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Original Contributions

PEDIATRIC CANNABIS SINGLE-SUBSTANCE EXPOSURES REPORTED TO THE MICHIGAN POISON CENTER FROM 2008–2019 AFTER MEDICAL MARIJUANA LEGALIZATION

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Abstract—Background: Legalization of medical and recreational cannabis is a major contributor to pediatric cannabis exposures. The trends and magnitude of pediatric cannabis exposures in Michigan after medical cannabis legalization in 2008 have not been assessed. **Objective:** To describe the temporal trends of pediatric cannabis exposures reported to the Michigan Poison Center (MiPC) after medical cannabis was legalized in 2008 and 1 year after legalization of recreational cannabis in 2018. **Methods:** Retrospective electronic chart review of pediatric (<18 years old) single-substance cannabis exposures reported to the MiPC from January 1, 2008 to December 31, 2019. Routes of cannabis exposure were reported as ingestion, inhalation, and unknown. Types of ingested cannabis products were also documented. **Results:** Between 2008 and 2019, 426 pediatric cannabis single exposures were reported. The median patient age was 6.0 years (interquartile range 2–15 years). Age distribution was bimodal. A total of 327 (76.8%) exposures were from cannabis ingestion, 79 (18.5%) from inhalation, 2 (0.5%) from both ingestion and inhalation, and 18 (4.2%) from unknown route. The doubling time for number

of cases was 2.1 years, and the total number of annual reported cases increased after 2016. Teenagers (13–17 years) had the highest number of inhalational exposures, whereas young children (0–5 years) had the highest number of ingestions. **Conclusion:** Single-substance pediatric cannabis exposures reported to the Michigan Poison Center increased after medical cannabis was legalized in 2008 through recreational legalization in 2018. © 2021 Elsevier Inc. All rights reserved.

Keywords—pediatrics; cannabis; marijuana; toxicology

INTRODUCTION

Cannabis, after alcohol, is the second most commonly used psychotropic substance in the United States (1). A 2018 national survey showed that 34.8% of young adults age 18 to 25 years and 12.5% of children age 12–17 had used marijuana in the past year (1). In 2017, 36% of U.S. students in grades 9–12 used marijuana, and the rate for students in Michigan was slightly higher at 41% (2). Although it is currently unknown whether adolescent use of marijuana will rise due to the increasing nationwide trend in marijuana legalization, there is concern that legalization provides greater opportunity for youth marijuana acquisition and subsequent toxic exposures.

A preliminary version of these results was presented as an abstract (“Trends in Marijuana Exposures Reported to Michigan Poison Center from 2014 to 2019”) at the Annual Scientific Meeting hosted by the American College of Medical Toxicology, virtually, in March 2020 (New York, NY).

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At the federal level, cannabis remains a schedule I drug, defined by the Drug Enforcement Administration as a substance “with no currently accepted medical use and a high potential for abuse” (3). At the state level, adult use of cannabis is currently legal in 11 states, including our state of Michigan, with anticipated additions of four more states after voter approval occurred in the November 2020 elections (Arizona, Montana, New Jersey, and South Dakota) (4).

A consequence of increased legalization and subsequent availability of cannabis products is a predictable parallel increase in unintentional pediatric exposures. A retrospective review of national poison center data that compared state trends in unintentional pediatric cannabis exposures with respect to state cannabis legislation status found that the rate of pediatric exposure increased over a 7-year period (2005–2011) in states that had passed cannabis legislation (5). Since then, studies in states where marijuana was legalized or decriminalized have continued to show a concomitant rise in pediatric cannabis exposures and increases in emergency department visits or hospitalizations (6–8). For example, a report that combined data from Rocky Mountain Poison and Drug Center and Children’s Hospital of Colorado found that calls to the state’s poison control center for unintentional pediatric cannabis exposures between 2009 and 2015—when medical dispensaries proliferated and recreational use was legalized—increased 34% annually, significantly greater than the 19% increase in cannabis-related calls received by poison control centers in the rest of the United States (9). A further analysis of billing codes from hospitalizations in Colorado related to cannabis exposure reported significant increases in patients aged 0–8 and 9–17 years after liberalization of medical cannabis laws in 2010, and an even further increase in exposure for these ages after enactment of legalized recreational use in 2014 (10). This suggests that liberalization of cannabis laws is temporally related to increases in childhood cannabis exposures (11). Although studies have shown that national surveys of adolescent cannabis use have remained stable, encounters with health care facilities have increased (12–14). Some states, such as Colorado, have passed legislation focused on preventive measures, such as child-proof packaging, opaque packaging, and limited marketing, which thus far, have not been shown to be effective at decreasing health care facility visits (15).

