *ICD-10-CM* diagnosis codes of any rank.

Marijuana-related diagnosis code(s)	Kappa	Sensitivity	Specificity	PPV	NPV	ROC
Nondependent cannabis abuse (F12.1xx)	0.12	8.97	99.12	73.23	80.22	0.54
Cannabis dependence (F12.2xx)	0.01	0.58	100.0	100.0	78.93	0.50
Cannabis use (F12.9xx)	0.20	17.84	97.13	62.50	81.49	0.57
Poisoning by cannabis (T40.7X1x, T40.7X2x, T40.7X3x, T40.7X4x)	0.005	0.29	100.0	100.0	78.88	0.50
Adverse effects of cannabis (T40.7X5x)	0.002	0.10	100.0	100.0	78.85	0.50
Underdosing of cannabis (T40.7X6x)	--	--	--	--	--	--
Any cannabis (F12, T40.7)	0.30	27.68	96.25	68.44	83.21	0.62

Table 9. Ten most common *ICD-9-CM* diagnosis codes among discordant pairs (Tox +/ICD -).

Diagnosis codes	Kappa	Sensitivity	Specificity	PPV	NPV	ROC
Tobacco use disorder (305.1)	0.13	29.7	83.7	30.2	83.4	0.57
Alcohol abuse, unspecified (305.00)	0.07	18.6	87.6	26.2	81.9	0.53
Acute posthemorrhagic anemia (285.1)	0.008	10.2	90.4	20.2	80.9	0.50
Contusion of lung without mention of open wound into thorax (861.21)	0.02	9.1	92.1	21.5	81.0	0.51
Traumatic pneumothorax without mention of open wound into thorax (860.0)	0.01	9.0	91.8	20.8	81.0	0.50
Unspecified essential hypertension (401.9)	-0.07	9.0	84.6	12.2	79.7	0.47
Acute respiratory failure (518.81)	0.008	8.1	92.5	20.4	80.9	0.50
Closed fracture of lumbar vertebra without mention of spinal cord injury (805.4)	-0.01	7.3	91.9	17.6	80.7	0.50
Open wound of scalp, without mention of complication (873.0)	0.003	7.2	93.1	19.6	80.9	0.50
Closed fracture of dorsal [thoracic] vertebra without mention of spinal cord injury (805.2)	-0.006	6.3	93.3	18.2	80.8	0.50
Any Cannabis or 305.1	0.22	40.7	82.9	36.0	85.5	0.62
Any Cannabis or top 10 *ICD-9-CM* code	0.05	73.3	36.7	21.6	85.3	0.55

Table 10. Ten most common *ICD-10-CM* diagnosis codes among discordant pairs (Tox +/ICD -).

Diagnosis codes	Kappa	Sensitivity	Specificity	PPV	NPV	ROC

Nicotine dependence, cigarettes, uncomplicated (F17.210)	0.13	31.1	81.2	36.5	77.2	0.56
Acute posthemorrhagic anemia (D62)	-0.003	21.1	78.6	25.5	74.2	0.50
Essential (primary) hypertension (I10)	-0.12	16.5	71.0	16.5	71.0	0.44
Encounter for immunization (Z23)	0.02	16.8	84.9	27.8	74.6	0.51
Alcohol abuse with intoxication, unspecified (F10.129)	0.04	11.6	91.8	33.0	74.9	0.52
Hypokalemia (E87.6)	-0.01	11.6	87.4	24.2	74.0	0.49
Traumatic pneumothorax, initial encounter (S27.0XXA)	0.02	10.9	91.0	29.6	74.6	0.51
Acute respiratory failure (J96.00)	0.02	8.8	92.5	29.0	74.5	0.51
Acute respiratory failure, with hypoxia (J96.01)	-0.03	8.0	89.6	21.1	73.7	0.49
Laceration without foreign body of scalp (S01.01XA)	-0.01	8.6	90.5	23.9	74.0	0.50
Any Cannabis (F12, T40.7) or Nicotine dependence, cigarettes, uncomplicated (F17.210)	0.25	47.3	78.8	43.6	81.1	0.63
Any Cannabis (F12, T40.7) or any top 10 ICD10-CM diagnosis codes	0.04	84.0	22.1	27.3	79.9	0.53

Table 11. Association of patient, facility, and visit factors to concordance of marijuana-related diagnosis codes and toxicology test results.

		Characteristic	**OR**	**95% CI**	**P-value**
Facility Characteristics	Facility Location	East	Ref		
		West	1.05	0.98 – 1.11	0.14
	Location Type	Rural	Ref		
		Urban	1.13	1.06 – 1.22	0.001
	Facility Type	Private	Ref		
		Public	1.27	1.21 – 1.33	<0.0001
	Facility Size	Small	Ref		
		Medium	0.99	0.84 – 1.16	0.88
		Large	1.10	0.95 – 1.28	0.20
	Facility Affiliation	Healthcare system	Ref		
		Independent	1.11	0.99 – 1.26	0.09
Patient Characteristics		Mean Age	1.03	1.03 – 1.03	<0.0001
	Age Category	<17	Ref		
		18-20	0.50	0.45 – 0.56	<0.0001
		21-30	0.63	0.57 – 0.69	<0.0001
		31-50	1.0	0.90 – 1.10	0.92
		51+	2.15	1.94 – 2.39	<0.0001
	Sex	Female	Ref		
		Male	0.56	0.53 – 0.59	<0.0001
	Race	White	Ref		
		Black	0.57	0.50 - 0.64	<0.0001
		Asian	3.06	2.16 - 4.35	<0.0001
		Pacific Islander	1.51	1.12 – 2.04	0.006
		Native American	0.67	0.57 – 0.78	<0.0001
		Other	0.85	0.53 - 1.37	0.50
	Ethnicity	Non-Hispanic	Ref		
		Hispanic	0.88	0.69 – 1.12	0.30
Injury Characteristics	Type of Injury	Cut/Pierce	Ref		
		Falls	2.28	2.03 – 2.55	<0.0001
		Fire/flame/heat	1.21	0.99 – 1.47	0.07
		Firearm	0.75	0.65 – 0.86	<0.0001
		Machinery	2.22	1.50 – 3.28	<0.0001
		Motor vehicle - occupant	1.41	1.26 – 1.57	<0.0001
		Motor vehicle - motorcyclist	1.29	1.13 - 1.48	<0.0001
		Motor vehicle – bicyclist	1.60	1.22 – 2.09	0.001

		Motor vehicle – pedestrian	1.88	1.61 – 2.20	<0.0001
		Motor vehicle - unspecified	1.01	0.68 – 1.50	0.95
		Bicyclist	1.56	1.27 – 1.93	<0.0001
		Pedestrian	2.74	1.37 – 5.50	0.004
		Transport	1.82	1.58 – 2.11	<0.0001
		Struck by/against	1.09	0.96 – 1.25	0.19
		Drowning	1.49	1.27 – 1.74	<0.0001
		Suffocation	2.72	1.30 – 5.68	0.008
		Other	1.43	1.01 – 2.04	0.05
		Severity of injury (ISS)	0.998	0.996 – 1.00	0.13
Visit Characteristics	Discharge Disposition	Home	Ref		
		Skilled Nursing Facility/Rehab	1.84	1.72 – 1.98	<0.0001
		Transfer	1.22	1.06 – 1.40	0.005
		Died	1.71	1.51 – 1.93	<0.0001
		Other	1.03	0.92 – 1.14	0.64
	Weekend Admission	No	Ref		
		Yes	0.89	0.85 – 0.94	<0.0001
		Mean Length of Stay	1.01	1.00 – 1.01	<0.0001
	Insurance Type	Public (e.g., Medicare, Medicaid, L & I)	Ref		
		Private	1.23	1.16 – 1.30	<0.0001
		Self-Pay	0.67	0.63 – 0.72	<0.0001
		Charity care	0.50	0.44 – 0.57	<0.0001
		Mean rank of marijuana-related diagnosis code	0.96	0.94 – 0.97	<0.0001
	Marijuana Policy	Medical Marijuana (Jan 2002-Nov 2012)	Ref		
		Recreational Marijuana (Dec 2012-Jun 2014)	0.96	0.88 - 1.04	0.34
		Retail Marijuana (Jul 2014-Dec 2016)	0.72	0.68 - 0.77	<0.0001

Table 12. Validity measures limiting to hospital discharge records with ≥1 factors related to concordance of marijuana-related diagnosis codes and toxicology test results.

	Kappa	Sensitivity	Specificity	PPV	NPV	ROC
Records with ≥1 characteristics significantly associated with concordance	0.26	20.5	98.4	73.3	85.3	0.59
Age <17 or 51+	0.28	20.6	99.0	73.3	90.3	0.60
Female	0.26	19.0	98.7	68.9	89.0	0.59
Asian	0.20	15.6	98.4	41.7	94.0	0.57
Falls, suffocation, machinery-related, transport-related, motor vehicle – pedestrian, pedestrian	0.27	19.8	99.0	75.9	88.3	0.59
Discharged to Skilled Nursing or Died	0.22	15.6	99.2	74.6	89.0	0.57
Public payer	0.27	22.1	98.0	73.1	83.7	0.60

Table 13. Association of patient, facility, and visit factors with having a toxicology test done.

Characteristic	No Toxicology (N=160,526)	Toxicology Test (N=49,781)	OR (95% CI)
Facility Characteristics			
Facility Location			
East	37,487 (23.4)	9,065 (18.2)	Ref
West	123,026 (76.7)	40,680 (81.8)	1.37 (1.33 – 1.40)
Location Type			
Rural	37,392 (23.3)	5,570 (11.2)	Ref
Urban	123,121 (76.7)	44,175 (88.8)	2.41 (2.34 – 2.48)
Facility Type			
Public	118,081 (73.6)	23,888 (48.0)	Ref
Private	42,432 (26.4)	25,857 (52.0)	3.01 (2.95 – 3.08)
Facility Size			
Small	9,853 (6.1)	1,210 (2.4)	Ref

Medium	39,766 (24.8)	8,066 (16.2)	1.65 (1.55 – 1.76)
Large	110,894 (69.1)	40,469 (81.4)	2.97 (2.80 – 3.16)
Facility Affiliation			
Healthcare system	145,114 (90.4)	47,732 (96.0)	Ref
Independent	15,399 (9.6)	2,013 (4.1)	0.40 (0.38 – 0.42)
Patient Characteristics			
Mean Age	54.2	41.3	0.98 (0.981 – 0.982)
Age Group			
<18	23,167 (14.4)	3,401 (6.8)	Ref
18-20	4,189 (2.6)	3,587 (7.2)	5.8 (5.5 – 6.2)
21-30	12,753 (8.0)	10,763 (21.6)	5.7 (5.5 – 6.0)
31-50	23,655 (14.7)	15,659 (31.5)	4.5 (4.3 – 4.7)
51+	96,749 (60.3)	16,335 (32.8)	1.2 (1.1 – 1.2)
Sex			
Female	74,937 (46.7)	14,222 (28.6)	Ref
Male	85,576 (53.3)	35,523 (71.4)	2.19 (2.14 – 2.24)
Race			
White	83,146 (90.1)	17,897 (85.4)	Ref
Black	3,072 (3.3)	1,334 (6.4)	2.0 (1.9 – 2.2)
Asian	2,664 (2.9)	463 (2.2)	0.8 (0.7 – 0.9)
Pacific Islander	1,406 (1.5)	369 (1.8)	1.2 (1.1 – 1.4)
Native American	1,691 (1.8)	801 (3.8)	2.2 (2.0 – 2.4)
Other	269 (0.3)	99 (0.5)	1.7 (1.4 – 2.2)
Ethnicity			
Non-Hispanic	22,443 (93.3)	5,173 (92.0)	Ref
Hispanic	1,625 (6.8)	451 (8.0)	0.8 (0.7 – 0.9)
Injury Characteristics			
Type of injury			
Cut/Pierce	3,119 (2.3)	2,319 (5.3)	Ref
Falls	78,473 (58.4)	11,112 (25.4)	0.19 (0.18 – 0.20)
Fire/flame/heat	5,615 (4.2)	791 (1.8)	0.19 (0.17 – 0.21)
Firearm	2,064 (1.5)	1,997 (4.6)	1.30 (1.20 – 1.41)
Machinery	1,536 (1.1)	256 (0.6)	0.22 (0.19 – 0.26)
Motor vehicle - occupant	12,109 (9.0)	12,532 (28.6)	1.39 (1.31 – 1.48)
Motor vehicle - motorcyclist	3,902 (2.9)	3,041 (7.0)	1.05 (0.98 – 1.13)
Motor vehicle – bicyclist	781 (0.6)	476 (1.1)	0.82 (0.72 – 0.93)
Motor vehicle – pedestrian	2,721 (2.0)	2,198 (5.0)	1.09 (1.01 – 1.17)
Motor vehicle - unspecified	177 (0.1)	151 (0.4)	1.15 (0.92 – 1.44)
Bicyclist	2,731 (2.0)	853 (2.0)	0.42 (0.38 – 0.46)
Pedestrian	183 (0.1)	93 (0.2)	0.68 (0.53 – 0.88)
Transport	7,181 (5.3)	2,807 (6.4)	0.53 (0.49 – 0.56)
Struck by/against	6,671 (5.0)	2,970 (6.8)	0.60 (0.56 – 0.64)
Drowning	199 (0.2)	82 (0.2)	0.55 (0.43 – 0.72)
Suffocation	118 (0.1)	235 (0.5)	2.68 (2.13 – 3.36)
Other	6,789 (5.1)	1,838 (4.2)	0.36 (0.34 – 0.39)
Mean Severity of injury (ISS)	9.5	14.7	1.06 (1.05 – 1.06)
Visit characteristics			
Discharge Disposition			
Home	93,509 (58.5)	33,952 (68.8)	Ref
Skilled Nursing Facility/Rehab	49,667 (31.1)	9,076 (18.4)	0.50 (0.49 – 0.52)
Transfer	8,152 (5.1)	1,541 (3.1)	0.52 (0.49 – 0.55)
Died	5,296 (3.3)	2,459 (5.0)	1.28 (1.22 – 1.34)
Other	3,359 (2.1)	2,329 (4.7)	1.91 (1.81 – 2.02)
Weekend			
No	109,240 (68.1)	32,520 (65.4)	Ref
Yes	51,273 (31.9)	17,225 (34.6)	1.13 (1.10 – 1.15)
Mean Length of Stay	5.11	7.31	1.03 (1.03 – 1.03)
Mean rank of marijuana-related diagnosis code	8.1	8.0	0.99 (0.98 – 1.00)
Insurance type			
Public (e.g., Medicare, Medicaid, L & I)	95,637 (59.6)	21,928 (44.1)	Ref
Private	54,707 (34.1)	19,668 (39.5)	1.6 (1.5 - 1.6)

Self-Pay	9,226 (5.8)	7,036 (14.1)	3.3 (3.2 - 3.4)
Charity care	956 (0.6)	1,113 (2.2)	5.1 (4.7 - 5.5)
Miscellaneous			
Marijuana Policy			
Medical Marijuana (Jan 2002-Nov 2012)	105,223 (65.6)	38,413 (77.2)	Ref
Recreational Marijuana (Dec 2012-Jun 2014)	21,305 (13.3)	4,099 (8.2)	0.53 (0.51 – 0.55)
Retail Marijuana (Jul 2014-Dec 2016)	33,985 (21.2)	7,233 (14.5)	0.58 (0.57 – 0.60)

Table 14. Association of patient, facility, and visit factors with having a marijuana-related diagnosis code among patients that test positive for marijuana.

Characteristic	**No Cannabis-related diagnosis code (N = 205,423)**	**Cannabis-related diagnosis code (N = 4,835)**	χ^2
Facility Characteristics			
Facility Location			<0.0001
East	1,474 (19.0)	693 (34.1)	
West	6.301 (81.0)	1,338 (65.9)	
Location Type			<0.0001
Rural	979 (12.6)	322 (15.9)	
Urban	6,796 (87.4)	1,709 (84.2)	
Facility Type			<0.0001
Public	3.560 (45.8)	610 (30.0)	
Private	4,215 (54.2)	1,421 (70.0)	
Facility Size			<0.0001
Small	202 (2.6)	63 (3.1)	
Medium	1,408 (18.1)	450 (22.2)	
Large	6,165 (79.3)	1,518 (74.7)	
Facility Affiliation			<0.0001
Healthcare system	7,483 (96.2)	1,903 (93.7)	
Independent	292 (3.8)	128 (6.3)	
Patient Characteristics			
Mean Age	33.8	31.8	<0.0001
Age Group			<0.0001
<18	530 (6.8)	208 (10.2)	
18-20	994 (12.8)	245 (12.1)	
21-30	2,454 (31.6)	690 (34.0)	
31-50	2.472 (31.8)	615 (30.3)	
51+	1,325 (17.0)	273 (13.4)	
Sex			0.04
Female	1,505 (19.4)	352 (17.3)	
Male	6,270 (80.6)	1,679 (82.7)	
Race			0.21
White	3,133 (82.7)	961 (81.4)	
Black	369 (9.7)	111 (9.4)	
Asian	27 (0.7)	5 (0.4)	
Pacific Islander	49 (1.3)	18 (1.5)	
Native American	192 (5.1)	75 (6.4)	
Other	17 (0.5)	10 (0.9)	
Ethnicity			0.54
Non-Hispanic	944 (91.8)	366 (90.8)	
Hispanic	84 (8.2)	37 (9.2)	
Injury Characteristics			
Type of injury			<0.0001
Cut/Pierce	475 (7.1)	133 (8.3)	
Falls	1,166 (17.4)	287 (17.9)	
Fire/flame/heat	132 (2.0)	23 (1.4)	
Firearm	525 (7.9)	132 (8.2)	
Machinery	29 (0.4)	4 (0.3)	
Motor vehicle - occupant	2,031 (30.4)	497 (30.9)	
Motor vehicle - motorcyclist	536 (8.0)	74 (4.6)	
Motor vehicle – bicyclist	67 (1.0)	21 (1.3)	

Motor vehicle – pedestrian	280 (4.2)	67 (4.2)	
Motor vehicle - unspecified	33 (0.5)	9 (0.6)	
Bicyclist	125 (1.9)	31 (1.9)	
Pedestrian	8 (0.1)	3 (0.2)	
Transport	372 (5.6)	81 (5.0)	
Struck by/against	586 (8.8)	160 (10.0)	
Drowning	8 (0.1)	1 (0.1)	
Suffocation	33 (0.5)	23 (1.4)	
Other	279 (4.2)	61 (3.8)	
Mean Severity of injury (ISS)	15.1	12.0	<0.0001
Visit characteristics			
Discharge Disposition			<0.0001
Home	5,900 (76.4)	1,567 (77.8)	
Skilled Nursing Facility/Rehab	955 (12.4)	187 (9.3)	
Transfer	230 (3.0)	56 (2.8)	
Died	284 (3.7)	42 (2.1)	
Other	356 (4.6)	161 (8.0)	
Weekend			0.15
No	4,883 (62.8)	1,311 (64.6)	
Yes	2,892 (37.2)	720 (35.5)	
Mean Length of Stay	6.9	5.2	<0.0001
Insurance type			0.004
Public (e.g., Medicare, Medicaid, L & I)	3,369 (43.3)	953 (46.9)	
Private	2,601 (33.5)	599 (29.5)	
Self-Pay	1,499 (19.3)	405 (19.9)	
Charity care	306 (3.9)	74 (3.6)	
Miscellaneous			
Marijuana Policy			<0.0001
Medical Marijuana (Jan 2002-Nov 2012)	5,878 (75.6)	1,285 (63.3)	
Recreational Marijuana (Dec 2012-Jun 2014)	601 (7.7)	233 (11.5)	
Retail Marijuana (Jul 2014-Dec 2016)	1,296 (16.7)	513 (25.3)	

Chapter 2: Marijuana-related Hospitalizations

Association of Marijuana Policy Changes with Risk of Marijuana-related Hospital Discharges, 1994-2016, Washington State

Background

Washington State has been at the forefront of modern-day marijuana legislation for over two decades. In November 1998, Washington State became one of the first states to legalize use, possession, and cultivation of marijuana for certain approved medical conditions (Washington Initiative 692). Over the next several years, additional legislation pertaining to medical marijuana was passed. These were primarily clarifications and modifications to the original initiative; changes of note during this time include expansions to the list of medical conditions eligible for marijuana treatment and in the classifications of healthcare professionals allowed to issue medical authorizations for use of marijuana (27). The proliferation of state-level medical marijuana legislation in Washington State and elsewhere prompted the United States Deputy Attorney General David Ogden to issue a memorandum in October 2009 that directed United States Attorneys not to get involved in enforcement of federal marijuana laws if individuals were compliant with the state laws regarding medical marijuana. In 2011, additional legislation was passed in Washington State which developed a framework for the establishment of collective gardens. These collective gardens evolved into dispensaries, which were essentially retail access points for medical marijuana and were not licensed or regulated. In November 2012, Washington State and Colorado became the first two states to pass legislation allowing the use, possession, and sale of marijuana for recreational purposes for adults 21 years of age or older (Washington Initiative 502 and Colorado Amendment 64, respectively). Such legislation was unprecedented not only in the United States but also internationally. Washington Initiative 502 came to full fruition in July 2014 when the first licensed retail marijuana outlets opened in Washington State.

