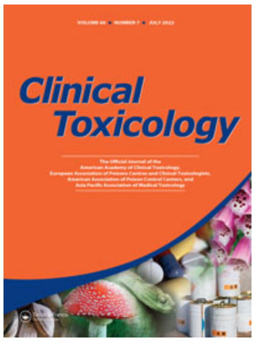

Clinical Toxicology

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ictx20

Synthetic cannabinoid poisonings and access to the legal cannabis market: findings from US national poison centre data 2016–2019

Tracy A. Klein, Julia A. Dilley, Janessa M. Graves & Erica L. Liebelt

To cite this article: Tracy A. Klein, Julia A. Dilley, Janessa M. Graves & Erica L. Liebelt (2022): Synthetic cannabinoid poisonings and access to the legal cannabis market: findings from US national poison centre data 2016–2019, Clinical Toxicology, DOI: 10.1080/15563650.2022.2099887

To link to this article: https://doi.org/10.1080/15563650.2022.2099887

CLINICAL TOXICOLOGY
https://doi.org/10.1080/15563650.2022.2099887

CLINICAL RESEARCH

Synthetic cannabinoid poisonings and access to the legal cannabis market: findings from US national poison centre data 2016–2019

Tracy A. Klein[a], Julia A. Dilley[b], Janessa M. Graves[c] and Erica L. Liebelt[d]

[a]College of Nursing, Washington State University, Vancouver, WA, USA; [b]Multnomah County Health Department, Oregon Health Authority, Portland, OR, USA; [c]College of Nursing, Washington State University, Spokane, WA, USA; [d]College of Medicine, University of Arkansas for Medical Sciences, Little Rock, AR, USA

ABSTRACT

Aim: To investigate trends in synthetic cannabinoid exposures reported to United States (US) poison control centres, and their association with status of state cannabis legalisation.

Methods: A retrospective study of National Poison Data System (NPDS) data from 2016 to 2019 identified and associated synthetic poisoning reports with annual state cannabis law and market status. State status was categorised as restrictive (cannabis illegal or limited medical legalisation), medical (allowing THC-containing medical cannabis use) and permissive (allowing non-medical use of THC-containing cannabis by adults). We categorised a subset of states with permissive policies by their implementation of legal adult possession/use and opening retail markets, on a quarterly basis. Mixed-effects Poisson regression models assessed synthetic exposures associated with legal status, first among all states using annual counts, and then among states that implemented permissive law alone using quarterly counts.

Results: A total of 7600 exposures were reported during the study period. Overall, reported synthetic exposures declined over time. Most reported exposures (64.8%) required medical attention, and 61 deaths were documented. State implementation of medical cannabis law was associated with 13% fewer reported annual exposures. Adoption of permissive state cannabis policy was independently and significantly associated with 37% lower reported annual synthetic exposures, relative to restrictive policies (IRR: 0.63, 95% CI: 0.50–0.79). Among states with permissive law during the period, implementation of legal adult possession/use was associated with 22% fewer reported quarterly exposures. Opening of retail markets was associated with 36% fewer reported exposures, relative to states with medical cannabis only.

Conclusions: Adoption of permissive cannabis law was associated with significant reductions in reported synthetic cannabinoid exposures. More permissive cannabis law may have the unintended benefit of reducing both motivation and harms associated with use of synthetic cannabis products.

ARTICLE HISTORY
Received 13 February 2022
Revised 12 May 2022
Accepted 2 July 2022

KEYWORDS
Synthetic cannabis; cannabis legalisation; poison centre

Introduction

Synthetic cannabinoids, such as "K2" or "spice", are used as an alternative to natural cannabis by an estimated 0.2–4% of the population, predominantly among those in their late teens and early twenties [1]. In 2014–2015, about half of high school seniors who self-reported using synthetic cannabinoids did so three or more times in the past month [2]. A high percentage (95.7%) has previously used cannabis products and many had used 2–4 other drugs of abuse [2]. Defining synthetic cannabinoids and their constituents are challenging due to variable and illicit production, and synthetic cannabinoid poisonings can often overlap with other drug poisonings [3]. People who use synthetic cannabinoids report a preference for natural cannabis products, due in part to its lower negative effect profile including less hangover effects, less paranoia and more ability to function [4]. Users of synthetic products therefore may use them for reasons other than preference, such as avoidance of detection in urine drug screens in a supervised setting such as during drug treatment [5].

Passage of the United States (US) Synthetic Drug Abuse Prevention Act in 2012 attempted to limit production of synthetic cannabinoids [6]. The greatest number of annual synthetic cannabinoid exposures reported to US Poison Centres since passage of this act were in 2015, with 7792 cases [7]. When compared to acute intoxication with natural cannabis, synthetic cannabinoids cause greater agitation and cardiotoxicity, in part due to their stronger binding with CB1 receptors and incorporation of many toxic compounds including atypical sympathomimetic toxidromes [2,8–10]. As new synthetic agents are developed, knowledge of their effects is still under study and long-term impact of use is therefore unknown [9].