Medical cannabis became legal in Michigan in 2008, and recreational cannabis became legal in 2018. As of December 1, 2019, recreational cannabis products were available for purchase. This manuscript reports the trend in unintentional pediatric (<18 years old) single-substance cannabis exposures at risk of toxicity reported

to the Michigan Poison Center with respect to the progression of laws pertaining to the changes in legal status of cannabis from 2008 to 2019.

METHODS

We conducted a retrospective review of all single-substance cannabis cases reported to the Michigan Poison Center (MiPC) from 2008 to 2019. Michigan has a population of approximately 10 million people covered by one poison center. The MiPC is staffed by nurses, pharmacists, and physicians (Poison Information Providers [PIPs] and Certified Specialists in Poison Information [CSPIs]) who take telephone calls from the public and health care providers. Calls originating from within Michigan or telephones with area codes from Michigan are routed to the MiPC call center. Human poisoning advice is provided free of charge 24 h a day, 365 days per year. The MiPC logs over 100,000 incoming and outgoing calls per year. CSPIs and PIPs create a chart for every exposure reported, and clinical and demographic data are entered into a secure electronic toxicology database. The MiPC changed databases in August of 2019 from ToxiCALL® (Computer Automation Systems Inc., Aurora, CO) to ToxSentry™ (Jacksonville, FL) (ToxiCALL 1999–8/2019 and ToxSentry 8/2019–present). This study was approved by the Detroit Medical Center and Wayne State University Institutional Review Boards.

To identify all cases of pediatric cannabis exposure, we queried both databases: ToxiCALL (January 1, 2008–July 31, 2019) and ToxSentry™ (August 1, 2019–December 31, 2019). Investigators searched using the following key words: “marijuana,” “marihuana,” “THC,” “cannabis,” and “cannabinoids.” Each chart generated by keyword searches was reviewed by authors (DD and AK) to confirm that they met the following inclusion criteria: 1) patients were exposed only to a cannabis product; 2) patients were intoxicated with symptoms consistent with cannabis exposure or were at high risk of developing symptoms (judged by the MiPC specialists), and 3) patients were age 17 years and younger. We excluded cases that were deemed to be of unlikely significance, such as tastes, licks, or secondhand smoke exposures. We chose to exclude cases that involved multiple substances because those cases may have represented toxicity that was not due to cannabis (e.g., ethanol, alprazolam), which would potentially confound interpretation of cannabis intoxication. Furthermore, it is important to note that charts are often coded for cannabis if a urine drug test is positive for tetrahydrocannabinol (THC), and this would decrease the specificity for cannabis intoxication/toxicity. Finally,

unintentional intoxication in young children was our main outcome of interest. We excluded cases of cannabinoid hyperemesis, calls regarding chronic usage, and information calls.

We collected the following data: unique case number, age, year of exposure, and type of exposure. Types of exposures were categorized as: 1) ingestion; 2) inhalation; and 3) unknown/not otherwise specified. Ingestions were further subcategorized into ingestion of 1) “edibles” and 2) nonfoodstuffs or ingestion detail not documented. “Edibles” were defined as foodstuff created to be ingested, such as cookies, candies, gummies, chocolates, and brownies.

A linear regression line was fit to log₁₀ cases over time. Given the exponential nature of the data, the estimated doubling time was calculated overall and for edible ingestion only, using the tangent line at time 0 on these semi-log graphs, where $\Delta(t) = \log(2)/\text{slope}$. All analyses were performed using SAS 9.4 (SAS Institute Inc, Cary, NC). We stratified the analysis into three age groups: 0–5 years, 6–12 years, and 13–17 years. We then calculated the median and interquartile range (IQR) of age for all exposures and the subcategory of edible ingestions.