Marijuana is harvested from the female *Cannabis sativa* plant. *Cannabis sativa* contains numerous chemical compounds, but the primary psychoactive compound is delta-9-tetra-hydrocannabidiol (THC) (26, 28). Once in the blood, THC stimulates a release of dopamine in addition to disrupting the function of several areas of the brain (29, 30). Marijuana intoxication results in one or more of the following: feelings of euphoria (associated with increases in dopamine), disinhibition, anxiety, paranoia, temporal slowing, depersonalization, derealization, hallucinations, and impaired judgment, attention, or reaction time (31). Additional signs of marijuana intoxication include increased appetite, dry mouth, bloodshot eyes, or rapid heart rate (31). The magnitude of these effects are highly dependent on the dose used, the route of administration, user's prior experience with cannabis, any concurrent drug use, the setting and the mindset of the user (32).

Supporters of marijuana often cite its therapeutic effects. These qualities include its ability to provide relief from chronic pain, nausea, or spasticity symptoms, especially in people experiencing chronic or debilitating medical conditions (33). Additionally, it may be used as a form of relaxation (31). While marijuana may elicit desirable effects, like most substances, it also has the potential to be provoke undesirable health effects. Studies have reported an association between marijuana intoxication and a collection of acute health consequences. These include stimulation of negative psychological effects such as feelings of anxiety, psychotic episodes, or severe paranoia instead of the euphoria reported by most users (34). Some studies have reported increased risk of cardiac events and stroke after cannabis use (16, 34, 35). Marijuana is sometimes used to relieve nausea, but some users, especially those with a history of chronic use, experience cyclic episodes of severe nausea and vomiting after smoking cannabis, a condition known as cannabinoid hyperemesis syndrome (36). Studies have reported up to two times increased risk of traffic crash if driving while intoxicated by marijuana (37, 38). While people tend to drive more cautiously while intoxicated, studies have reported increases in lane-weaving and reduced reaction times, which may lead to increased risk for traffic crash (37-39). When marijuana is used in combination with alcohol, the risk of car crash is increased above use of either substance independently (39). Potential health effects associated with long-term marijuana use include chronic bronchitis, lower birthweight of offspring with maternal use, impairments in learning and memory, increased risk of development of schizophrenia or other psychoses, and increased risk of substance dependence (33).

Due to the complete novelty of legalizing recreational marijuana, researchers were only able to speculate about the potential impacts of such legislation on marijuana usage rates and public health prior to its enactment. Early reports from Washington State and Colorado indicate there may be some negative health consequences associated with legalization of marijuana. The Rocky Mountain Poison and Drug Center and Washington Poison Center have both reported increases in marijuana exposure calls since recreational marijuana became commercially available in 2014 (8, 40, 41). The number of marijuana-related hospitalizations in Colorado has increased significantly each year since 2000, when Colorado legalized marijuana for medical use (8, 40). Marijuana-related emergency department visits in Colorado have significantly increased annually since 2012, when marijuana was legalized (8). Tefft, Arnold and Grabowski (42) reported a noticeable increase in the number and proportion of drivers involved in fatal crashes testing positive for THC in Washington State in 2014, compared to 2010 through 2013. Additionally, Colorado reported one self-inflicted death after consumption of an edible marijuana product in 2014 (43).

In summary, legalization may lead to increased marijuana usage and, in turn, increased rates of adverse health effects associated with both acute and chronic marijuana use, which could have significant negative effects on the population's health and place additional burden on the healthcare system. The objective of this study is to assess the impact of various key marijuana policies on the likelihood of marijuana-related hospital discharges in Washington State.

To our knowledge, this study will be the first evaluation of the liberalization of marijuana policies on severe health events in Washington State.

Methods

Study Design

This interrupted time series study used 23 years (1994 – 2016) of Washington State hospital discharge records from the Comprehensive Hospital Abstract Reporting System to assess whether major changes in marijuana policy were associated with the experiencing a marijuana-related hospitalization.

Data Collection

Hospital discharge records are collected by the Washington State Department of Health through the Comprehensive Hospital Abstract Reporting System (CHARS). This administrative dataset contains information on all hospitalizations that occur in Washington State, with the exception of those occurring at federal hospitals. CHARS records were obtained for discharges occurring January 1994 – December 2016. Approval to use these data was obtained from the Washington State Institutional Review Board (Study ID: D-021116-H).

Study Subjects

All hospital discharges that had at least one coded diagnosis or external cause of injury were included. Cannabis-related hospital discharges were identified by isolating records with a diagnosis indicating cannabis dependence (*ICD-9-CM*: 304.3x), non-dependent cannabis abuse (*ICD-9-CM*: 305.2x), cannabis-related disorder (*ICD-10-CM*: F12.xxx), or poisoning by cannabis (*ICD-10-CM*: T40.7xxx). In addition, hospital discharges for poisonings and adverse effects of psychodysleptic drugs (*ICD-9-CM*: 969.6, E854.1, E939.6) were included in an attempt to capture unintentional cannabis poisonings or adverse effects of cannabis. A secondary, control, outcome was defined as a hospital discharge with a diagnosis of poisoning by primarily systemic and hematological agents (*ICD-9-CM*: 963.x, 964.x, or 960.7, *ICD-10-CM*: T45.xxx).

Statistical Analysis

Descriptive statistics were calculated for patient characteristics (e.g. age, gender, race, ethnicity, rural/urban residence, geographic region of residence) and hospitalization characteristics (e.g. severity of illness measured by length of stay, category of illness or injury – based on Medicare major diagnostic category). Characteristics of marijuana-related hospital discharges were assessed for each of the following time periods: pre-medical marijuana (January 1994 - November 1998), medical marijuana (December 1998 - September 2009), Ogden Memorandum (October 2009 - November 2012), legalization of recreational marijuana (December 2012 - June 2014), and opening of retail marijuana sales (July 2014 - December 2016). The mean rate of monthly marijuana-related hospital discharges for each policy

timeframe was calculated and an analysis of variance test was conducted to evaluate for significant differences in the mean monthly marijuana-related hospital discharge rate across policy timeframes.

Logistic regression was used to assess the log odds of a marijuana-related hospital discharge being associated with each marijuana policy change. The model had the following structure:

$$ln\left[\frac{\Pr(Y)}{1-\Pr(Y)}\right] = \beta_0 + \beta_1 X_1 + + \beta_2 X_2 + \beta_3 X_3 + \beta_4 X_4 + \beta_5 Z$$

with Y being an indicator of marijuana-related hospital discharge $(0/1)$, X_{1-4} being an indicator (0/1) for the marijuana policy (i.e., Pre-medical, Medical, Ogden Memorandum, Legalization, Retail) in effect at the time of hospital discharge, with the pre-medical marijuana timeframe serving as the reference timeframe, and Z is an indicator variable $(0/1)$ that indicates whether the hospital discharge occurred before or after the change from *ICD-9-CM* to *ICD-10-CM* coding on October 1, 2015. The coefficient β_0 represents the log odds ratio of marijuana-related hospital discharge at baseline (i.e., pre-medical), β_{1-4} describe the log odds ratios of marijuana-related hospital discharge during each subsequent timeframe (i.e., Medical, Ogden Memorandum, Legalization, and Retail using pre-medical as the reference timeframe), and β_5 describes the log odds ratio of outcome associated with the transition to *ICD-10-CM* (a potential confounder).

To further investigate the potential effects of marijuana policy changes on subpopulations, the logistic regression was repeated by stratifying the models by patient and hospitalization characteristics that substantially differed in the pre- and post-legalization periods, as identified during the descriptive analysis of marijuana-related hospital discharges.
To assess whether associations between marijuana-related hospital discharges and marijuana policy changes were spurious, the logistic regression analysis was repeated using hospital discharges with a diagnosis of poisoning by primarily systemic and hematological agents (e.g., antiallergic, antiemetic, antineoplastic, immunosuppressive, vitamins, enzymes, iron, anticoagulants, antithrombotic, fibrinolysis-affecting, anticoagulant antagonists, vitamin K) as a control outcome. Since the number of hospital discharges related to systemic and hematological agents was expected to be relatively stable during the study period, it was anticipated that no significant effect would be seen at any of the time points of interest in the marijuana analysis, and thus give further evidence of causality between marijuana policy changes and the effects observed. All statistical analyses were performed in Stata 14 (College Station, TX).

Results

Between 1994 and 2016, there were 14,670,164 hospital discharge records. Discharge records that were missing both diagnosis and external cause codes (N=1,854) were removed from the dataset, resulting in 14,668,310 records. 154,001 (1.0%) hospital discharge records contained a marijuana-related diagnosis code (Table 1).

Hospital discharge records with a diagnosis code for cannabis abuse, cannabis dependence, or cannabis use accounted for 98% of all marijuana-related hospital discharges (Table 2). Table 3 compares characteristics of hospital

discharge records with a marijuana-related diagnosis code to those without. Patients with a marijuana-related diagnosis code were younger, more likely to be male, have a concurrent alcohol or tobacco-related diagnosis, and be treated in a psychiatric unit or hospital.

Table 4 describes the patient, clinical, and facility characteristics of the marijuana-related hospital discharge records during each significant time period. The proportion of minors decreased over time while an increase occurred in patients over the age of 50. The mean length of stay decreased while the proportion of admissions that were classified as emergency increased over time. The proportion of patients who were transferred to other care or died increased over time. The proportion of discharges with an alcohol-related diagnosis decreased while hospitalizations with tobacco-related diagnosis increased. Hospitalizations with a major diagnostic category of mental health or substance abuse decreased while other categories increased. The proportion of acute care hospitalizations increased compared to psychiatric hospitalizations.

The monthly rate of marijuana-related hospitalizations increased over time, most noticeably after 2009 (Figure 1). An analysis of variance test indicated there was a significant change in the mean rate of marijuana-related hospital discharges across the policy timeframes (Table 5).

The logistic regression model indicated the odds of a marijuana-related hospital discharge significantly increased with each increasingly lenient change in marijuana-related policy compared to before November 1998, when there were no legal allowances for marijuana (Table 6). The model was adjusted for the change in diagnosis coding from *ICD-9-CM* to *ICD-10-CM* on October 1, 2015.

There were 8,770 hospital-discharges related to systemic drugs identified during the study timeframe. Hospital discharges related to systemic drugs were rare and relatively stable between 1994 and 2016 (Figure 2). The logistic regression model for the control outcome indicated the odds of systemic drug-related hospitalizations significantly changed with each modification to marijuana policy, but these changes were slight compared to the changes in the odds of marijuana-related hospital discharge (Table 7, Figure 3).

The odds of a marijuana-related hospital discharge increased more dramatically for people over 21 years of age than for patients under 21 with each change in marijuana policy (Figure 4). Breaking patients down into finer age groups, the largest increases were observed in patients over 50 years of age (Figure 5). Stratifications of the logistic model by patient urbanicity, care setting, and major diagnostic category were unremarkable.

Discussion

A very small proportion of all hospital discharges in Washington State are related to marijuana, but the proportion has increased from less than 0.5% prior to 1999 to nearly 3% after 2014. This correlates to a 613% increase in the

proportion of marijuana-related hospital discharges in 15 years. The passage of legislation allowing use of marijuana for medical purposes was associated with a subtle increase in marijuana-related hospital discharge rates; however, rates started to increase much more dramatically after the release of the Ogden Memorandum in 2009 and continued to increase substantially through 2016. The logistic regression model also indicated that each marijuana-related policy increased the odds of a marijuana-related hospital discharge relative to when there were no marijuana-tolerant policies (i.e., prior to 1998).

Similarly, Colorado has reported significant increases in the rate of marijuana-related hospitalizations with each more permissive phase of marijuana policy (8). After the Ogden Memorandum in 2009, Colorado reported a large increase in the number of medical marijuana applications received and dispensaries established (9). Colorado also noted a significant increase in marijuana-related hospitalization rates in 2010 compared to 2009, with subsequently increasing annual hospitalization rates through 2015 (10).

Increasingly tolerant marijuana laws reflect increased societal acceptance of marijuana and a perception that marijuana is low risk. Legalization is also likely to further reduce stigma and fear of legal consequences. These factors may encourage people who may not have previously used marijuana to do so. Data from the Washington Liquor and Cannabis Board indicates sale of cannabis in Washington State increased through 2016 from less than $5 million dollars in sales in July 2014 to nearly $100 million in sales in September 2016 (44, 45). Such increases may indicate both increasing consumption (frequency and dose) of marijuana by any individual user as well as expansion in the number of people using marijuana. The 2013-2014 National Survey on Drug Use and Health (NSDUH) indicated significantly increased reporting of past year (+8.1%), past month (+7.9%) and daily marijuana use (+4.4%) among Washington State adults 26 years of age or older compared to survey results obtained in 2002-2003 (46). Another analysis of NSDUH data indicated adults over the age of 21, who had prior experience with marijuana, were at increased risk of daily marijuana use after passage of medical marijuana laws (47). Additionally, increased potency of marijuana may increase the likelihood of adverse consequences from marijuana (48). In Washington, cannabis flower contained an average of 21% THC while inhalable extracts contained an average of nearly 69% THC in 2016 (44), whereas the THC content of seized marijuana was only 12% in 2014 (49). This reflects a sharp increase in potency of both legal and illegal marijuana products compared to seized marijuana products from the 1990s that contained an average of 4% THC. Increased numbers of marijuana users, frequency of use among existing marijuana users and increased potency may all contribute to increased risk of marijuana-related hospital discharge.

Stratified analysis indicated the associations between marijuana-related hospital discharge and marijuana policy changes were magnified among patients 21 years of age or older compared to minors. However, with finer age breakdowns, it is evident that the most dramatic increases in odds ratios occurred in patients over the age of 50. Previous

studies have reported that while older adults represent a small proportion of total marijuana users, the greatest increases in use between 2002 and 2014 were observed in this population (50). In this study, the proportion of marijuana-related hospital discharges involving older adults increased from 2.2% prior to 1998 to 32.5% after 2014. Older adults are more likely to report using marijuana for medicinal purposes than for nonmedicinal reasons (51). Older adults may view marijuana as a safer alternative to alcohol, illicit drugs or prescription drugs (52).There is evidence that marijuana may relieve chronic pain, neuropathic pain, and spasticity due to multiple sclerosis; however, older adults may also be more likely to experience adverse effects of marijuana (33, 53). People who use marijuana for medicinal purposes are doing so without evidence-based guidelines on specific strains or dosage (54). Marijuana use may also increase risk of injury among older adults (55). Older adults are already at increased risk of motor vehicle injuries and falls; marijuana may simply magnify this increased risk due to physical and cognitive alterations (56). Compounds in marijuana may also modify metabolism of prescription medications, increasing likelihood of drug interactions (57). Some studies indicate marijuana use may increase risk of cardiovascular events (e.g., stroke, cardiac arrest), outcomes for which older age is also an important risk factor (16, 34, 35, 58). The increased odds of marijuana-related hospital discharge may be a reflection of both increased use among older adults and increased risk of adverse events among older users of marijuana.

Both legalization of marijuana and the increased availability of marijuana products have raised much concern about potential negative consequences for minors. The proportion of marijuana-related hospital discharges that involved patients <21 years of age actually decreased from 26% prior to 1998 to 9.5% after 2014. The odds of minors experiencing a marijuana-related hospital discharge doubled after the release of the Ogden Memorandum, but the risk only slightly increased after legalization of marijuana and opening of retail stores, indicating that while these policy changes may have had some additional negative impact on minors, the impacts were minimal. In fact, the 2014 Washington Healthy Youth survey indicated little change in marijuana use among minors since 2012 (59).

The impact of legalization on children is of special interest because marijuana exposures may lead to severe adverse health effects (sometimes requiring medical intervention) and, because children are natural explorers, they may be at increased risk of accidental exposure (40, 60, 61). In this study, marijuana-related hospital discharges involving children under the age of 12 were extremely rare, with only 135 hospital discharges identified in 23 years. The proportion of marijuana-related hospital discharges that involved children <12 years of age remained stable throughout the entire study; however, logistic regression models indicated that the odds of marijuana-related hospital discharge in children <12 years of age increased fourfold after the Ogden Memorandum but there was no further increase in odds after legalization and opening of retail stores. This suggests that allowances for recreational marijuana may have had little impact on young children beyond the effects of legalized medical marijuana in the era after the Ogden Memorandum.