RESULTS

Between 2008 and 2019, a total of 1392 cannabis exposures in children younger than 18 years old were reported to the MiPC. We excluded 743 cases of co-exposures and 220 cases that were judged to be insignificant (licks, tastes, secondhand smoke) or were lost to follow-up, resulting in 426 cases of single-substance pediatric cannabis exposures. Total exposures reported to the MiPC ranged from 47,908 in 2008 to 54,717 in 2019, with a peak in 2010 at 72,792 reported exposures (Table 1). Despite the inconsistent trend in exposure vol-

ume reported to the MiPC over the study time period, the percentage of isolated pediatric cannabis exposures has increased over the study time period (0.01% to 0.24%).

The median age of children who had isolated cannabis exposures was 6.0 years (IQR 2–15), with 209 cases for children age 0–5 years (49.1%), 45 cases for children age 6–12 years (10.6%), and 172 cases for children age 13–17 years (40.3%). The cases exhibited a bimodal age distribution (Figure 1), with the fewest cases reported for the age range of 6–12 years and the most cases reported for children 0–5 years and 13–17 years.

From 2008 to 2019, the number of isolated pediatric cannabis cases reported to MiPC consistently increased each year, following an exponential pattern, with a doubling time of 2.1 years (Figure 2). Ingestion was the most common route of exposure (327 [76.8%]), followed by inhalation (79 [8.5%]), unknown (18 [4.2%]), and combination ingestion and inhalation (2 [0.5%]) (Figure 3). From 2008 until 2016, the total number of cases reported per year was consistently below 30. In 2016, the number of total annual reported cases began to rise and was driven by edible cannabis items (Figure 2): the number of annual reports for ingestions rose between 2016 and 2019, whereas the number of inhalational exposures remained somewhat steady throughout the entire study period (mean 6.6 inhalations per year). One exception of 21 inhalational exposures was reported in 2019.

The ingestion data (not including the two ingestion and inhalation events) were further subdivided into “edible” vs. “nonedible” sources (see Methods). Of the 327 ingestion events recorded, 227 (69.4%) were from edible products, and 100 (30.5%) were from nonedible sources. The median age of children exposed to edible cannabis products was 5 years (IQR 3–14), and the distribution of age of exposure to edible cannabis was also bimodal (Figure 1). The doubling time between 2008 and 2019

Table 1. Site of Origin of Call to MiPC by Year

	Year	Total MiPC Exposures	Total Pediatric Isolated Cannabis Exposures	Origin of Call	
				HCF	Home
MML	2008	47,908	7	1	6
	2009	61,786	4	2	2
	2010	72,492	12	9	3
	2011	69,540	14	9	5
	2012	67,284	29	18	11
	2013	61,727	15	11	4
	2014	57,919	23	20	3
	2015	60,162	21	16	5
	2016	61,211	33	24	9
	2017	58,232	49	42	7
RML	2018	55,771	86	66	20
	2019	54,717	133	96	37
Total		728,749	426	314	112

MiPC = Michigan Poison Center; HCF = health care facility; MML = medical marijuana legalization; RML = recreational marijuana legalization.

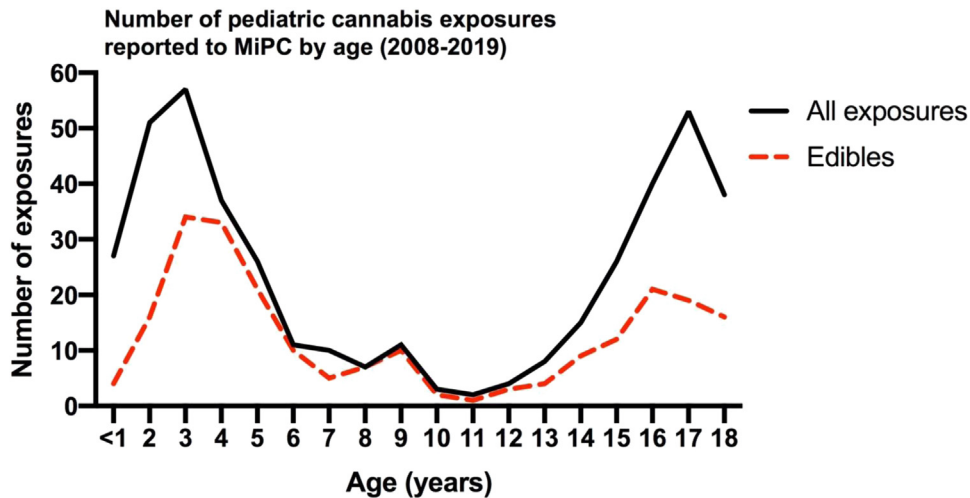


Figure 1. Bimodal distribution of pediatric cannabis exposures by age (2008–2019). MiPC = Michigan Poison Center.

for reported edible cannabis exposures among pediatric patients was 2.3 years, slightly longer than for overall exposures, again fitting an exponential pattern (Figure 2).

Inhalational exposures were highest in teenagers (13–17 years), whereas ingestions from both edible and nonedible sources were highest in young children (0–5 years) (Figure 3). Most calls originated from a health care facility (314 [74%]), and the remaining calls originated from home or school (112 [26%]) (Table 1).

DISCUSSION

Analysis of the MiPC pediatric cannabis single-agent exposure data, the largest case series to our knowledge to date, revealed an overall increase in annual pediatric exposures of cannabis in Michigan in the years from medical cannabis legalization in 2008 through recreational cannabis legalization in 2018. A bimodal distribution in age groups showed that children ages 0–5 and teenagers

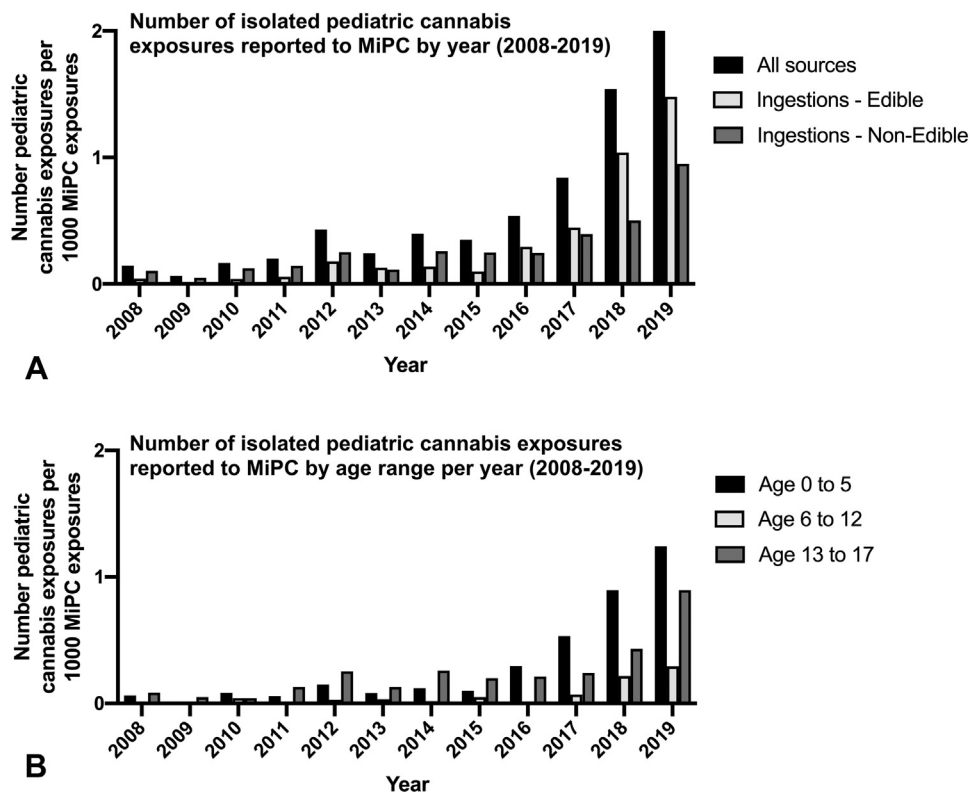


Figure 2. Pediatric single-substance cannabis exposures reported to Michigan Poison Center (MiPC) by exposure type (A) and by age range (B) from 2008–2019.