These findings are consistent with what has been reported from Colorado. Wang, Roosevelt and Heard (62) reported that no children under age 12 had been treated for marijuana ingestion between 2005 and 2009 at a large children's hospital, but that number rose to 14 between 2009 and 2011. Colorado also noted a significant increase in hospitalizations of young children once medical marijuana became commercially available (2010 – 2013) compared to legalized medical marijuana (2001 – 2009) (8). The Rocky Mountain Poison Center reported that the greatest increases in marijuana exposure calls between 2000 and 2015 occurred in children 0–8 years of age (10). Increases in poison center calls suggest that the number of marijuana exposures in young children may actually be increasing with each increasingly permissive marijuana policy change, but that these exposures are being managed outside of the hospital. With increased awareness of marijuana intoxication as the potential cause of symptoms, the number of children that end up being hospitalized for marijuana intoxication may be reduced. This may explain why legalization was not associated with an additional increased risk of marijuana-related hospital discharge in young children.

Since the initial law (I-502) was passed in 2012, lawmakers in Washington State have been continually revising marijuana laws in an attempt to reduce or prevent adverse impacts on children and minors. The initial law instituted a buffer zone around schools, playgrounds, and other places where children may be present; retail stores and their advertising are prohibited within these buffer zones (Revised Code of Washington 69.50). Additionally, the law included restrictions on advertising to control the amount of advertising, its content, and format. Products which are especially appealing to children are prohibited (Washington Administrative Code 314-55-077(7)). As recently as late 2018, in response to complaints about safety, the Washington Liquor and Cannabis Board re-evaluated products for their appeal to children and revised guidance on what is acceptable. There are also packaging and labeling requirements intended to reduce unintentional exposures. Specifically, marijuana-containing products shall be packaged in child-resistant packaging and each individual serving packaged. Packages and labeling shall not be appealing to children and, beginning in February 2017, were required to contain a standardized "not for kids" label that includes the Poison Center phone number. These laws have continued to be refined in an effort to improve protections for children.

Contemporaneous interventions may obscure the true effects of marijuana policy changes. Such interventions might include local moratoriums or bans on retail marijuana outlets which would lessen the potential statewide impact of marijuana legislation. In 2014, 14 cities or counties had permanently prohibited retail sales of recreational marijuana and 57 jurisdictions had instituted temporary moratoriums (63). By mid-2016, 60 cities or counties had instituted a permanent ban on marijuana retail sales and 7 jurisdictions had temporary bans (64). This equated to 30% of Washington's population residing in a location with either a temporary or permanent ban. As a result, the full impact of marijuana legalization on the risk of marijuana-related hospitalization may have been muted.

The significant increases in the odds of a marijuana-related hospital discharge with each change in marijuana

policy is not sufficient evidence for causal association. To assess the potential of a spurious association, the relationship between systemic drug-related hospital discharges, an outcome that would not be expected to be influenced by marijuana policy, and marijuana policies were assessed using the same logistic regression model that was used to assess marijuana-related hospital discharges. Associations between systemic drug-related hospital discharges and marijuana policies were significant, but the magnitude of the associations were much smaller than those observed for marijuana-related hospital discharges. Additionally, the values of the odds ratios did not increase substantially with each change in marijuana policy, like they did for marijuana-related hospital discharges. Potential explanations for the significant associations that were observed for systemic drug-related hospital discharges may include contemporaneous changes in the systemic drugs themselves or policies entirely unrelated to marijuana. The significance of the odds ratios in the control model does indicate that at least a portion of the association between marijuana-related hospital discharge and marijuana policy may be explained by factors unrelated to marijuana policy; however, it also supports the theory that these other factors are unlikely to fully explain the association between marijuana-related hospital discharge and marijuana policy changes.

Limitations

The legalization of marijuana in December 2012 may have impacted the willingness of patients to disclose use of marijuana, physician documentation and coding practices, and the frequency of physician inquiries about marijuana use. As such, any associations observed between marijuana policy and marijuana-related hospital discharge could instead be tied to changes in the underlying population, openness to marijuana usage, clinical practice, or hospitalization trends rather a true increased risk of marijuana-related hospital discharge.

Diagnosis codes were the primary method for identifying hospitalizations in which marijuana exposure was responsible, at least partially, for admission. These codes may not be used consistently when marijuana is involved, and their use may not indicate marijuana is an underlying or contributing cause of hospitalization. Instead they may only indicate a patient's history of usage. While codes for non-dependent marijuana abuse were, by far, the most common marijuana-related diagnosis code identified in marijuana-related hospital discharge records, the second and third most common marijuana-related codes identified were for cannabis dependence and use. For at least a fraction of marijuana-related hospital discharges, the presence of such codes may be a reflection of the patient's current or past use of cannabis rather than an indication that cannabis was an underlying or contributing cause to the current hospitalization.

Finally, *ICD-10-CM* is an entirely different code-set than *ICD-9-CM* and contains entirely different codes to reflect marijuana involvement. Data included after the change to *ICD-10-CM* may have reflected a transition period for hospitals that were still familiarizing themselves with the new coding standard and how to properly assign these codes to a hospital discharge. The potential impact of the change in *ICD* coding standard from *ICD-9-CM* to *ICD-10-CM* on October 1, 2015

was controlled for by including the change in the regression models. Additionally, a previous study (see Chapter 1) indicated the change in coding standard did not markedly change the validity of marijuana-related *ICD-CM* codes.

Future directions

The odds of a marijuana-related hospital discharge increased with each change in marijuana policy. It will be important to explore mechanisms for reducing the odds of a marijuana-related hospital discharge in the future and in other states that choose to legalize marijuana.

Since older adults appear to be at increasing risk of experiencing a marijuana-related hospital discharge, it is important to conduct additional studies to confirm these associations and investigate explanations for these possible associations. There are a number of potential explanations: 1) expansion of use in older adult populations 2) increases in the frequency or dose of marijuana 3) changes in the type of marijuana products used 4) increased risks of drug-drug interactions 5) increased risk of injuries from falls or motor vehicles or 6) exacerbations of pre-existing chronic illnesses requiring hospitalization. Regardless of the underlying mechanism, interventions among this population should be prioritized. Educational campaigns targeted towards older adult communities warning about risks associated with marijuana use in older age and increased potency of modern day marijuana may prove successful at reducing risks in this population. Healthcare providers could screen older adult patients for marijuana use and discuss potential risks with those reporting use. It may also be helpful for retailers, especially those which are “medically endorsed”, to provide education to older adult customers about their unique risks. Finally, while information may be limited, guidance on how to conscientiously use marijuana may also be of value to this population.

Many people are using marijuana for medicinal purposes, but they are doing so without any evidence-based guidance on which strains of marijuana or dosage of marijuana to use. Additionally, marijuana may interact with other drugs, causing changes in metabolism of drugs or possibly adverse events. More research on drug interactions with marijuana, especially in older adults, who may be physiologically different from younger people, is needed. Research on marijuana continues to be limited due to marijuana’s status as a schedule 1 substance under the federal Controlled Substances Act, so this will likely remain a critical need.

While recreational marijuana laws did not appear to have any different risk for young children than the release of the Ogden Memorandum, the presence of marijuana tolerant policies may have increased the risk of young children being exposed to marijuana. It is important to evaluate whether additional measures can be taken to further reduce the risk of young children experiencing accidental exposures to marijuana.

Conclusions

Increasingly lenient marijuana policies may be associated with increased risk of marijuana-related hospitalization, particularly in older adults and, to a lesser degree, young children. As such policies continue to proliferate, it will be critical to explore the likelihood that these associations are causally related. Additionally, policy makers and public health practitioners should be advised to identify and test potential interventions that may reduce the risk of adverse health consequences associated with marijuana legalization.

Figures

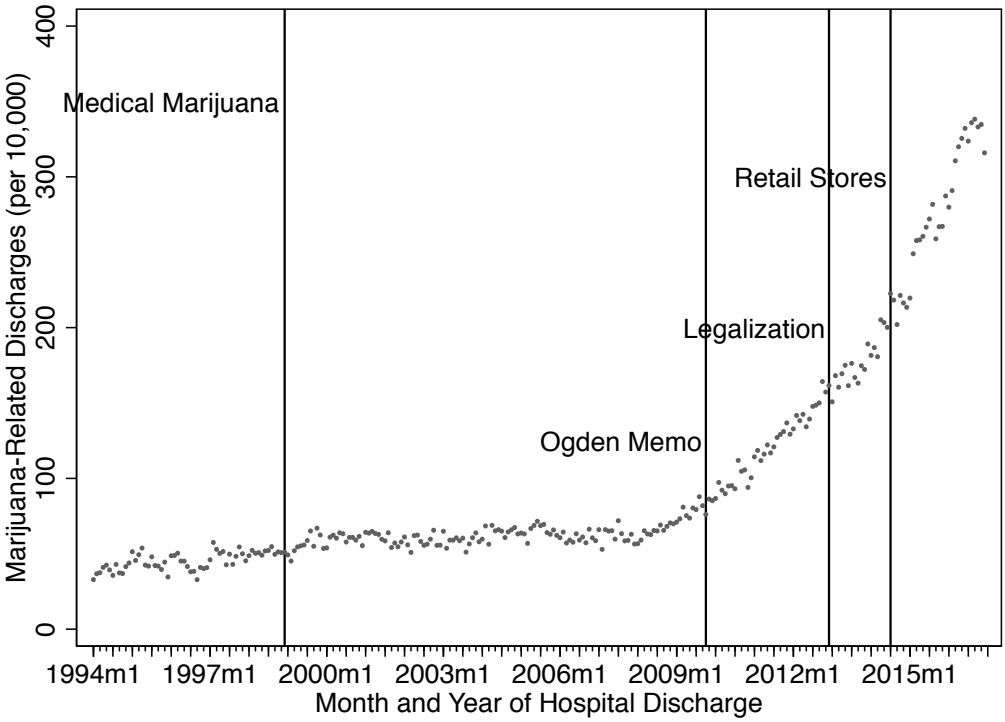

Figure 1. Monthly rate of marijuana-related hospital discharges per 10,000 total hospital discharges.

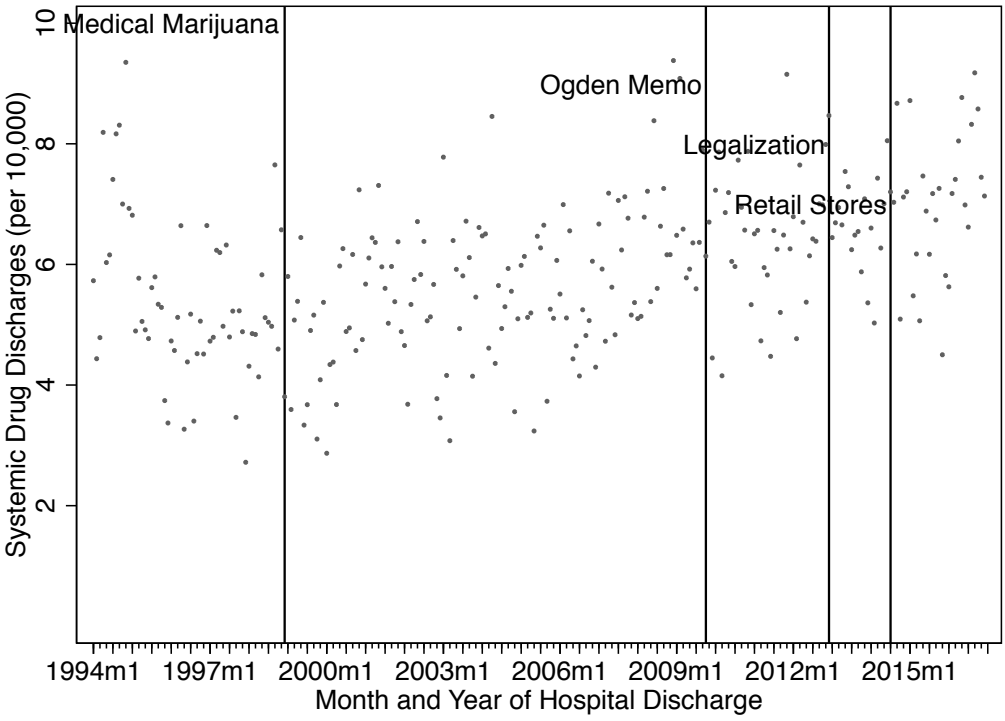

Figure 2. Monthly rate of systemic drug-related hospital discharges per 10,000 total hospital discharges.

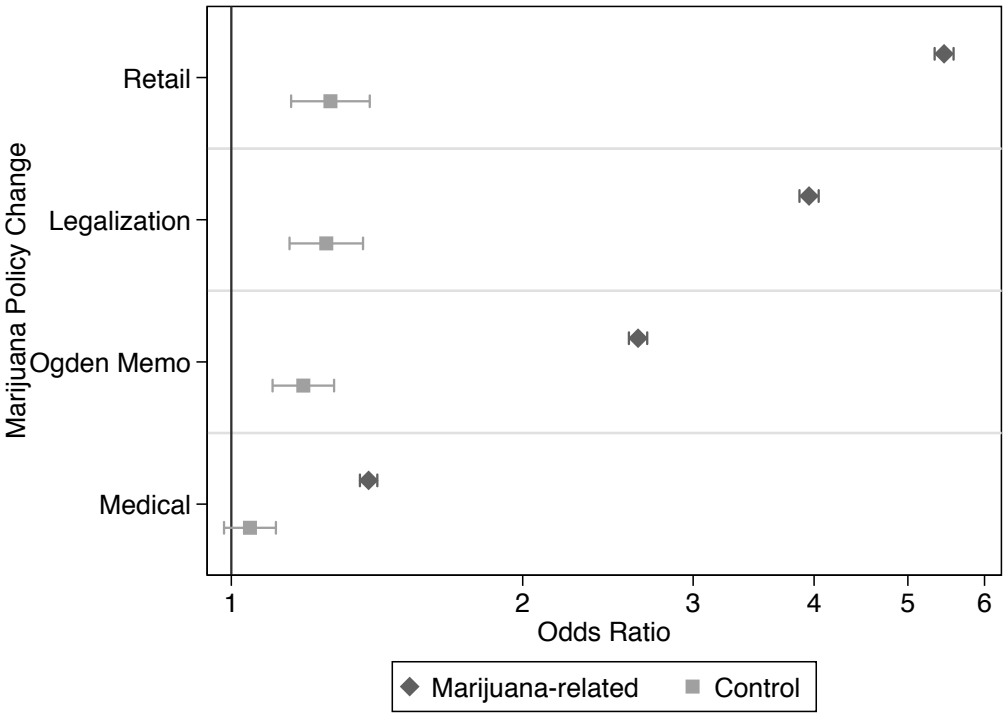

Figure 3. Point estimates of odds ratios with 95% confidence intervals for each change in marijuana policy obtained from logistic regression models.

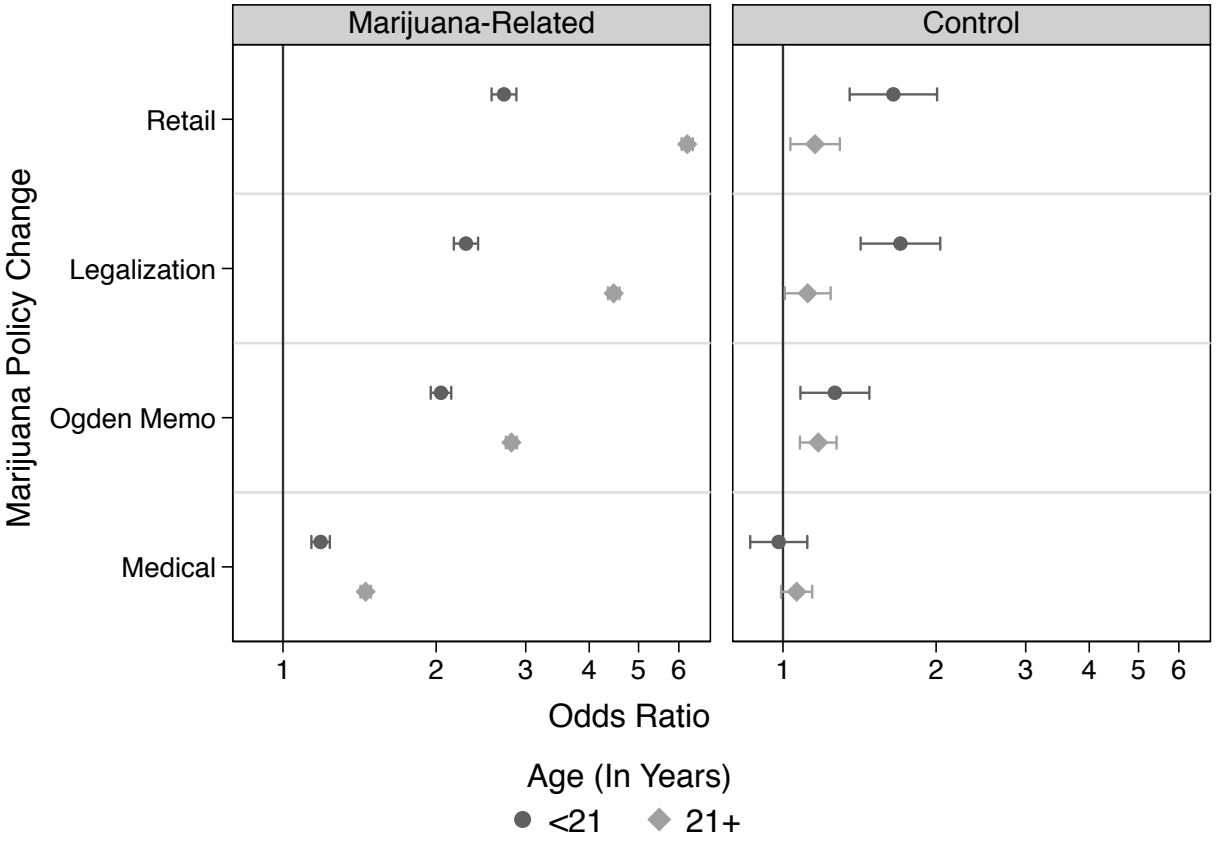

Figure 4. Point estimates of odds ratios with 95% confidence intervals for each change in marijuana policy obtained from logistic regression models, stratified by minor status.