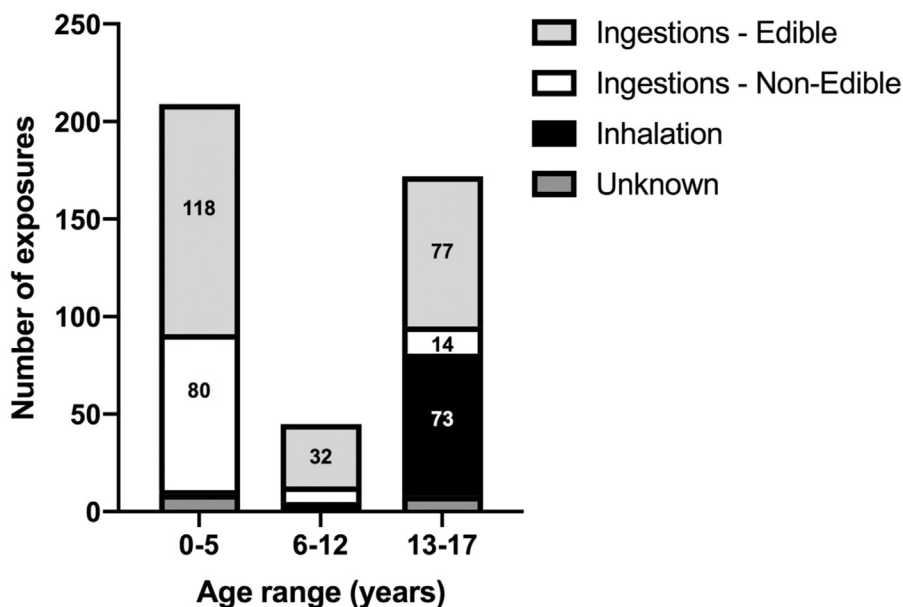


Figure 3. Cannabis exposures by age group and route (2008-2019). Breakdown of main exposure routes per age group showing predominant route of exposure for young children 0–5 years old was ingestions, whereas teenagers 13–17 years old had the highest number of reported inhalation exposures. Number of nonedible ingestions for age 6–12 was eight.

13–17 years were most affected, and that the trend was driven by ingested edible cannabis products. We hypothesize that this distribution is predictable and conforms to normal human development: oral exploratory behaviors in very young children; affinity for cookies and candy in slightly older children; and autonomy, peer pressure, and experimental behavior in teens.

This study was not designed to identify the cause of the rapid increase in poison center calls of cannabis exposure in Michigan. However, exposure to edibles was the main driver. This may be due to one or a combination of factors: 1) edible products are increasingly available, 2) edibles continue to mimic mainstream noncannabis sweets and candy and are not sold or distributed in child-resistant packaging (despite state-mandated packaging restrictions to the contrary), 3) residents are making homemade edible products that are not subject to state regulations, 4) cannabis has increased in potency, and 5) reporting of toxic exposures has increased (16).

Acute toxicity in teens is problematic; teens are having cannabis-related health events significant enough to be evaluated in a health care setting at an increasing rate, occurring at a time of rapid brain development and differentiation. Both ingestion and inhalational exposures can lead to anxiety, panic attacks, psychosis, altered mental status, dangerous behaviors, and a number of other health and psychiatric effects. Edible products are more likely to result in accidental overdose than inhaled products due to slow onset of action of THC after consumption and subsequent “dose-stacking” effects. Cannabis potency

(percent concentration of THC by volume) and use of concentrated products (e.g., “dab,” “wax,” “honey”) likely play a role as well.

Cannabis has become a major industry in states where its recreational use is now legal. For example, in Colorado, legal cannabis generated over \$300 million in tax revenue for the state in 2019 alone, and this has been increasing yearly since the state began reporting on the subject (17). As of the writing of this manuscript, medical cannabis is available within Michigan at 213 provisioning centers, 61 recreational cannabis retailers, and with 111 recreational cannabis licenses granted (18). Michigan sold nearly \$32 million worth of recreational marijuana in its first 3 months of operation (December 2019 to February 2020), with March and April 2020 demonstrating consistent upward trends of \$21.9 and \$27.8 million, respectively, generating \$1.2–1.55 million in monthly tax revenue (18,19). This industry will likely continue to be a significant portion of Michigan’s economy going forward, and its legal status is unlikely to change. This upward sales trend represents increased availability and risk for unintentional pediatric exposure.