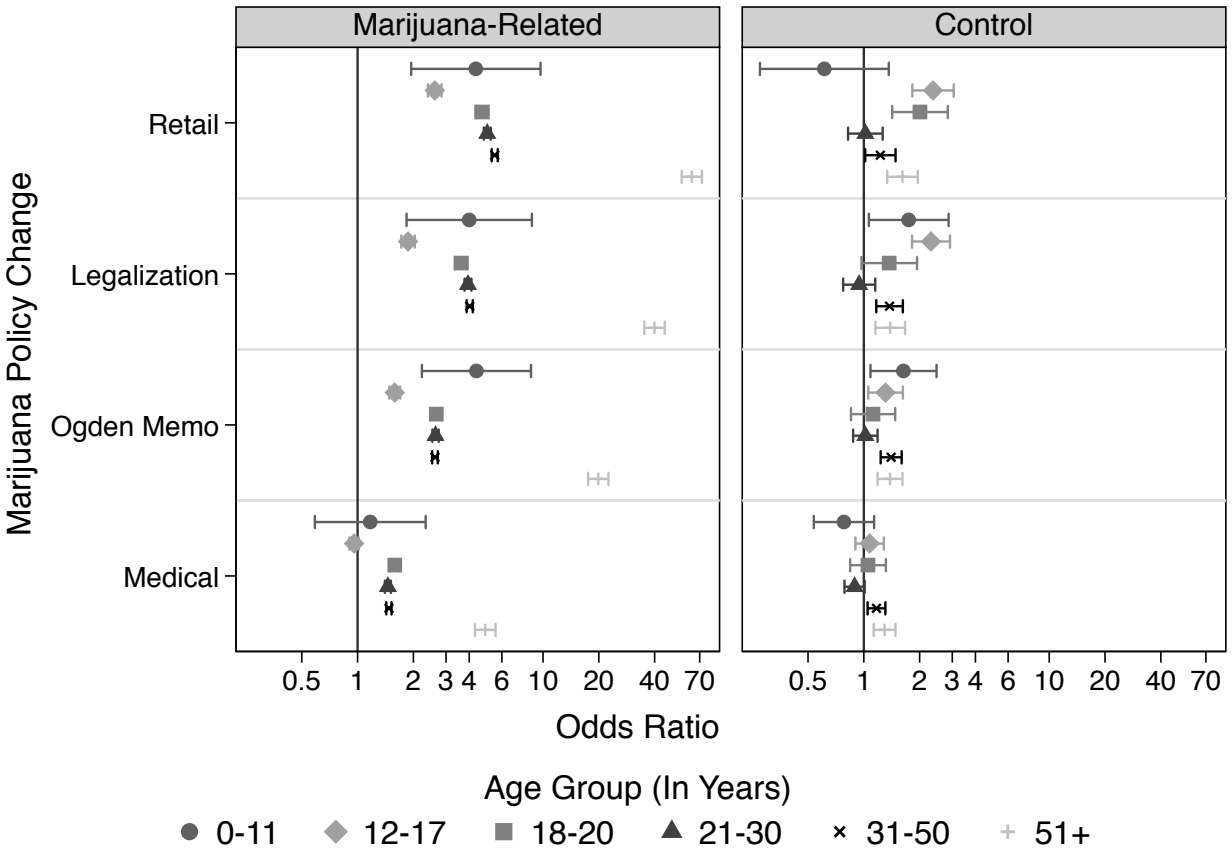

Figure 5. Point estimates of odds ratios with 95% confidence intervals for each change in marijuana policy obtained from logistic regression models, stratified by age group.

Tables

Table 1. Pertinent marijuana policy changes in Washington and count (percentage) of marijuana-related hospital discharges occurring during each timeframe.

Policy	Timeframe	Marijuana-related Hospitalizations N (%)
Prior to medical marijuana (Pre-Medical)	1/1994 – 11/1998	11,549 (0.45)
Medical marijuana becomes permissible (Medical)	12/1998 – 9/2009	41,814 (0.62)
Federal Ogden Memorandum (Ogden Memo)	10/2009 – 11/ 2012	27,749 (1.18)
Legalization of recreational marijuana (Legalization)	12/2012 – 6/2014	20,700 (1.76)
Opening of retail marijuana stores (Retail)	7/2014 – 12/2016	52,189 (2.76)

Table 2. Distribution of marijuana-related diagnosis codes among marijuana-related hospital discharge records.

Diagnosis Code	N	%
[Nondependent] cannabis abuse (305.2 or F12.1)	105,282	68.4
Cannabis dependence (304.3 or F12.2)	26,451	17.2
Cannabis use, unspecified (F12.9)	19,027	12.4
[Accidental] poisoning by psychodysleptics (969.6 or E854.1)	1,077	0.7
Psychodysleptics causing adverse effects in therapeutic use (E939.6)	124	0.1
Poisoning by cannabis (T40.7X1 - T40.7X4)	155	0.1
Adverse effect of cannabis (T40.7X5)	82	0.1
Underdosing of cannabis (T40.7X6)	0	0
Multiple cannabis codes	1,803	1.2

Table 3. Patient and hospitalization characteristics of hospital discharge records with and without a marijuana-related diagnosis code.

	Marijuana-related (N=154,001)		Not Marijuana-related (N=14,514,309)	
	N	%	N	%
Patient Characteristics				
Age Category				
0-11	135	0.1	2,373,900	16.4
12-17	9,906	6.4	279,501	1.9
18-20	13,224	8.6	328,423	2.3
21-30	42,890	27.9	1,578,153	10.9
31-50	56,064	36.4	2,796,863	19.3
51+	31,749	20.6	6,971,169	48.0
Unknown	33	0.0	186,300	1.3
Male	89,776	58.3	5,945,648	41.0
Visit Characteristics				
Insurance Type				
Public	88,470	57.4	7,565,843	52.1
Private	31,914	20.7	4,052,805	27.9
Self-pay	14,458	9.4	437,756	3.0
Other/Unknown	19,159	12.4	2,457,905	16.9
Type of Admission				
Emergency	85,200	55.3	5,336,669	36.8
Urgent	29,272	19.0	2,831,810	19.5
Elective	37,972	24.7	4,547,722	31.3
Trauma	1,156	0.8	41,222	0.3
Other/Unknown	401	0.3	1,756,828	12.1
Alcohol-Related Diagnosis	22,495	14.6	534,747	3.7
Tobacco-Related Diagnosis	82,675	53.7	2,164,147	14.9
Major Diagnostic Category				
Disease/Disorder of Body System	55,101	35.8	8,468,898	58.3
Infectious Disease	5,250	3.4	433,815	3.0
Mental Health	37,896	24.6	402,458	2.8

Substance-Related	19,585	12.7	144,636	1.0
Injury/Poisoning	9,054	5.9	238,484	1.6
Pregnancy/Childbirth	14,033	9.1	1,920,297	13.2
Other	1,529	1.0	2,077,236	14.3
Unknown	11,553	7.5	828,480	5.7
Facility Characteristics				
Care Setting				
Acute Care	122,073	79.3	14,034,934	96.7
Psychiatric	31,199	20.3	309,463	2.1
Other/Unspecified	729	0.5	162,856	1.1

Table 4. Patient and hospitalization characteristics of marijuana-related hospital discharges by marijuana policy timeframe.

	Pre-medical		Medical		Ogden Memo		Legalization		Retail	
Characteristic	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Patient Characteristics										
Minor (<21 years)	3,003	26.0	8,476	20.3	4,448	16.0	2,390	11.5	4,948	9.5
Visit Characteristics										
Mean length of stay (95% CI)	7.9 (7.7 – 8.0)		6.2 (6.1 – 6.3)		5.5 (5.4 – 5.5)		5.0 (4.9 – 5.1)		5.0 (5.0 – 5.1)	
Type of Admission										
Emergency	4,061	35.2	19,502	46.6	16,571	59.7	13,216	63.8	31,850	61.0
Urgent	2,913	25.2	9,324	22.3	5,004	18.0	2,965	14.3	9,066	17.4
Elective	4,563	39.5	12,759	30.5	5,955	21.5	4,340	21.0	10,355	19.8
Trauma	9	0.1	218	0.5	201	0.7	136	0.7	592	1.1
Other/Unknown	3	0.0	11	0.0	18	0.1	43	0.2	326	0.6
Discharge Disposition										
Discharged	9,435	81.7	34,608	82.8	22,771	82.1	16,343	79.0	41,267	79.1
Admitted	0	0.0	1	0.0	18	0.1	37	0.2	69	0.1
Transferred to Hospital	200	1.7	775	1.9	425	1.5	347	1.7	952	1.8
Transferred to Other Care	797	6.9	3,405	8.1	2,537	9.1	2,336	11.3	6,000	11.5
Died	28	0.2	117	0.3	179	0.6	154	0.7	495	0.9
Other/Unknown	1,089	9.4	2,908	7.0	1,819	6.6	1,483	7.2	3,406	6.5
Alcohol-Related Diagnosis	2,034	17.6	8,325	19.9	4,435	16.0	2,887	13.9	4,814	9.2
Tobacco-Related Diagnosis	3,288	28.5	15,765	37.7	16,408	59.1	13,399	64.7	33,815	64.8
Major Diagnosis Category										
Disease/Disorder of Body System	1,100	9.5	10,671	25.5	10,685	38.5	8,776	42.4	23,869	45.7
Infectious Disease	52	0.5	341	0.8	687	2.5	952	4.6	3,218	6.2
Mental Health	4,157	36.0	15,469	37.0	6,604	23.8	3,398	16.4	8,268	15.8
Substance-related	4,366	37.8	6,739	16.1	3,126	11.3	2,161	10.4	3,193	6.1
Injury or Poisoning	547	4.7	2,887	6.9	1,959	7.1	1,129	5.5	2,532	4.9
Pregnancy or Childbirth	1,295	11.2	4,424	10.6	2,158	7.8	1,696	8.2	4,460	8.5
Other	32	0.3	833	2.0	198	0.7	171	0.8	295	0.6
Unknown	0	0.0	450	1.1	2,332	8.4	2,417	11.7	6,354	12.2
Facility Characteristics										
Care Setting										
Acute Care	8,890	77.0	28,454	68.0	21,605	77.9	17,779	85.9	45,345	86.9
Psychiatric	2,572	22.3	13,223	31.6	6,023	21.7	2,792	13.5	6,589	12.6
Other/Unspecified	87	0.8	137	0.3	121	0.4	129	0.6	255	0.5

Table 5. Mean monthly marijuana-related hospital discharges (per 10,000).

Policy	Mean	95% Confidence Interval
Pre-Medical	45.1	43.5 – 46.7
Medical	62.1	60.9 – 63.3
Ogden Memo	118.0	110.4 – 125.5
Legalization	176.1	168.8 – 183.5
Retail	276.0	259.8 – 292.2

*Significant by ANOVA, p<0.0001

Table 6. Logistic Regression Model Results for Marijuana-Related Hospital Discharges

	Odds Ratio	Standard Error	P-value	95% Confidence Interval
Medical Marijuana	1.39	0.01	<0.0001	1.36 – 1.42
Ogden Memo	2.63	0.03	<0.0001	2.57 – 2.69
Legalization	3.95	0.05	<0.0001	3.86 – 4.04
Retail Stores	5.45	0.06	<0.0001	5.33 – 5.57
ICD change	1.30	0.01	<0.0001	1.28 – 1.32

Table 7. Logistic Regression Model Results for Systemic Drug-Related Hospital Discharges.

	Odds Ratio	Standard Error	P-value	95% Confidence Interval
Medical Marijuana	1.05	0.03	0.16	0.98 – 1.11
Ogden Memo	1.19	0.04	<0.0001	1.10 – 1.28
Legalization	1.25	0.06	<0.0001	1.15 – 1.37
Retail Stores	1.27	0.06	<0.0001	1.15 – 1.39
ICD change	1.07	0.06	0.25	0.96 – 1.19

Appendix A: Extended Results

Table 3a. Patient and hospitalization characteristics of discharge records with and without a marijuana-related diagnosis code.

	Marijuana-related (N=154,001)		Not Marijuana-related (N=14,514,309)	
Characteristic	**N**	**%**	**N**	**%**
Patient Characteristics				
Median Age (IQR)	34 (24, 48)	--	49 (25, 70)	--
Minor (<21 years)	23,265	15.1	2,981,824	20.5
Age Category				
0-11	135	0.1	2,373,900	16.4
12-17	9,906	6.4	279,501	1.9
18-20	13,224	8.6	328,423	2.3
21-30	42,890	27.9	1,578,153	10.9
31-50	56,064	36.4	2,796,863	19.3
51+	31,749	20.6	6,971,169	48.0
Unknown	33	0.0	186,300	1.3
Male	89,776	58.3	5,945,648	41.0
Race*				
White	79,744	51.8	4,484,662	30.9
Black	9,001	5.8	233,955	1.6
American Indian	4,124	2.7	90,633	0.6
Asian	928	0.6	215,397	1.5
Hawaiian/Pacific Islander	1,134	0.7	71,482	0.5
Other	542	0.4	17,836	0.1
Unknown	58,528	38.0	9,400,344	64.8
Ethnicity*				
Not Hispanic	91,542	59.4	4,652,664	32.1
Hispanic	4,674	3.0	396,152	2.7
Unknown	57,785	37.5	9,465,493	65.2
Patient Urbanicity				
Urban	117,028	76.0	10,893,508	75.1
Suburban	15,659	10.2	1,310,806	9.0
Large rural	12,735	8.3	1,321,342	9.1
Small town/rural	8,178	5.3	954,063	6.6
Unknown	401	0.3	34,590	0.2
Washington Resident	149,259	96.9	14,000,625	96.5
Washington Geography				
Eastern Washington	33,596	21.8	3,421,474	23.6
Western Washington	115,575	75.0	10,574,024	72.9
Non-Washington/Unknown	4,830	3.1	518,811	3.6
Visit Characteristics				
Weekend Admission	34,795	22.6	2,811,635	19.6
Time of Admission*				
Morning (5am – 11am)	18,766	12.2	1,616,761	11.1
Afternoon (11am – 5pm)	32,110	20.9	1,791,231	12.3
Evening (5pm – 11pm)	31,101	20.2	1,544,493	10.6
Late Night (11pm – 5am)	19,166	12.4	938,019	6.5
Unknown	52,858	34.3	8,623,805	59.4
Insurance Type				
Public	88,470	57.4	7,565,843	52.1
Private	31,914	20.7	4,052,805	27.9
Self-pay	14,458	9.4	437,756	3.0
Other/Unknown	19,159	12.4	2,457,905	16.9
Median Length of Stay (IQR)	3 (2, 7)	--	2 (1, 4)	--
Patient Type				
Inpatient	142,448	92.5	13,685,829	94.3
Observation*	11,553	7.5	828,480	5.7
Type of Admission				

Emergency	85,200	55.3	5,336,669	36.8
Urgent	29,272	19.0	2,831,810	19.5
Elective	37,972	24.7	4,547,722	31.3
Trauma	1,156	0.8	41,222	0.3
Other/Unknown	401	0.3	1,756,828	12.1
Discharge Disposition				
Discharged	124,424	80.8	11,459,178	79.0
Admitted	125	0.1	5,234	0.0
Transferred to Hospital	2,699	1.8	258,572	1.8
Transferred to Other Care	15,075	9.8	2,307,393	15.9
Died	973	0.6	285,610	2.0
Other/Unknown	10,705	7.0	198,180	1.4
Alcohol-Related Diagnosis	22,495	14.6	534,747	3.7
Tobacco-Related Diagnosis	82,675	53.7	2,164,147	14.9
Major Diagnostic Category				
Disease/Disorder of Body System	55,101	35.8	8,468,898	58.3
Infectious Disease	5,250	3.4	433,815	3.0
Mental Health	37,896	24.6	402,458	2.8
Substance-Related	19,585	12.7	144,636	1.0
Injury/Poisoning	9,054	5.9	238,484	1.6
Pregnancy/Childbirth	14,033	9.1	1,920,297	13.2
Other	1,529	1.0	2,077,236	14.3
Unknown	11,553	7.5	828,480	5.7
Facility Characteristics				
Care Setting				
Acute Care	122,073	79.3	14,034,934	96.7
Psychiatric	31,199	20.3	309,463	2.1
Other/Unspecified	729	0.5	162,856	1.1
Facility Urbanicity				
Urban	142,259	92.4	13,143,547	90.6
Suburban	371	0.2	96,073	0.7
Large Rural	9,614	6.2	948,078	6.5
Small Town/Rural	1,711	1.1	318,504	2.2
Unknown	46	0.0	8,107	0.1

*Information not collected until 2008

Table 4a. Patient and hospitalization characteristics of marijuana-related hospital discharges by marijuana policy timeframe.

	Pre-medical		**Medical**		**Ogden Memo**		**Legalization**		**Retail**	
Characteristic	N	%	N	%	N	%	N	%	N	%
Median age	28		30		33		37		39	
Minor (<21 years)	3,003	26.0	8,476	20.3	4,448	16.0	2,390	11.5	4,948	9.5
Age category										
0-11	11	0.1	31	0.1	35	0.1	17	0.1	41	0.1
12-17	1,692	14.7	3,486	8.3	1,781	6.4	908	4.4	2,039	3.9
18-20	1,300	11.3	4,959	11.9	2,632	9.5	1,465	7.1	2,868	5.5
21-30	3,611	31.3	12,735	30.5	8,047	29.0	5,661	27.3	12,836	24.6
31-50	4,683	40.5	17,088	40.9	9,799	35.3	7,055	34.1	17,439	33.4
51+	252	2.2	3,515	8.4	5,428	19.6	5,588	27.0	16,966	32.5
Unknown	0	0.0	0	0.0	27	0.1	6	0.0	0	0.0
Male	6,543	56.7	24,131	57.7	16,573	59.7	12,235	59.1	30,294	58.0
Race*										
White	-	-	-	-	19,549	70.4	15,801	76.3	40,294	77.2
Black	-	-	-	-	2,356	8.5	1,761	8.5	4,396	8.4
American Indian	-	-	-	-	1,281	4.6	773	3.7	1,795	3.4
Asian	-	-	-	-	160	0.6	185	0.9	533	1.0
Hawaiian/Pacific Islander	-	-	-	-	258	0.9	197	1.0	607	1.2
Other	-	-	-	-	38	0.1	64	0.3	433	0.8
Unknown	-	-	-	-	4,107	14.8	1,919	9.3	4,131	7.9
Ethnicity*										
Not Hispanic	-	-	-	-	20,849	75.1	18,494	89.3	47,958	91.9
Hispanic	-	-	-	-	1,092	3.9	942	4.6	2,429	4.7

Unknown	-	-	-	-	5,808	20.9	1,264	6.1	1,802	3.5
Urbanicity										
Urban	9,043	78.3	32,537	77.8	21,025	75.8	15,189	73.4	39,234	75.2
Suburban	927	8.0	3,798	9.1	2,654	9.6	2,413	11.7	5,867	11.2
Large rural	931	8.1	3,241	7.8	2,399	8.6	1,849	8.9	4,315	8.3
Small town/rural	606	5.2	2,120	5.1	1,589	5.7	1,179	5.7	2,684	5.1
Unknown	42	0.4	118	0.3	82	0.3	70	0.3	89	0.2
Washington Resident	11,066	95.8	40,693	97.3	26,936	97.1	20,041	96.8	50,523	96.8
Washington Geography										
Eastern Washington	2,391	20.7	8,083	19.3	6,468	23.3	5,085	24.6	11,569	22.2
Western Washington	8,669	75.1	32,576	77.9	20,451	73.7	14,937	72.2	38,942	74.6
Non-Washington/Unknown	489	4.2	1,155	2.8	830	3.0	678	3.3	1,678	3.2
Visit Characteristics										
Weekend Admission	2,092	18.1	8,884	21.2	6,530	23.5	4,973	24.0	12,316	23.6
Time of Admission*										
Morning (5am-11am)	-	-	-	-	4,921	17.7	3,531	17.1	9,206	17.6
Afternoon (11am-5pm)	-	-	-	-	9,045	32.6	6,255	30.2	14,830	28.4
Evening (5pm-11pm)	-	-	-	-	8,609	31.0	6,127	29.6	14,344	27.5
Late Night (11pm-5am)	-	-	-	-	5,148	18.6	3,739	18.1	9,017	17.3
Unknown	-	-	-	-	26	0.1	1,048	5.1	4,792	9.2
Insurance										
Public	5,456	47.2	22,175	53.0	14,397	51.9	11,533	55.7	34,909	66.9
Private	2,655	23.0	8,435	20.2	5,315	19.2	4,405	21.3	11,104	21.3
Self-pay	1,239	10.7	4,927	11.8	3,833	13.8	2,513	12.1	1,946	3.7
Other	2,199	19.0	6,277	15.0	4,204	15.2	2,249	10.9	4,230	8.1
Mean length of stay	7.9		6.2		5.5		5.0		5.0	
Patient Type										
Inpatient	11,549	100.0	41,364	98.9	25,417	91.6	18,283	88.3	45,835	87.8
Observation*	0	0.0	450	1.1	2,332	8.4	2,417	11.7	6,354	12.2
Type of Admission										
Emergency	4,061	35.2	19,502	46.6	16,571	59.7	13,216	63.8	31,850	61.0
Urgent	2,913	25.2	9,324	22.3	5,004	18.0	2,965	14.3	9,066	17.4
Elective	4,563	39.5	12,759	30.5	5,955	21.5	4,340	21.0	10,355	19.8
Trauma	9	0.1	218	0.5	201	0.7	136	0.7	592	1.1
Other/Unknown	3	0.0	11	0.0	18	0.1	43	0.2	326	0.6
Discharge Disposition										
Discharged	9,435	81.7	34,608	82.8	22,771	82.1	16,343	79.0	41,267	79.1
Admitted	0	0.0	1	0.0	18	0.1	37	0.2	69	0.1
Transferred to Hospital	200	1.7	775	1.9	425	1.5	347	1.7	952	1.8
Transferred to Other Care	797	6.9	3,405	8.1	2,537	9.1	2,336	11.3	6,000	11.5
Died	28	0.2	117	0.3	179	0.6	154	0.7	495	0.9
Other/Unknown	1,089	9.4	2,908	7.0	1,819	6.6	1,483	7.2	3,406	6.5
Alcohol-Related Diagnosis	2,034	17.6	8,325	19.9	4,435	16.0	2,887	13.9	4,814	9.2
Tobacco-Related Diagnosis	3,288	28.5	15,765	37.7	16,408	59.1	13,399	64.7	33,815	64.8
Major Diagnosis Category										
Disease/Disorder of Body System	1,100	9.5	10,671	25.5	10,685	38.5	8,776	42.4	23,869	45.7
Infectious Disease	52	0.5	341	0.8	687	2.5	952	4.6	3,218	6.2
Mental Health	4,157	36.0	15,469	37.0	6,604	23.8	3,398	16.4	8,268	15.8
Substance-related	4,366	37.8	6,739	16.1	3,126	11.3	2,161	10.4	3,193	6.1
Injury or Poisoning	547	4.7	2,887	6.9	1,959	7.1	1,129	5.5	2,532	4.9
Pregnancy or Childbirth	1,295	11.2	4,424	10.6	2,158	7.8	1,696	8.2	4,460	8.5
Other	32	0.3	833	2.0	198	0.7	171	0.8	295	0.6
Unknown	0	0.0	450	1.1	2,332	8.4	2,417	11.7	6,354	12.2
Facility Characteristics										
Care Setting										
Acute Care	8,890	77.0	28,454	68.0	21,605	77.9	17,779	85.9	45,345	86.9
Psychiatric	2,572	22.3	13,223	31.6	6,023	21.7	2,792	13.5	6,589	12.6
Other/Unspecified	87	0.8	137	0.3	121	0.4	129	0.6	255	0.5
Hospital Urbanicity										
Urban	10,996	95.2	39,129	93.6	25,251	91.0	18,718	90.4	48,165	92.3
Suburban	17	0.1	86	0.2	66	0.2	83	0.4	119	0.2
Large rural	397	3.4	2,167	5.2	2,092	7.5	1,604	7.7	3,354	6.4
Small town/rural	133	1.2	410	1.0	332	1.2	290	1.4	546	1.0
Unknown	6	0.1	22	0.1	8	0.0	5	0.0	5	0.0

*Information not collected until 2008

Chapter 3: Marijuana Poison Center Calls

Interrupted Time-series Analysis of Marijuana Exposures, 1999-2016, Washington State

Background

Washington State has been at the forefront of modern-day marijuana legislation for over two decades. In November 1998, Washington State became one of the first states to legalize use, possession, and cultivation of marijuana for certain approved medical conditions (Washington Initiative 692). Over the next several years, additional legislation pertaining to medical marijuana was passed including expansions to the list of medical conditions eligible for marijuana treatment and in the classifications of healthcare professionals allowed to issue medical authorizations for use of marijuana (27). By 2009, 13 states had legalized marijuana for medical purposes (47). This proliferation of state-level medical marijuana legislation prompted the United States Deputy Attorney General David Ogden to issue a memorandum in October 2009 that directed United States attorneys not to get involved in the enforcement of federal marijuana laws if individuals were compliant with state-level medical marijuana laws. In 2011, additional legislation was passed in Washington State which developed a framework for the establishment of collective gardens. These collective gardens evolved into dispensaries, which were essentially retail access points for medical marijuana; they were neither licensed nor regulated. In November 2012, Washington and Colorado became the first states to pass legislation allowing the use, possession, and sale of marijuana for recreational purposes for adults 21 years of age or older (Washington Initiative 502 and Colorado Amendment 64, respectively). Such legislation was unprecedented not only in the United States but also internationally. Washington Initiative 502 came to full fruition in July 2014 when the first licensed retail marijuana outlets opened in Washington State.

Marijuana is harvested from the female *Cannabis sativa* plant. *Cannabis sativa* contains numerous chemical compounds, but the primary psychoactive compound is delta-9-tetra-hydrocannabidiol (THC) (26, 28). Once in the blood, THC stimulates a release of dopamine in addition to disrupting the function of several areas of the brain (29, 30). Marijuana intoxication results in one or more of the following: feelings of euphoria (associated with increases in dopamine), disinhibition, anxiety, paranoia, temporal slowing, depersonalization, derealization, hallucinations, and impaired judgment, attention, or reaction time (31). Additional signs of marijuana intoxication include increased appetite, dry mouth, bloodshot eyes, or rapid heart rate (31). The magnitude of these effects are highly dependent on the dose used, the route of administration, user's prior experience with cannabis, any concurrent drug use, the setting and the mindset of the user (32).

Supporters of marijuana often cite its therapeutic effects. These qualities include its ability to provide relief from chronic pain, nausea, or spasticity symptoms, especially in people experiencing chronic or debilitating medical conditions (33). Additionally, it may be used as a form of relaxation (31). While marijuana may elicit desirable effects, like most substances, it also has the potential to be provoke undesirable health effects. Studies have reported an association of marijuana intoxication with a collection of acute health consequences. This includes stimulating negative psychological effects such as feelings of anxiety, psychotic episodes, or severe paranoia instead of the euphoria reported by most users (34). Some studies have reported increased risk of cardiac events and stroke after cannabis use (16, 34, 35). Marijuana is sometimes used to relieve nausea, but some users, especially those with a history of chronic use, experience cyclic episodes of severe nausea and vomiting after smoking cannabis, a condition known as cannabinoid hyperemesis syndrome (36). Studies have reported up to two times increased risk of traffic crash if driving while intoxicated by marijuana (37, 38). When marijuana is used in combination with alcohol, the risk of car crash is increased above use of either substance independently (39). Long-term use of marijuana may lead to chronic bronchitis, lower birthweight of offspring, impairments in learning and memory, increased risk of development of schizophrenia or other psychoses, and increased risk of substance dependence (33).

Implementation of policies favorable to marijuana increases the availability and, potentially, the usage of marijuana, including among previously inexperienced users. As a result, an increase in the number of people experiencing acute adverse health consequences associated with THC intoxication following relaxation of marijuana policies may be expected (65). Of specific interest is the impact of edible marijuana products being readily available in retail stores. Attractiveness of these products to inexperienced users combined with the delayed effects of THC when ingested, may increase the likelihood of overdose on these products (66). In addition to an increase in intentional exposures, the overall increased availability of marijuana and increased availability of child-appealing marijuana products (e.g., candies, cookies) may lead to an increase in unintentional ingestion among children, occasionally resulting in serious health consequences (62, 66-68).

Due to the complete novelty of legalizing recreational marijuana, researchers were only able to speculate about the potential impact of such legislation on marijuana usage rates and public health prior to its enactment. Early reports from Washington State and others that were early adopters of legalization of marijuana for recreational purposes indicate it may be associated with some negative health consequences. Colorado, Washington State, and Oregon have reported increases in the number of marijuana exposure calls made to poison centers after a retail marijuana market was established (8, 40, 41, 69). The number of marijuana-related hospitalizations in Colorado has increased significantly each year since 2000, when medical marijuana was legalized in Colorado (8, 40). Marijuana-related emergency department visits in Colorado have also significantly increased annually since 2012, when recreational marijuana was legalized (8).

Tefft, Arnold and Grabowski (42) reported a noticeable increase in the number and proportion of drivers involved in fatal crashes testing positive for THC in Washington State in 2014, compared to 2010 through 2013. Additionally, since marijuana was legalized, there has been one report of a death associated with marijuana intoxication in the literature and a handful of marijuana-related deaths reported in the media (43, 70, 71).

In summary, increases in acute marijuana-related adverse health events could have significant negative effects on the population's health and place additional burden on the healthcare system. While Washington was one of the first states to legalize marijuana for recreational use, several other states have since passed similar legislation. Thus, it is critical to understand the potential health impacts of such legislative changes and to recognize which populations are most impacted by the changes so that appropriate public health interventions can be put into place. This study will be the first study, to our knowledge, that assesses the impact of key marijuana policy changes on trends in marijuana-related poisonings in Washington State.

Methods

Study Design

This study employed an interrupted time series (ITS) design to assess the impact of significant changes in marijuana policies in Washington State (October 2009: Ogden Memorandum; December 2012: legalization of recreational marijuana possession and use; July 2014: opening of non-medical marijuana retail stores) on marijuana-related poisonings.

Data Collection

The Washington Poison Center (WAPC) is a non-profit agency that provides immediate, free, and expert treatment advice and assistance, via telephone, in case of exposure to poisonous, hazardous, or toxic substances. The WAPC is available twenty-four hours a day, 365 days a year and has served the residents of Washington State since 1956. The WAPC maintains an electronic medical record system of all calls to the poison center (toxiCALL). All human exposures reported to the WAPC from January 1999 through December 2016 and entered into toxiCALL were considered for this analysis. The dataset contained limited patient information (e.g., age, gender, weight), call information (date and time of the poison center call, type of call, location of caller, relationship of caller to patient, caller site), exposure information (e.g., number of substances, route, reason, site, time, duration, chronicity), exposure management (e.g., management site, healthcare outcome, therapies recommended and administered), details about the substances involved (standard text description, verbatim description, Poisindex code, generic code, quantity, concentration, dose, certainty of amount, form of substance), clinical effects (i.e., presence of symptoms arranged into categories such as cardiovascular, dermal, gastrointestinal, heme/hepatic, neurological, ocular, renal, respiratory, and miscellaneous), outcome information

(e.g., medical outcome, duration of effects), and recommendations or actions taken for all exposure calls. All fields, with the exception of caller location information and verbatim substance description, were coded. Approval to use this data was obtained from the University of Washington Institutional Review Board (Study ID: STUDY00000050).

Marijuana-related exposures were defined as patients who reported exposure to marijuana (American Association of Poison Control Centers [AAPCC] generic codes: 083000 - "Marijuana: Dried Plant" and 310096 - "eCigarettes: Marijuana Device Flavor Unknown"). These codes are part of a coding system of nearly 2000 products used by poison control centers nationwide to codify substances involved in exposures. The code set is actively maintained by the AAPCC – Micromedex Joint Coding Group (72). Standardized substance descriptions as well as free-text verbatim substance descriptions were reviewed to further categorize marijuana substances. Patients whose only marijuana exposure appeared to involve synthetic marijuana or a pharmaceutical preparation of marijuana were removed from the dataset. Additionally, records that indicated there was a confirmed non-exposure were excluded.

Statistical Analysis

Descriptive statistics were calculated for patient characteristics (e.g., age, gender), product type, cannabis type, number of products involved, exposure characteristics (e.g., chronicity, exposure route, intent of exposure), and clinical effects (e.g., clinical effect category, management site, medical outcome) for the time periods before and after each significant marijuana policy change: the Ogden Memorandum (October 2009), legalization of non-medical marijuana (December 2012), and the opening of retail marijuana sales (July 2014). The mean rate of monthly marijuana exposure calls for each policy timeframe was calculated and an analysis of variance test was conducted to evaluate for significant differences in the mean monthly marijuana exposure call rate across policy timeframes.

Interrupted time-series analysis was conducted to determine whether there was a significant shift in the level of cannabis poisonings after the Ogden Memorandum (October 2009), legalization of non-medical marijuana (December 2012), and the opening of retail marijuana sales (July 2014). The *a priori* assumption was that a shift, most likely toward the positive, in the number of marijuana-related poisonings would occur at each of these time points.

To ensure there were sufficient marijuana exposure calls per month (≥ 5) for a monthly time series analysis, the count of cannabis-related exposure calls per month was calculated and assessed. If several months had < 5 marijuana exposure calls, the unit of time for the time-series analysis would have been coarsened to quarters rather than months, which would have been undesirable because it would limit the number of points available for analysis during each timeframe of interest. Additionally, the monthly rate of cannabis-related poisonings was plotted against time to assess underlying trends, seasonal patterns, overall variability, and identify outliers.

A Poisson regression model was used. The model had the following basic structure:

$$Y_t = \beta_0 + \beta_1 T + \beta_2 X_t + \beta_3 Z_t + \beta_4 W_t$$

where T represents time elapsed since the start of the study in months, X_t is a binary (0/1) variable indicating the months in which the Ogden memorandum was in effect (October 2009 – November 2012), Z_t is a binary (0/1) indicator variable indicating the time points that legalization was in effect (December 2012 – June 2014), W_t is a binary (0/1) indicator variable indicating time points when retail stores were open (July 2014 – December 2016), Y_t is the monthly count of marijuana exposure calls at time t, β_0 represents the baseline level of marijuana-related poisonings at time zero, β_1 describes the change in outcome per time unit (i.e., pre-intervention trend), and β_2, β_3, or β_4 describe the level changes during each intervention relative to the pre-intervention timeframe (January 1999 - October 2009). The total count of exposure calls to the poison center per month was included in the model as an offset to account for changes in overall poison center call trends.

Adherence to Poisson model assumptions was evaluated. Overdispersion was assessed by applying a negative binomial model and evaluating the dispersion (alpha) parameter. To assess whether the assumption of independence was violated as a result of autocorrelation, response residuals were plotted against both the number of study months elapsed and the predicted mean monthly marijuana exposure call count to identify potential trends. Additionally, correlograms were produced to assess autocorrelation and partial autocorrelation. Sensitivity analyses included evaluation of a Poisson model with parameters allowing for changes in slope after each policy change, in addition to level shifts, and a Poisson model that included a covariate that accounted for the statewide number of licensed retailers that reported non-zero product sales each month after July 2014. None of the models were able to account for the number of unlicensed and unregulated medical marijuana dispensaries that were open between 2011 through 2016.

The interrupted time series analysis was repeated using the monthly count of exposure calls to the Washington Poison Center that were related to 3% hydrogen peroxide solution (AAPCC subgeneric code 143790), as a control, to assess whether there were changes in overall poison center call patterns, unrelated to the legislation change, that may have impacted the results. The final model that was fit to the cannabis poisoning data was fit to the hydrogen peroxide data. Since hydrogen peroxide exposures were expected to be relatively stable during the study period [personal communication with Washington Poison Center staff], it was expected that no significant effect would be seen at any of the time points of interest in the marijuana analysis, and thus give further evidence of causality between legislation and effects observed. All statistical analyses were performed in Stata 14 (College Station, TX).

Results

There were 2371 calls to the Washington Poison Center about marijuana exposures between 1999 and 2016. After review of standardized and verbatim substance descriptions, 76 exposures originally identified as marijuana exposures were found to involve exposures to synthetic marijuana (e.g., spice) or a pharmaceutical preparation of

marijuana (e.g., dronabinol). These records were removed from the dataset. An additional four exposures were confirmed non-exposures and were removed from the dataset. The final dataset contained 2291 marijuana exposure calls. Marijuana exposure calls comprised a small proportion (0.2%) of all exposure calls to the poison center. The proportion of marijuana exposure calls increased between the medical marijuana era (0.12%) to the opening of retail stores (0.49%) (Table 1).

Table 2 describes the patient, exposure, and clinical characteristics of marijuana exposure calls to the Washington Poison Center during each marijuana policy period. Slightly more than half of exposures occurred in males. The proportion of marijuana exposure calls involving minors decreased by 9% across the time periods; however, the proportion of marijuana exposure calls involving patients under five years of age increased from 5% to 16%. The proportion of older adults (those 50 years of age or older) calling about a marijuana exposure also increased from 3% to 13%. Specific marijuana product information was missing or unspecified for 74% of all marijuana exposure calls. The availability of marijuana product type increased with time from only 10% of marijuana exposures calls during the medical era to 64% of calls after July 2014. After marijuana retail sales began, edible marijuana products (e.g. baked good, candy, other food/drink) were reported in 62% (N=235) of marijuana exposures in which the marijuana product type was specified (N=378). Changes in the routes of marijuana exposure between the medical marijuana era and the retail era include a 10% decrease in both inhalation (from 26% to 16%) and multiple routes of exposure (from 25% to 15%) while ingestion increased 19% (from 46% to 65%). Additionally, unintentional exposures and adverse reactions increased 22% across time periods, from 16% to 38%. Approximately 82% of all marijuana exposures were associated with a clinical effect, of which the most common effects identified were neurological, followed by cardiovascular and gastrological effects. The percentage of marijuana exposure patients that sought medical care increased and the majority of those were evaluated and released. The bulk of marijuana exposures resulted in outcomes classified as minor effects (e.g., symptoms that are minimally bothersome, such as drowsiness or mild gastrointestinal symptoms), but over the entire study period, 300 people were admitted to the hospital and nearly half of those were treated in intensive care.