Many states have adopted rules and regulations that comport with the 2015 American Academy of Pediatrics policy statement on cannabis to forbid direct advertising to children and to require packaging practices to prevent unintentional pediatric use and poisoning (20). Indeed, as of April 2020, 15 states (AL, CA, CO, CT, HI, IL, MA, MD, ME, MN, MT, NM, NV, NY, WA) have childproof

packaging requirements, and 13 (AL, AZ, CO, CA, FL, MA, MD, MN, NM, NV, NY, OR, WA) have specific labeling instructions to keep products away from children (3,21). In Michigan, the Marijuana Regulatory Agency within the Department of Licensing and Regulatory Affairs was created to establish rules for edible cannabis. These rules state: 1) “No edible marijuana product package can be in a shape or labeled in a manner that would appeal to minors aged 17 years or younger,” 2) “No edible marijuana product can be easily confused with commercially sold candy,” and 3) “An edible marijuana product must be in opaque, child-resistant packages or containers that meet the effectiveness specifications outlined in 16 CFR 1700.15” (18). However, even in states that have enacted such regulations, increases in unintentional exposures and health care facility visits still have occurred at substantial rates (7,15). It remains unclear what impact packaging rules and legislation will have on reported pediatric exposures, and further study may reveal differences in younger vs. adolescent pediatric populations.

Going forward, preemptive and planned regulations to ensure proper labeling and packaging is logical and recommended by the American Academy of Pediatrics and these authors, and the effectiveness of preventive measures should continue to be evaluated and reported. Preventing teenage exposures may require tactics other than regulation of labeling or child-proof packaging, such as peer-to-peer health educational programs and campaigns. Future research should examine the influence of specific policies to determine which strategies are most effective for preventing pediatric exposures and to develop evidence-based recommendations. Prospective enumeration of product type, manufacturer (including homemade), potency, and distributor is also suggested to identify responsible parties.

States that are considering medical or recreational cannabis legalization should be aware of the trends demonstrated in Michigan and other states. Poison centers and acute care facilities located in those states should expect to see a continued increase in pediatric cannabis exposures, regardless of associated regulatory safeguards.

Limitations

Limitations to Poison Center data have been extensively reviewed (22). As with other poison center-based studies, our results are subject to selection and reporting bias. Specifically, disease severity may be overestimated because severe cases are more likely to be reported to the poison center and may be provider and institution dependent. Additionally, poison center charts are of variable quality. Details of ingestion exposure can some-

times be limited, and therefore we may not have captured all of the edible exposures.

We chose to exclude all reported exposures that reported any type of co-ingestants. Although this choice limits the number of cases, it also removes confounding ingestions and toxicities. We limited our search terms to “cannabinoid, cannabis, THC, marijuana, and marijuana” because these are the terms most often used by poison center staff to code exposure. Other terms may have been used, and we assume these terms to be infrequently used and their exclusion unlikely to affect results.

CONCLUSION

Cannabis exposures reported to the MiPC consistently increased among pediatric patients in the period after medical cannabis legalization (2008) and leading up to recreational cannabis legalization (2019) in the state of Michigan. The mitigating effects of aggressive education campaigns, product labeling, and childproof/resistant packaging are unknown. Future research is needed to evaluate the effects of cannabis regulations and public health campaigns on unintentional pediatric cannabis exposures to inform the development of prevention and mitigation strategies.

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ARTICLE SUMMARY

1. Why is this topic important?

As the legislative landscape of marijuana use is changing, focusing on decriminalization, legalization, and overall movements of liberalization of cannabis use, it is important to discuss potential unintended consequences of these changes, especially among our vulnerable pediatric population. Pediatric cannabis exposures, both intentional and unintentional, have the potential to cause negative unintended health consequences—including intoxications, hospital visits, and intensive care unit stays among the most dramatic. Monitoring exposure cases in the context of the legislative changes at the level of one state has the potential to guide future legislations to aid in the risk/benefit discussions that can be used by other states considering future changes.

2. What does this study attempt to show?

We propose that the increasing liberalization of the attitudes around adult cannabis use, reflected by state legislative actions, has unintended consequences leading to increases in (both intentional and unintentional) pediatric cannabis exposures.

3. What are the key findings?

We demonstrate a large increase in exposures across pediatric age groups spanning the time between medical marijuana legalization in 2008 and legalization of recreational marijuana in 2018. All age groups were affected, and a dramatic increase in edible exposure was noted.

4. How is patient care impacted?

Health care providers should be aware of the increased numbers of exposures to cannabis in the pediatric population, as it is important to include this intoxication in the differential of altered pediatric patients.