An analysis of variance test indicated there was a significant change in the mean number of monthly marijuana exposure calls across the policy timeframes (Table 3).

There was no evidence of seasonality nor were any outliers identified that required removal (Figure 1). Of 216 observation months, there were two months in which no marijuana exposure calls occurred. The plot of marijuana exposure calls suggests the monthly rate of marijuana exposures began to increase after the release of the Ogden Memorandum and continued to increase through 2016. The Poisson model indicated each marijuana policy change after 1999 was associated with significant increases in marijuana exposure calls (Table 4). The largest shifts in level occurred after the Ogden Memorandum and after retail stores opened.

Sensitivity analyses included models that assessed changes in slope after each policy change as well as a covariate that accounted for the number of stores that were open each month. The incident rate ratios for slope changes and number of stores were trivial. For simplicity, the results of the model with only shifts in levels are presented. Model assessment indicated there was no autocorrelation nor over-dispersion obscuring the validity of the Poisson model.

There were 4886 calls to WAPC regarding exposures to hydrogen peroxide during the study period. The Poisson model fit to hydrogen peroxide exposure call counts indicated there were significant shifts in hydrogen peroxide call counts in correspondence with significant marijuana interventions, but the shifts were small compared to those observed in the marijuana model (Table 5, Figure 2).

Discussion

A very small proportion of all exposure calls to the Washington Poison Center were related to marijuana. Even so, there was a fourfold increase in the proportion of exposure calls involving marijuana over the course of the study. The rate of marijuana exposure calls began to increase after the release of the Ogden Memorandum in late 2009 and continued to increase substantially through 2016. The Poisson model indicated that each marijuana-related policy was associated with a significant increase in the incidence rate ratio of a marijuana exposure relative to when medical marijuana alone was permissible. The legalization of marijuana possession had the smallest individual impact compared to the release of the Ogden Memorandum and the opening of marijuana retail stores. These trends align with what has been reported from other states that have legalized marijuana for medical or recreational purposes (9, 10, 69). While the significant increases in incidence rate ratios of marijuana exposure calls associated with each change in marijuana policy does not indicate causation, similar increases were not observed in the Poisson model for hydrogen peroxide poisonings. This helps to rule out the possibility that changes in poison center exposure call patterns or other contemporaneous events, unrelated to marijuana, were entirely responsible for the increases in incidence rate ratios observed, and supports the likelihood that marijuana policy changes could be causatively associated with changes in the incident rate ratio of marijuana exposures.

Reduced perception of risk associated with marijuana use, increased numbers of marijuana users, increased frequency of use among existing marijuana users and increased potency of marijuana products may all contribute to increased risk of marijuana poisonings. Increasingly tolerant marijuana laws reflect increased societal acceptance of marijuana and increased perception that marijuana is low risk. Additionally, legalization reduces fear of legal consequences and increases access to marijuana (73). The combination of these factors may increase use and encourage people who may not have previously used marijuana to do so. In fact, after a number of marijuana policy changes in 2009, Colorado, which had legalized medical marijuana nearly a decade earlier, reported a large increase in the number of medical marijuana applications received each month (from 485 in January 2009 to over 10,155 in

December 2009) and dispensaries established (from 0 in 2008 to 900 in mid-2010) (9, 74). Data from the Washington Liquor and Cannabis Board indicates sale of cannabis in Washington State increased through 2016 from less than $5 million dollars in sales in July 2014 to nearly $100 million in sales in September 2016 (44, 45). Such increases may indicate both increasing consumption (frequency and dose) of marijuana by each individual user as well as expansion in the number of people using marijuana (45). The 2013-2014 National Survey on Drug Use and Health (NSDUH) indicated significantly increased reporting of past year (+8.1%), past month (+7.9%) and daily marijuana use (+4.4%) among Washington State adults 26 years of age or older compared to survey results obtained in 2002-2003 (46). Another analysis of NSDUH indicated adults over the age of 21, who had prior experience with marijuana, were at increased risk of daily marijuana use after passage of medical marijuana laws (47). Additionally, increased potency of marijuana may increase the likelihood of adverse consequences from marijuana (48). In Washington, cannabis flower contained an average of 21% THC while inhalable extracts contained an average of nearly 69% THC in 2016 (44) whereas the THC content of seized marijuana was only 12% in 2014 (49). This reflects a sharp increase in potency of both legal and illegal marijuana products compared to seized marijuana products from the 1990s that contained an average of 4% THC. Of note, there is also now commercial availability of THC concentrates and products containing multiple doses. Increased number of marijuana users, frequency of use among existing marijuana users and increased potency may all contribute to increased risk of marijuana poisoning.

Specific marijuana product type was largely missing or unspecified in this dataset, especially prior to retail sales of marijuana, but there was an apparent increase in marijuana exposure calls involving edible (e.g., baked goods, candy, other food/drink) products. Additional evidence of this shift is supported by the increase in marijuana exposures that were through ingestion, as opposed to inhalation. Cao, Srisuma, Bronstein and Hoyte (75) reported a five-fold increase in the number of calls to U.S. poison centers involving edibles between 2013 – 2015, with the highest rates occurring in the three states that had legalized marijuana for recreational purposes. Lamy, Daniulaityte, Sheth, Nahhas, Martins, Boyer and Carlson (76) evaluated a sample of tweets for three months in 2015 and observed the highest proportion of tweets mentioning edible marijuana originated from these same three states. The change from smoking to ingesting marijuana is likely due to increased availability of a much wider variety of marijuana products. In addition to their palatability, edibles may have an appeal because of the perception that it is healthier than smoking and facilitate discreet consumption of marijuana (76, 77).

Despite the apparent shift toward poisonings involving consumption of edible marijuana products, they comprised only 10% of the total market share for cannabis sales in Washington in 2016 (78). This apparent incongruity may be a reflection of the pharmacokinetic properties of THC that is ingested (75). When marijuana is smoked, THC is rapidly absorbed into the blood, allowing the dose and its effects to be quickly and easily regulated by the user (66). When THC

is ingested, its effects are delayed, which may result in a person to inadvertently consuming high levels of THC before experiencing any effects (75). Additionally, the THC content of an edible may not be known if homemade, THC may be unevenly distributed throughout an edible if it is poor quality, or the edible may be insufficiently/incorrectly labeled (76). These factors make it more difficult for people to regulate their dose, which can increase the likelihood of an overdose. The unanticipated health effects of an overdose may also increase the likelihood that a person will call the poison center or seek medical care. Monte, Shelton, Mills, Saben, Hopkinson, Sonn, Devivo, Chang, Fox, Brevik, Williamson and Abbott (24) reported that 10.7% of emergency department visits attributable to cannabis at a Colorado hospital were due to exposure to edibles, despite edibles only representing an estimated 0.3% of total cannabis sales in Colorado from 2014 - 2016. While several factors may explain this apparent imbalance, this observation suggests that edibles may have a propensity for generating acute adverse effects. Clear and accurate labeling of THC content, clear demarcation of individual doses in multi-dose packages, assurance of product quality, and limits on total THC content of a product may reduce the likelihood of overdose from edible marijuana products (76). Additionally, educating people about the delayed effect of edibles and the importance of not taking multiple doses may help avoid THC toxicity. Oregon, Washington, and Colorado have all placed limits on the total and per serving THC content to try to prevent inadvertent over-consumption of edibles: Oregon allows only a total of 5 mg per serving, while Washington and Colorado allow 10 mg (79-81).

Increased proportions of older adults reporting a marijuana exposure were observed. Previous studies have reported that while older adults represent a small proportion of total marijuana users, the greatest increases in use between 2002 and 2014 were observed in this population (50). In this study (see Chapter 2), the proportion of older adults with a marijuana-related hospital discharge increased from 3% prior to 2010 to 13% after 2014. Older adults are more likely to report using marijuana for medicinal purposes than for nonmedicinal reasons (51). Older adults may view marijuana as a safer alternative to alcohol, illicit drugs or prescription drugs (52).There is evidence that marijuana may relieve chronic pain, neuropathic pain, and spasticity due to multiple sclerosis; however, older adults may also be more likely to experience adverse effects of marijuana (33, 53). People who use marijuana for medicinal purposes are doing so without evidence-based guidelines on specific strains or dosage (54). Compounds in marijuana may also modify metabolism of prescription medications, increasing likelihood of drug interactions (57).

Both legalization of marijuana and the increased availability of marijuana products raised much concern about potential negative consequences for minors. The proportion of marijuana exposure calls involving patients <21 years of age decreased with each increasingly lenient marijuana policy change. In fact, the 2014 Washington Healthy Youth survey indicated little change in marijuana use among adolescents since 2012 (59). While adolescents and young adults represented an increasingly smaller proportion of all marijuana exposures, the proportion of marijuana exposure calls involving children, especially those <5 years of age increased substantially in Washington State. These findings are in line

with what has been reported previously in states allowing medical or recreational marijuana (8, 10, 40, 61, 62, 82). Cao, Srisuma, Bronstein and Hoyte (75) reported the highest rate of calls to U.S. poison centers involving marijuana edibles between 2013 through 2015 were for children ≤ 5 years of age.

Young children are particularly at risk of accidental ingestion of marijuana-containing products as well as severe adverse events requiring medical intervention (40, 60, 61, 67, 83, 84). Children who have been exposed to marijuana often present with neurological abnormalities, such as lethargy or somnolence, but may occasionally experience respiratory insufficiency (62, 85). Additionally, children presenting to emergency departments with marijuana intoxication are prone to receiving extensive and invasive work-ups in order to determine marijuana to be the causative agent (62, 85). Marijuana-infused products may be indistinguishable from the same items without marijuana, especially if products or packaging are designed to mimic mainstream products (e.g., gummy bears). They are appealing to children, palatable, and may contain high concentrations of THC, especially if multiple doses are consumed. All of these features may increase the likelihood of unintentional intoxication in young children. An additional contributing factor to the increase of exposures being reported in children may include increased availability of the products in the home (61).

Limitations

While interrupted-time series analysis controls for overall secular trends in marijuana exposure calls, contemporaneous interventions may obscure the true effects of marijuana policy changes. Such interventions might include local moratoriums or bans on retail marijuana outlets, which would lessen the potential statewide impact of marijuana legislation. In 2014, 14 cities or counties had permanently prohibited retail sales of recreational marijuana and 57 jurisdictions had instituted temporary moratoriums (63). By mid-2016, 60 cities or counties had instituted a permanent ban on marijuana retail sales and 7 jurisdictions had temporary bans (64). This equated to 30% of Washington's population residing in a location with either a temporary or permanent ban. As a result, the full impact of marijuana legalization on the risk marijuana poisonings may have been muted.

Calls to WAPC are voluntary and may originate from either a member of the public or a clinician. Call patterns may be sensitive to fear of legal consequences, familiarity with the clinical presentation and management of marijuana exposures, availability of alternative sources of information (such as Google), as well as publicity and awareness of poison center services. In fact, there was a general decrease in total exposure calls (for any substance) to WAPC between 1999 through 2016. Calls to the poison center may be skewed towards those events that are more severe. Additionally, coding and recording of specific details, such as product type, likely changed over the study period. As a result of these factors, calls to the poison center may not reflect the true burden of marijuana poisonings or distribution of people experiencing adverse marijuana events, and observed trends may be influenced by factors other than marijuana policy changes.

Nearly three-quarters of all marijuana exposure calls were missing information about the specific type of marijuana involved in the exposure. The completeness of this information did increase over time (from 10% to 64%), but the missing information limited the ability to analyze trends in marijuana products and assess the products involved in exposures during each timeframe. Despite this limitation, route of exposure was over 97% complete, which allowed the type of marijuana involved in poisonings to be inferred to some degree.

Record-level information was obtained for all marijuana exposure calls, but only aggregate data about total exposure calls was available. As a result, it was not possible to assess the underlying composition of people who called WAPC about an exposure or to determine if the population meaningfully changed during the course of the study. Additionally, this prevented trends in patient, exposure, or clinical characteristics from being assessed beyond changes in the overall proportion.

Future directions

Calls to the poison center regarding marijuana poisonings have increased after each major change in marijuana policy. General education efforts about safe, legal, and responsible use of marijuana may avoid some these adverse events.

Descriptive analyses of these data indicated some significant differences in certain patient, product, exposure route, or clinical characteristics in the pre- and post-legalization periods. It is important to conduct additional studies to confirm these associations. Of note, young children and older adults appear to be at increasing risk of exposure. Protections for children will likely need to expand beyond existing legal restrictions on advertising, product type, and requirements for packaging of commercial products, since these do not protect children from home-made goods, items stored in secondary containers or improperly secured items. Such strategies may include educating parents and caregivers about the effects of marijuana on children and how to avoid unintentional exposures in the home. This could be accomplished through general public education campaigns or at the point of sale by providing pamphlets, having signage, or providing education about the unique risks to children. Targeted outreach could also be accomplished during pediatric healthcare visits by conducting screening for children at risk of marijuana exposure and providing caretakers with counseling on ways to protect children from accidental marijuana exposures.

Since older adults appear to be at increasing risk of experiencing a marijuana poisoning, interventions among older adults should also be prioritized. Educational campaigns targeted towards older adult communities warning about risks associated with marijuana use in older age and increased potency of modern day marijuana may prove successful at reducing risks in this population. Healthcare providers could screen older adult patients for marijuana use and discuss potential risks with those reporting use. It may also be helpful for retailers, especially those which are “medically

endorsed", to provide education to older adult customers about their unique risks. Finally, while information may be limited, guidance on how to conscientiously use marijuana may also be of value to this population.

Conclusions

The rate of marijuana exposure calls to the Washington Poison Center have been increasing for the past several years and time series models indicate that progressively tolerant marijuana legislation may be associated with these increases. Young children are particularly at risk of exposures, presumably as a result of the increased availability of edible marijuana-containing products. Intervention strategies should be explored and implemented to reduce the likelihood of people experiencing marijuana-related adverse health events.

Figures

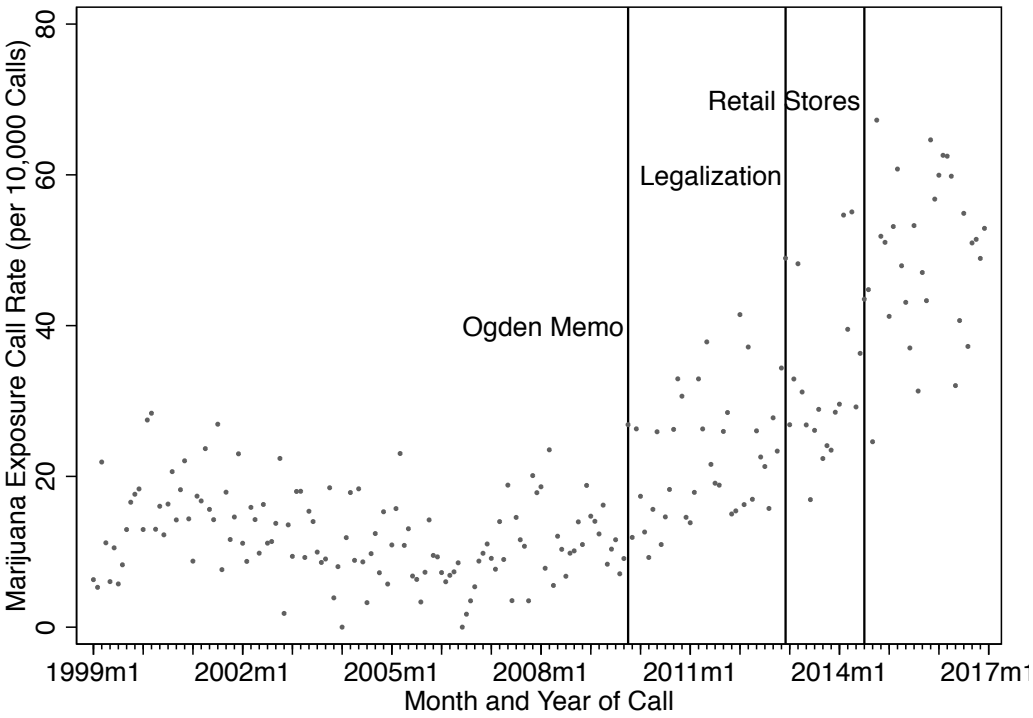

Figure 1. Monthly marijuana exposure calls per 10,000 total exposure calls to the Washington Poison Center.

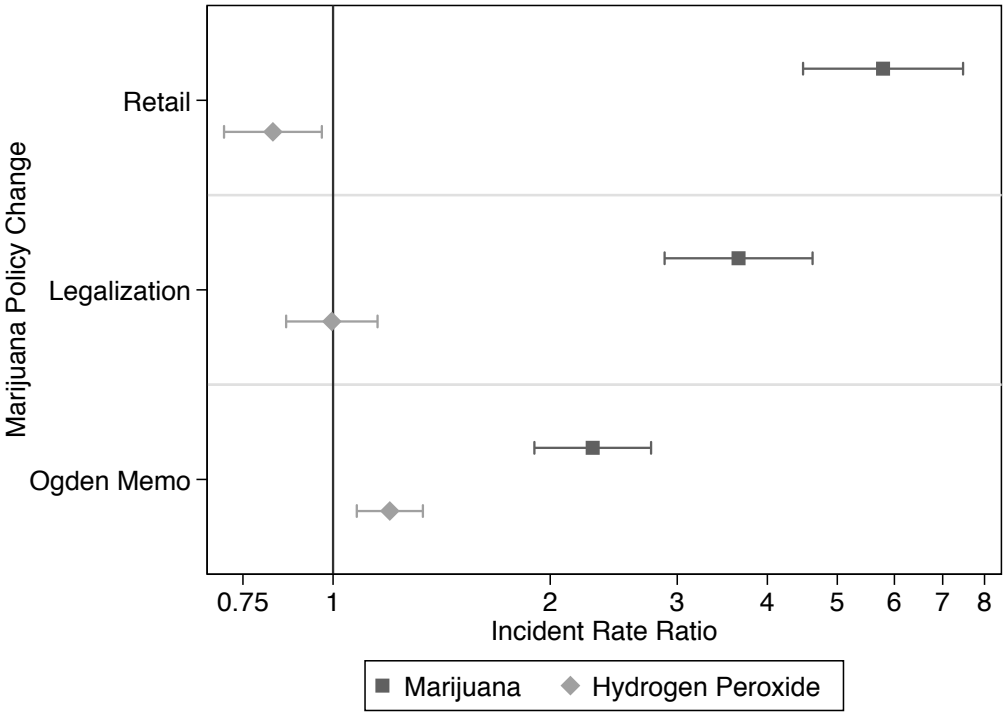

Figure 2. Incident rate ratio point estimates and 95% confidence intervals from Poisson models for marijuana and hydrogen peroxide.

Tables

Table 1. Pertinent marijuana policy changes in Washington State and count (percentage) of calls to Washington Poison Center regarding marijuana during each timeframe.

Policy	Timeframe	Marijuana Exposure Calls N (%)
Medical marijuana becomes permissible (Medical)	1/1999 – 9/2009	911 (0.12)
Federal Ogden Memorandum (Ogden Memo)	10/2009 – 11/ 2012	423 (0.22)
Legalization of recreational marijuana (Legalization)	12/2012 – 6/2014	282 (0.33)
Opening of retail marijuana stores (Retail)	7/2014 – 12/2016	675 (0.49)

Table 2. Patient and exposure characteristics of marijuana exposure calls.

Characteristic	Medical Marijuana (N=911) N, %	Ogden Memo (N=423) N, %	Legalization (N=282) N, %	Retail (N=675) N, %
Patient Characteristics				
Sex				
Male	533, 59	247, 58	167, 59	362, 54
Female	372, 41	172, 41	114, 40	309, 46
Unknown	6, <1	4, 1	1, <1	4, <1
Age category				
< 5	42, 5	30, 7	38, 13	109, 16
5 - 11	4, 0.4	9, 2	10, 4	23, 3
12 - 17	294, 32	89, 21	55, 20	112, 17
18 - 20	151, 17	71, 17	27, 10	58, 9
21 - 24	103, 11	49, 12	34, 12	62, 9
25 - 49	206, 23	116, 27	65, 23	173, 26
50+	25, 3	35, 8	31, 11	90, 13
Unknown	86, 9	24, 6	22, 8	48, 7
Child (<12 years)	46, 5	39, 9	48, 17	132, 20
Minor (<21 years)	493, 54	199, 47	130, 46	307, 45
Exposure Characteristics				
Product type*				
Baked good	22, 2	26, 6	24, 9	128, 19
Candy	0, 0	2, 0.5	6, 2	65, 10
Other food/drink	2, 0.2	2, 0.5	20, 7	42, 6
Concentrate	8, 0.9	5, 1	25, 9	103, 15
Cannabidiol	0, 0	0, 0	1, 0.4	10, 1
Marijuana vaporizer	0, 0	0, 0	0, 0	5, 1
Plant/Smokeable	49, 5	5, 1	6, 2	16, 2
Topical	1, 0.1	1, 0.2	1, 0.4	4, 0.6
Other	13, 1	4, 0.9	9, 3	5, 1
Unspecified/Unknown	816, 90	378, 89	192, 68	314, 46
Exposure Route				
Ingestion	421, 46	220, 52	173, 61	440, 65
Inhalation	236, 26	108, 26	53, 19	107, 16
Multiple	229, 25	83, 20	47, 17	103, 15
Other	5, 0.6	3, 0.7	4, 1	8, 1
Unknown	20, 2	9, 2	5, 2	17, 3
Intent				
Unintentional	112,12	68, 16	64, 23	189, 28
Intentional	726, 80	297, 70	171, 61	384, 57
Adverse reaction	33, 4	24, 6	32, 11	70, 10
Other	22, 2	20, 5	8, 3	19, 3
Unknown	18, 2	14, 3	7, 2	13, 2
Exposure Site				
Own residence	540, 59	277, 65	203, 72	534, 79
Other residence	87, 10	35, 8	28, 10	45, 7
School	13, 1	19, 4	8, 3	8, 1
Public area	29, 3	19, 4	6, 2	28, 4
Other (HCF, Work, Rest)	25, 3	11, 3	5, 1	8, 1
Unknown	217, 24	62, 15	32, 11	52, 8
Clinical Characteristics				

Clinical Effect Category**				
Cardio	180, 20	102, 24	75, 27	182, 27
Dermal	28, 3	8, 2	7, 2	16, 2
Gastro	159, 17	79, 19	63, 22	165, 24
Liver	2, 0.2	6, 1	0, 0	6, 1
Neurological	524, 58	260, 61	175, 62	419, 62
Ocular	67, 7	44, 10	33, 12	68, 10
Renal	4, 0.4	8, 2	3, 1	12, 2
Respiratory	47, 5	30, 7	14, 5	46, 7
Other	257, 28	134, 32	68, 24	194, 29
No clinical effects noted	154, 17	64, 15	51, 18	114, 17
Unknown clinical effects	33, 4	0, 0	0, 0	0, 0
Clinical Management				
Not medically attended	484, 53	168, 40	111, 39	271, 40
Evaluated/Treated and Released	232, 25	153, 36	102, 36	268, 40
Admitted to hospital	52, 6	39, 9	28, 10	56, 8
Admitted to intensive care	71, 8	39, 9	17, 6	40, 6
Psychiatry	23, 3	6, 1	7, 2	9, 1
Lost to follow-up or AMA	49, 5	18, 4	17, 6	31, 5
Medical Outcome				
No effect	33, 4	10, 2	17, 6	33, 5
Minor effect	545, 60	259, 61	159, 56	394,58
Moderate effect	152, 17	94, 22	65, 23	154, 23
Major effect	15, 2	18, 4	8, 3	20, 3
Death	4, 0.4	3, 1	1, 0.4	2, 0.3
Unable to follow	110, 12	22, 5	22, 8	41, 6
Unrelated	52, 6	17, 4	10, 4	30, 4
Clinical Effects Duration				
<=2 hours	28, 3	19, 4	15, 5	43, 6
<= 8 hours	92, 10	73, 17	54, 19	161, 24
<= 24 hours	111, 12	63, 15	46, 16	115, 17
<= 3 days	44, 5	30, 7	21, 7	33, 5
>3 days	18, 2	11, 3	4, 1	16, 2
Unknown or NA	618, 68	227, 54	142, 50	307, 45

*Columns for Legalization and Retail timeframes sum to more than 100% of exposure calls due to multiple marijuana products being reported during a single exposure call. Percentages for each product type are calculated from the total number of marijuana exposure calls occurring during each timeframe.
**Clinical effect categories are not mutually exclusive. A single exposure can be assigned to multiple clinical effect categories. Percentages for each clinical effect are calculated from the total number of marijuana exposure calls occurring during the timeframe.

Table 3. Mean monthly marijuana exposure calls per 10,000 exposure calls.

Policy	Mean	95% Confidence Interval
Medical	12.1	11.1 – 13.1
Ogden Memo	22.4	19.7 – 25.1
Legalization	33.1	27.8 – 38.5
Retail	49.2	45.3 – 53.1

*Significant by ANOVA, p<0.0001

Table 4. Interrupted time series model results for marijuana exposure calls to the Washington Poison Center.

	IRR	95% Confidence Interval	P-value
Pre-intervention slope (Time)	0.997	0.996 – 0.999	0.002
Ogden Memo	2.291	1.901 – 2.760	<0.0001
Legalization	3.659	2.881 – 4.621	<0.0001
Retail stores	5.787	4.483 – 7.471	<0.0001

Table 5. Interrupted time series model results for hydrogen peroxide exposure calls to the Washington Poison Center.

	IRR	95% Confidence Interval	P-value
Pre-intervention slope (time)	1.003	1.003 – 1.005	<0.001
Ogden Memo	1.199	1.079 – 1.332	0.001
Legalization	0.996	0.861 – 1.153	0.959
Retail stores	0.825	0.706 – 0.965	0.016

Chapter 4: Pediatric Marijuana Exposures

Pediatric Marijuana Exposure Calls, Washington Poison Center, 2016

Background

Marijuana is harvested from the female *Cannabis sativa* plant. *Cannabis sativa* contains numerous chemical compounds, but the primary psychoactive compound is delta-9-tetra-hydrocannabidiol (THC) (26, 28). Once in the blood, THC stimulates a release of dopamine in addition to disrupting the function of several areas of the brain (29, 30). Marijuana intoxication results in one or more of the following: feelings of euphoria (associated with increases in dopamine), disinhibition, anxiety, paranoia, temporal slowing, depersonalization, derealization, hallucinations, and impaired judgment, attention, or reaction time (31). Additional signs of marijuana intoxication include increased appetite, dry mouth, bloodshot eyes, or rapid heart rate (31). The magnitude of these effects are highly dependent on the dose used, the route of administration, user's prior experience with cannabis, any concurrent drug use, the setting and the mindset of the user (32).

Washington State has been at the forefront of modern-day marijuana legislation for over two decades. In November 1998, Washington State became one of the first states to legalize use, possession, and cultivation of marijuana for certain approved medical conditions (Washington Initiative 692). Over the next several years, additional legislation pertaining to medical marijuana was enacted including expansions to the list of medical conditions eligible for marijuana treatment and in the classifications of healthcare professionals allowed to issue medical authorizations for use of marijuana (27). The proliferation of state-level medical marijuana legislation across the United States prompted the United States Deputy Attorney General David Ogden to issue a memorandum in October 2009 that directed United States attorneys not to get involved in the enforcement of federal marijuana laws if individuals were compliant with state-level medical marijuana laws. In 2011, additional legislation (ESSB 5073) was passed in Washington State which developed a framework for the establishment of collective gardens. These collective gardens evolved into dispensaries, which essentially created retail access points for medical marijuana; they were neither licensed nor regulated. In November 2012, Washington and Colorado became the first two states to pass legislation allowing the use, possession, and sale of marijuana for recreational purposes for adults 21 years of age or older (Washington Initiative 502 and Colorado Amendment 64, respectively). Such legislation was unprecedented not only in the United States but also internationally. Washington Initiative 502 came to full fruition in July 2014 when the first licensed retail marijuana outlets opened in Washington State. As of 2019, 34 states and the District of Columbia have legalized marijuana to some degree; 10 states

and the District of Columbia have legalized marijuana for recreational purposes (6).

There is great concern about the effects that liberalization of marijuana policies and establishment of a marijuana retail market will have on minors (85, 86). These changes in policies may lead to decreased risk perceptions surrounding marijuana among both minors and adults (73, 87, 88). Also, marijuana is more widely available, which may increase opportunities for exposure. In addition to marijuana plant material, there is increased accessibility of marijuana-containing edible products. Edibles are of particular concern for minors due to their resemblance of similar non-marijuana-containing products, palatability and high THC content (89).

Young children are prone to accidental ingestion of marijuana-containing products as well as severe adverse events requiring medical intervention (40, 60, 61, 67, 83, 84). Cannabis toxicity in children usually presents as lethargy, nausea, tachycardia, or bradycardia with more serious consequences such as respiratory depression or seizures being reported occasionally (90). Additionally, children presenting to emergency departments with marijuana intoxication are prone to receiving extensive and invasive work-ups in order to determine marijuana to be the causative agent (62, 85).

Calls to poison centers about unintentional marijuana ingestions in children have been increasing for a number of years (61, 62, 82). Wang, Roosevelt and Heard (62) reported that a major pediatric hospital in Denver, Colorado had not seen any children for marijuana exposures prior to 2009, when Colorado experienced a major expansion in medical marijuana, and that the number of children seen with marijuana exposures had risen since. When surveying states by legalization status, researchers have reported substantially greater increases in the number of poison center calls regarding pediatric exposures to marijuana occurring in states that have legalized marijuana for medical or recreational purposes compared to those that have not legalized marijuana (61, 82). Washington State has experienced a similar increase. Of the marijuana exposure calls regarding children under the age of 12 that occurred from 1999 – 2016, nearly 68% of marijuana exposure calls to the Washington Poison Center occurred after legalization in November 2012, which represented less than a quarter of the total study period (See Chapter 3).

Since marijuana was legalized in 2012, lawmakers in Washington State have been continually revising marijuana laws in an attempt to reduce or prevent adverse impacts on children and minors. The initial law instituted a buffer zone around schools, playgrounds, and other places where children may be present; retail stores and their advertising are prohibited within these buffer zones (Revised Code of Washington 69.50). Additional restrictions on advertising are in place to control the amount of advertising, its content, and format. Products which are especially appealing to children are prohibited (Washington Administrative Code 314-55-077). The Washington State Liquor and Cannabis Board must approve all marijuana-infused products, labeling, and packaging prior to the product being available for purchase. As recently as late 2018, in response to complaints about safety, the Washington Liquor and Cannabis Board re-evaluated products for their appeal to children and revised guidance on what is acceptable. There are also packaging and labeling

requirements intended to reduce unintentional exposures (Washington Administrative Code 314-55, 246-70). Specifically, marijuana-containing products shall be packaged in child-resistant packaging and each individual serving packaged (e.g., a single candy bar with multiple servings is not allowed). Packages and labeling shall not be appealing to children and, beginning in February 2017, were required to contain a standardized “not for kids” label that includes the phone number for Poison Control. These laws continue to be clarified and refined in an effort to improve protections for children.

While there has been an attempt to minimize exposure of minors to marijuana, such events continue to occur and may be increasing in states with more tolerant marijuana policies (61, 62). The objectives of this research were to evaluate and describe all Washington Poison Center calls for marijuana exposures among children under age 12 in 2016 (four years after marijuana was legalized and nearly 2 years after legal sales began in Washington State), for the purpose of identifying mechanisms of exposure in order to inform efforts to reduce the number of marijuana exposures.

Methods

This case series study used call records from the Washington Poison Center (WAPC) to describe child marijuana exposures four years after marijuana was legalized in Washington State. The WAPC is a non-profit agency that provides immediate, free, and expert treatment advice and assistance, via telephone, in case of exposure to poisonous, hazardous, or toxic substances. The WAPC is available twenty-four hours a day, 365 days a year and has served the residents of Washington State since 1956. The WAPC enters information about each call they receive into an electronic medical record system. For this study, all calls made to the Washington Poison Center in 2016 regarding marijuana exposures (subgeneric code=083000) among children under the age of 12 were identified. A dataset containing patient information (e.g., age, gender, weight), call information (date and time of the poison center call, type of call, location of caller, relationship of caller to patient, caller site), exposure information (e.g., number of substances, route, reason, site, time, duration, chronicity), exposure management (e.g., management site, healthcare outcome, therapies recommended and administered), details about the substances involved (standard description, verbatim description, Poisindex code, generic code, quantity, concentration, dose, certainty of amount, form of substance), clinical effects (i.e., presence of symptoms arranged into categories such as cardiovascular, dermal, gastrointestinal, heme/hepatic, neurological, ocular, renal, respiratory, and miscellaneous), and outcome information (e.g., medical outcome, duration of effects) was obtained. Additionally, call notes were extracted from the medical records of these patients and patient identifiers were manually redacted by the WAPC. All fields, with the exception of caller location information, verbatim substance description, and the call notes were coded values.

Patient demographics, exposure details, clinical effects, and therapies were summarized using descriptive statistics. Call notes for each marijuana exposure were reviewed by the researcher to gather information about four

characteristics of the event: the specific form of marijuana involved (e.g., brownie, cookie, joint), intent for which marijuana was originally obtained (e.g., medical, recreational), the source of the marijuana (e.g., parent, friend, babysitter), as well as any additional details about circumstances leading to exposure (e.g., substance left on counter). Approval to use these data was obtained from the University of Washington Institutional Review Board (Study ID: STUDY00000050). All statistical analyses were performed in Stata 14 (College Station, TX).

Results

In 2016, there were fifty-nine calls to the Washington Poison Center about marijuana exposures among children under the age of 12 years. Nine records were removed from the dataset because calls were made from outside Washington State (N=4), marijuana exposure was ruled out by the Poison Center (N=4), or the exposure substance was misclassified as marijuana (N=1). Details about each child's exposure are available in Table 1.

The median age of children with a reported marijuana exposure was two years. Only six children (12%) were over the age of 5. None of the exposures were reported to be intentional. Of those where the source of marijuana could be determined (N=29, 58%), a family member, either parent (N=20, 69%) or grandparent (N=6, 21%), was the most common source of marijuana (Table 2). Nearly all of the exposures (94%) occurred at the patient's own home and involved only a single substance (90%). Very few records allowed ascertainment of whether the marijuana involved was intended for medical or recreational marijuana (N=13, 26%). Of those that noted the type, 85% indicated that the marijuana was obtained for medical purposes.

Ingestion (N=43, 86%) far exceeded any other exposure route (e.g., inhalation, dermal contact). Edibles were the most frequently reported form of marijuana (N=26, 63%) among cases where product type could be determined (N=41, 82%). Brownies, cookies, and candies were the most common form of edible (N=25, 96%). Baked goods were reported to be both homemade and purchased. A small number of exposures (N=9, 18%) involved oil, marijuana vaporizers, ointment, or plant material (either in original state or prepared for smoking). There were three exposures to cannabidiol (CBD) among children being treated for seizures by parents. One was the result of therapeutic error, one an adverse reaction, and the third was an unintentional exposure. A single child was reported to have been exposed to marijuana through breastmilk. The child experienced a seizure; however, the child had a history of seizures and the mother had consumed other substances that could potentially cause seizures. A single report of second-hand smoke was identified in an apartment building. While scent of marijuana was observable in the child's room, the child was asymptomatic.

Of those whose medical outcome was known (N=33), nearly all exposures were considered to have caused no or minor health effects (78%). Three of these children were asymptomatic and the symptoms experienced by another three children were determined to be unrelated to their marijuana exposure. Symptoms generally lasted less than 24 hours.

Neurological symptoms, typically drowsiness or lethargy, were the most commonly reported symptoms (N=25, 50%). Cardiovascular effects (e.g., tachycardia, hypotension, hypertension) and gastrointestinal symptoms (i.e., vomiting, abdominal pain) were reported less commonly (14% and 12%, respectively). Twenty-nine children (58%) were evaluated at a healthcare facility. While most were released after evaluation, five children (10%) were admitted to non-critical care. The single incident of major health effect requiring intensive care and intubation involved a toddler with a history of seizures who was given cannabidiol oil containing 22% THC.

Discussion

The patient, exposure, and clinical characteristics described in this study are similar to those reported by others that have evaluated marijuana exposures in young children (82, 90). Compared to statistics for all exposures, to any substance, involving children ≤12 years reported to U.S. Poison Centers, exposures involving marijuana have a tendency toward more severe effects and place a greater burden on the healthcare system. Fifty-four percent of children sought treatment in a healthcare facility compared to 30% of all child exposures reported to U.S. poison centers in 2016 (72). Onders, Casavant, Spiller, Chounthirath and Smith (82) hypothesized that the proportion of children referred to healthcare facilities and admitted for marijuana exposures may be inflated due to marijuana's status as a U.S. Drug Enforcement Administration Schedule 1 drug and the requirement to report any pediatric exposures to such substances to child protective services. Referring an exposed child to a healthcare facility allows for child protective services (CPS) agencies to become involved and conduct an assessment of the exposure circumstances before the child is released home. With regard to severity of symptoms, only 2.6% of all exposure calls to U.S. poison centers involving children ≤12 years resulted in a moderate or major medical outcome as opposed to 14% of exposures observed in this study (72). Several studies have reported that children exposed to marijuana may experience severe, potentially life-threatening health effects including respiratory depression, which sometimes requires intubation, seizures, or coma (40, 62, 82, 91). A single adverse reaction requiring intubation and care in a critical care unit was identified in this study. This exposure was unique in that the child was intentionally given a THC-containing cannabidiol product and the child's reaction may have also been exacerbated by simultaneous exposure to multiple other medications. Little is known about the interaction of marijuana with other medications and scientific evidence validating the use of cannabidiol oil for seizure treatment is limited (92), although the U.S. Food and Drug Administration (FDA) did recently approve a cannabidiol oral solution for the treatment of seizures associated with two rare and severe forms of epilepsy (Lennox-Gastaut syndrome and Dravet syndrome) in patients two years of age and older (93). Official validation of cannabidiol for treatment of specific epilepsy disorders by the FDA may strengthen caregiver belief in the utility and safety of cannabidiol treatments for seizures in general. Even so, caregivers who choose to administer cannabidiol oil for seizures should be aware about of the dearth of evidence

regarding effectiveness of cannabidiol oil for seizures, in general, and that young children are particularly susceptible to adverse consequences of THC, even from low doses, as a result of their small size and naivety to marijuana (67, 94).

While ingestion has long been the most common route of marijuana exposure in young children, the primary form of marijuana ingested historically, and in countries where marijuana is still illegal, was resin (90, 91, 95). Only one exposure in this study involved resin. Instead, edibles, particularly baked goods and candies were the most frequently reported form of marijuana involved in this sample of exposures, despite only comprising 10% of the total market share of cannabis sales in Washington in 2016 (78). Cao, Srisuma, Bronstein and Hoyte (75) reported that over 90% of calls to U.S. poison centers between 2013 through 2015 that involved edible marijuana products occurred in states that have legalized marijuana. The popularity of edible marijuana in states that have legalized marijuana is likely due to wide commercial availability, palatability of these products, perception that ingestion is healthier than smoking, and the ability to discretely consume marijuana (76, 77). Unfortunately, the appeal of these products is not limited to adults. Brownies, cookies, chocolate, gummy candies, and other candies are attractive to children and may be indistinguishable from the same products that do not contain marijuana. Children are natural explorers and are likely consuming these items without knowing they contain marijuana (82). Even if children are aware a marijuana-containing edible is supposed to be off-limits, they may find them too attractive to resist. Edibles are particularly dangerous because they may contain high concentrations of THC. A child may consume large quantities of THC before experiencing any effect. Oregon, Washington, and Colorado have all placed limits on the total and per serving THC content allowed in edibles to try to prevent inadvertent over-consumption of edibles by adult consumers (79-81). Additionally, Washington State has put into place additional regulations related to packaging and labeling to discourage children from accessing these products or from consuming multiple doses (e.g., requiring edible products be wrapped as single servings).

One child in this study, who experienced a seizure, was found to have been exposed through breastmilk. Seizures have been documented in other children exposed to marijuana (82) and it has been reported that marijuana may increase the likelihood of seizures in people predisposed to seizures (96). It is unknown whether the THC alone caused the child's seizure since the child had a history of seizures and may have also been exposed to fennel oil, which has been previously reported to cause seizures (97). Multiple studies have reported that THC is transferred to breastmilk after a breastfeeding mother smokes marijuana, with infants estimated to receive 0.8 - 2.5% the dose of their mother (98, 99), but little scientific evidence exists regarding health effects from exposure to marijuana through breastfeeding (33, 100). Despite the potential for negative health effects through breastmilk exposure, a survey of women from Colorado in 2014 indicated that 3% of women who had ever used marijuana and nearly 14% of women who currently use marijuana used marijuana postpartum while breastfeeding (100). Results from the Colorado Pregnancy Risk Assessment Monitoring System estimated that an average of 3.6% of currently breastfeeding women used marijuana, with no significant

increases observed across 2014 through 2016 (101). It may be beneficial to increase awareness among breastfeeding mothers that infants can be exposed to THC through breastmilk and to educate them both about what is known and not known about the risks to their child.

Since marijuana was legalized in 2012, lawmakers in Washington State have been attempting to reduce or prevent adverse impacts on children and minors through legislation; however, it is unknown which specific policies or combinations of policies provide optimal protection for children and there may still continue to be gaps in the protection such regulations can provide. For example, edibles may be homemade, rendering all legal protections related to packaging and labeling of edibles useless at preventing child exposures to these items. Additionally, most concern and regulations intended to prevent pediatric exposures relate to direct exposures to marijuana, but children may also be exposed to marijuana through secondhand smoke. One study reported identification of marijuana metabolites in the urine of children whose parents reported use of marijuana in the child's home or by a caregiver (102). While effects may be muted, secondhand exposures to marijuana may have short and long term health effects akin to direct intoxication (103). The child that was exposed to secondhand smoke in this study was asymptomatic, but there is at least one account of secondhand smoke causing serious acute effects on a young child (104). Current regulations exist to reduce exposures to children in public spaces, but no protections exist for the home setting. The exposure in this study originated from a neighboring unit at a multi-family home, which may need to be of special consideration in future policy-making. Without thoughtful consideration of additional mechanisms to prevent unintended exposures, increases in marijuana use may lead to growing numbers of minors being inadvertently exposed to secondhand smoke.

The proliferation of tolerant marijuana policies may be an indication of decreased risk perceptions surrounding marijuana among both minors and adults (73, 87, 88). As a result, adults may not consider marijuana to be a risk to children or view it as a drug that must be kept away from children (86). Caregivers, such as parents or grandparents, were identified as a primary source of marijuana involved in pediatric unintentional exposures. Efforts need to be in place to teach parents and children alike that marijuana can be dangerous for children (105). Future interventions may include increased outreach to caregivers, perhaps by pediatricians at well-child visits, about marijuana and the risks to children. Specifically, caregivers should be informed of potential routes of exposure that they may not have been aware of or thought harmful (e.g., secondhand smoke, breastmilk), the potential detrimental effects of exposures on young children, safe storage practices, advisement not to use marijuana around children and, if possible, to keep marijuana out of the home entirely (90). Increasing awareness of the general public through educational campaigns or direct interventions by healthcare providers may also help to reduce laissez faire attitudes surrounding the risks of marijuana when it comes to children (90). Educational campaigns should motivate people to avoid using marijuana in front of children or spaces where

children will be, as well as keeping children away from places where people are actively smoking or previously smoked marijuana.

Limitations

Calls to the poison center are voluntary and may come from either clinicians or the public. As a result, the data obtained from WAPC may not be representative of the true assortment of marijuana exposures occurring in young children. Clinicians may be familiar with the typical clinical effects of marijuana intoxication and only call WAPC when more severe medical outcomes are observed, resulting in an over-representation of serious events. Exposures involving young children may also be over-represented as a result of reporting behaviors, more so than exposure patterns, due to additional fear of more serious adverse health effects in these patients. In addition, as children age, there is a shift from unintentional to intentional exposures (90). Older children may be more aware that they may have done something wrong and may be too fearful to notify an adult or the poison center about their exposure. Some exposures may go unrecognized or be unreported altogether. Members of the public may be reluctant to call the poison center for fear of legal consequences or social stigmatization. Additionally, members of the public may be less likely to call as they become more familiar or comfortable with the effects of marijuana and perceive that nothing needs to be done when a child is exposed beyond letting them sleep through the effects. These factors increase the likelihood that the reported cases of marijuana exposure are an under-representation of the true number of marijuana exposures occurring in young children and an over-representation of more severe clinical effects.

Very few records mentioned the original intent under which the marijuana product was obtained nor its source. This prevented the ability to tease out the independent effects of legalization for medical versus recreational purposes on pediatric exposures. Of those records that did include this information, the majority indicated it was obtained for medical purposes; however, it's possible people are more likely to indicate the intent of the marijuana as being medical due to stigma or fear of negative repercussions. This fear may not be entirely unfounded: four calls noted involvement or possibility of involving child protective services.

Conclusions

Young children continue to experience unintentional exposures to marijuana, despite increasing efforts to minimize risks, within a legalized retail marijuana state. It is important to understand and mitigate the effects of liberal marijuana policies and social perceptions that marijuana is of low risk to children. States need to anticipate the risks for child exposure, apply strong policies, monitor trends in child exposure, and consider dedicating resources for additional efforts that help families and caregivers to understand dangers and protect their children from exposure.

Tables

Table 1. Case series of pediatric marijuana exposure calls, Washington State, 2016.

Case Number	Age Group (Years)	Sex	Intent	Source	Product	Medically Attended	Medical Outcome (if medically attended)	Organ systems Impacted	Symptoms (Marijuana exposure-related or unknown relationship)
1	< 1	M	Unintentional	Unknown	Plant - Blunt	N	--	Gastrointestinal, Neurological	Vomiting, drowsiness/lethargy
2	< 1	F	Adverse Reaction	Parent	Breastmilk	Y	Evaluated/Treated and Released	Neurological	Seizures
3	1 – 3	F	Unintentional	Parent	Brownie	N	--	Neurological	Drowsiness/lethargy
4	1 – 3	F	Unintentional	Stranger	Brownie	Y	Evaluated/Treated and Released	Cardiovascular, Neurological	Tachycardia, agitated/irritable, other
5	7 - 11	F	Unintentional	Unknown	Brownie	Y	Admitted to noncritical care	Neurological	Drowsiness/lethargy
6	4 - 6	M	Unintentional	Parent	Brownie	Y	Lost to follow-up or AMA	Gastrointestinal, Neurological	Abdominal pain, drowsiness/lethargy
7	1 - 3	F	Unintentional	Grandparent	Brownie	N	--	Neurological	Drowsiness/lethargy
8	4 - 6	M	Unintentional	Parent	Brownie	N	--	Neurological	Drowsiness/lethargy
9	4 - 6	M	Unintentional	Grandparent	Brownie	N	--	Neurological, Respiratory	Drowsiness/lethargy, dyspnea
10	1 – 3	F	Unintentional	Unknown	Candy	Y	Evaluated/Treated and Released	Neurological	Drowsiness/lethargy, other
11	1 – 3	F	Unintentional	Grandparent	Candy	Y	Admitted to noncritical care	Neurological	Ataxia, drowsiness/lethargy
12	1 – 3	M	Unintentional	Parent	Candy	Y	Admitted to noncritical care	Cardiovascular, Neurological	Bradycardia, hypotension, drowsiness/lethargy
13	4 - 6	F	Therapeutic error	Parent	Cannabidiol	N	--	--	--
14	1 – 3	F	Unintentional	Parent	Cannabidiol Oil	Y	Admitted to noncritical care	Cardiovascular	Hypertension, Tachycardia
15	1 – 3	F	Unintentional	Unknown	Candy - Chocolate	Y	Evaluated/Treated and Released	Cardiovascular, Neurological	Tachycardia, drowsiness/lethargy
16	1 – 3	F	Unintentional	Parent	Candy - Chocolate	N	--	--	--
17	4 - 6	F	Unintentional	Parent	Cookie	Y	Evaluated/Treated and Released	Neurological	Drowsiness/lethargy
18	1 – 3	M	Unintentional	Unknown	Cookie	Y	Evaluated/Treated and Released		Other
19	1 – 3	F	Unintentional	Unknown	Cream	N	--	--	--
20	1 – 3	M	Unintentional	Unknown	E-marijuana	N	--	--	--
21	1 – 3	F	Unintentional	Unknown	Candy - Gummies	N	--	--	--
22	1 – 3	F	Unintentional	Unknown	Candy - Gummies	Y	Evaluated/Treated and Released		
23	1 – 3	M	Unintentional	Parent	Brownie	Y	Evaluated/Treated and Released	Cardiovascular, Gastrointestinal, Neurological, Respiratory	Tachycardia, abdominal pain, vomiting, drowsiness/lethargy, tachypnea
24	1 – 3	F	Unintentional	Parent	Cookie	N	--	--	--
25	1 – 3	F	Unintentional	Parent	Cookie	N	--	--	--
26	1 – 3	F	Unintentional	Unknown	Cookie	N	--	--	--
27	4 - 6	M	Unintentional	Unknown	Brownie	N	--	Gastrointestinal, Neurological	Nausea, vertigo
28	7 - 11	F	Unintentional	Parent	Candy - Mints	Y	Evaluated/Treated and Released	Neurological	Agitated/irritable, drowsiness/lethargy
29	1 – 3	M	Unintentional	Grandparent	Candy	Y	Evaluated/Treated and Released	Neurological	Agitated/irritable
30	1 – 3	F	Unintentional	Parent	Oil	Y	Lost to follow-up or AMA	Neurological	Drowsiness/lethargy
31	1 – 3	M	Unintentional	Parent	Oil	N	--	Neurological	Drowsiness/lethargy
32	< 1	M	Unintentional	Unknown	Oil	Y	Evaluated/Treated and Released	Neurological	Drowsiness/lethargy
33	1 – 3	M	Adverse Reaction	Parent	Cannabidiol Oil	Y	Admitted to critical care	Neurological, Respiratory	Coma, drowsiness/lethargy, respiratory depression

Case Number	Age Group (Years)	Sex	Intent	Source	Product	Medically Attended	Medical Outcome (if medically attended)	Organ systems Impacted	Symptoms (Marijuana exposure-related or unknown relationship)
34	1 – 3	M	Unintentional	Parent	Plant - Roach	Y	Evaluated/Treated and Released	--	--
35	1 – 3	F	Unknown	Parent	Brownie	Y	Evaluated/Treated and Released	Neurological	Seizure
36	1 – 3	F	Unintentional	Stranger	Pretzel	Y	Evaluated/Treated and Released	Neurological	Drowsiness/lethargy
37	< 1	M	Unintentional	Parent	Resin	Y	Admitted to noncritical care	Dermal, Neurological	Pallor, coma, drowsiness/lethargy, other
38	1 – 3	M	Unintentional	Neighbor	Second-hand Smoke	N	--	--	--
39	1 – 3	F	Unintentional	Unknown	Candy - Chocolate	N	--	--	--
40	1 – 3	M	Unintentional	Parent	E-marijuana	Y	Evaluated/Treated and Released		Other
41	1 – 3	F	Unintentional	Unknown	Lotion	N	--	--	--
42	1 – 3	M	Unknown	Unknown	Unknown	Y	Evaluated/Treated and Released	Gastrointestinal, Neurological	Vomiting, drowsiness/lethargy
43	1 – 3	M	Unintentional	Unknown	Unknown	Y	Evaluated/Treated and Released	Cardiovascular, Neurological	Tachycardia, drowsiness/lethargy
44	1 – 3	M	Unintentional	Unknown	Unknown	Y	Evaluated/Treated and Released	Cardiovascular, Gastrointestinal, Neurological, Ocular, Renal	Hypotension, Dehydration, drowsiness/lethargy, mydriasis, nystagmus, urinary retention, other
45	7 - 11	F	Unintentional	Unknown	Unknown	Y	Evaluated/Treated and Released	Neurological	Drowsiness/lethargy, Seizure
46	1 – 3	F	Unintentional	Grandparent	Unknown	Y	Evaluated/Treated and Released	Cardiovascular, Neurological, Respiratory	Tachycardia, agitated/irritable, tachypnea
47	Unknown	M	Unintentional	Grandparent	Unknown	N	--	Neurological	Drowsiness/lethargy, other
48	1 – 3	F	Unintentional	Unknown	Unknown	Y	Evaluated/Treated and Released	--	--
49	1 – 3	M	Unintentional	Unknown	Unknown	N	--	--	--
50	< 1	F	Unknown	Unknown	Unknown	N	--	--	--

Table 2. Characteristics of pediatric marijuana exposures reported to WAPC (N=50), 2016.

Characteristic	N, %
Median Age in years (IQR)	2 (1 – 3)
Age in years	
0-2	31, 62
3-5	13, 26
6-8	3, 6
9-11	2, 4
Unknown	1, 2
Male	22, 44
Exposure Reason	
Unintentional	44, 88
Adverse Reaction/Therapeutic error	3, 6
Unknown	3, 6
Exposure Site	
Own residence	47, 94
Other residence	2, 4
Public Area	1, 2
Source	
Parent	20, 40
Grandparent	6, 12
Other	3, 6
Unknown	21, 42
Product type	
Medical	11, 22
Recreational	2, 4
Unknown	37, 74
Product category	
Edible	26, 52
Smokable	3, 6
Topical	2, 4
Inhalation	2, 4
Other	8, 16
Unknown	9, 18
Cannabis type	
Baked good (brownie, cookie)	15, 30
Candy (chocolate, gummies)	10, 20
Oil	3, 6
Cannabidiol	3, 6
Plant	2, 4
Ointment	2, 4
E-marijuana pen	2, 4
Resin	1, 2
Breastmilk	1, 2
Other food	1, 2
Second-hand Smoke	1. 2
Unknown	9, 18
Number of substances	
1	45, 90
2	2, 4
3	1, 2
4	2, 4
Exposure Route	
Ingestion	43, 86
Inhalation	2, 4
Dermal	2, 4
Unknown	3, 6
Clinical Effect Duration	

<2 hours	3, 6
<=8 hours	16, 32
<=24 hours	6, 12
<=3 days	1, 2
Unknown	1, 2
NA	23, 46
Clinical Effect Category	
Cardiovascular	7, 14
Dermal	1, 2
Gastrointestinal	6, 12
Neurological	25, 50
Ocular	1, 2
Renal	1, 2
Respiratory	3, 6
Other	6, 6
Management Site	
Non-healthcare facility	21, 42
En-route to healthcare facility	23, 46
Referred to healthcare facility	6, 12
Medical Treatment	
Not treated in healthcare facility	21, 42
Evaluated and/or treated and released	21, 42
Admitted to non-critical care	5, 10
Admitted to critical care	1, 2
Lost to follow-up or AMA	2, 4
Therapy	
Observation	10, 20
Patient refused help	1, 2
Unknown	18, 36
Missing	21, 42
Treatment	
Charcoal	1, 2
Other Emetic	2, 4
Dilute/Irrigate/Wash	13, 26
Fresh air	1, 2
Food/snack	8, 16
Benzodiazepine	1, 2
IV Fluids	4, 8
Intubation	1, 2
Oxygen	1, 2
Other	3, 6
Medical Outcome	
Symptoms un-related to exposure	3, 6
No effect	3, 6
Minor effect	20, 40
Moderate effect	6, 12
Major effect	1, 2
Unable to follow	17, 34

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