Studies on synthetic cannabinoids are often case-based due in part to limitations in reporting and confirmation

CONTACT Tracy A. Klein taklein@wsu.edu College of Nursing, Washington State University, Vancouver, WA, USA

Supplemental data for this article is available online at here

[11,12]. Few data sources provide consistent and reliable information to allow for surveillance on synthetic cannabinoid use, in part due to challenges related to testing, presentation and documentation [13]. One data source is the US Toxicology Investigators Consortium (ToxIC), a database of prospectively collected data from patients seen at the bedside by medical toxicologists at selected sites in US. ToxIC data show an upward trend in synthetic cannabinoid poisonings from 2010 to 2015 [13]. During 2010–2015 most sites reported <20 synthetic cannabinoid cases though clusters were observed in large cities [13]. Cases involving synthetic cannabinoid use reported to Poison Centres have been associated with male gender, intentional use/misuse and chronic use characteristics [14]

Some trends in synthetic cannabinoids can be monitored across the US using syndromic surveillance, based on discharge codes and text from clinical summaries for patients seen in emergency departments (EDs). Regional U.S. trend data from 2016 to 2019 using such syndromic data noted a small national decrease in synthetic cannabinoid ED visits as well as decreasing incidence in the Southeast and the West, but statistically significant increases in both the Midwest and Northeast and wide variation by region [15].

One key data source that provides both comprehensive coverage of the US and detailed exposure information is the National Poison Data System (NPDS), a data management system owned by the American Association of Poison Control Centres (AAPCC) [16]. NPDS is used to track potentially toxic exposures which are reported by clinicians and the general public to regional poison control centres; case information, such as route of exposure, reported amount, clinical effects, health outcomes and limited demographic information about exposed individuals are included. Relevant to synthetic cannabinoids, NPDS characterises exposures based both on self-reported consumption and analytical data, including post-mortem assessment, when applicable [17,18]. NPDS data have been used to document outbreaks of synthetic cannabinoids, as well as general trends.

Identification of current potential predictors and correlates of natural and synthetic cannabinoid poisonings are important to evaluate and to implement harm reduction interventions. Medical cannabis laws have been negatively associated with synthetic cannabis exposure reports for adults age 50 and over [14], suggesting that cannabis policies may influence synthetic cannabinoid use. Legalisation of adult use (recreational or non-medical) cannabis may reasonably affect use of synthetic cannabinoids as well as recreational drugs or alternatives to cannabis. Examination of state legalisation of medical or retail cannabis use and market variations may help explain regional differences observed in synthetic cannabinoid health event trends [15].

Purpose

To investigate trends in synthetic cannabinoid exposures reported to US poison control centres, and their association with status of state cannabis legalisation. We hypothesised that more liberal cannabis state policies which allow access to THC-containing products would decrease the incidence of synthetic cannabinoid poisoning reports, and that restrictive policies would be predictive of higher synthetic cannabinoid poisoning rates.

Methods

Study setting and design

This study analysed data from the NPDS. We obtained deidentified data on synthetic cannabinoid exposure reports, characterised by NPDS using the relevant system code for synthetic cannabinoids (generic code 0200617). The Washington State University Office of Research Assurances has found that the project is exempt from the need for Institutional Review Board review (IRB #17473).

We examined all unique synthetic cannabis exposures reported during 2016–2019, a total of 7600 cases. These years included when multiple states had or were implementing adult use cannabis retail markets. Beginning analysis with 2016 data eliminated confounding effects from known major synthetic cannabinoid cluster outbreaks in 2015, which affected at least two states (New York and Louisiana) and is reflected in the peak number of annual poisonings of the last decade [7]. Our study frame concluded on 31 December 2019 and therefore did not include the effect of changes in cannabis law and distribution pursuant to the COVID-19 pandemic which impacted both use and distribution of cannabis [19].

Cases were characterised by the state in which the exposure occurred. We first coded state cannabis law into three categories, based on the most liberal guidance in place during each year: restrictive, medical, and permissive (see Supplemental Table 1). *Restrictive* states were defined as those where cannabis is either illegal or restricted to CBD only or very low concentration THC products for narrow medical use. *Medical* states were those which allow for use of THC products with broad medical authorisation. *Permissive* states were those which had adult use cannabis for non-medical purposes. Classification of each state law or policy, and dates of implementation, was based on reports from the National Conference of State Legislatures website [20] and annual state report data from the Americans for Safe Access reports (2015–2020) [21], both of which comprehensively track state law and implementation regarding cannabis. Additional cross checking of original state statutes and regulations was completed using links from these sources. We also used policy resources and state websites to determine the date of onset of legal adult possession and use and retail market opening in states with permissive policies, categorising these on a quarterly basis (see Supplemental Table 2).

Analyses

We described the synthetic cannabis exposure cases by year, state legal status at the time of the exposure (assigned per year), medical outcome, sex and age group. We used multilevel statistical models that predicted numbers of synthetic cannabis exposure based on state legal status, while accounting for historical trends and state-level influences (i.e., nesting). State was included as a random effect in all models, allowing each state to have a different baseline measure. Natural log of year-specific state population was included as an offset.

We first used a mixed effects Poisson regression model to estimate the annual number of synthetic cannabis exposures among all states as categorised by restrictive, medical and permissive legal status. Legal status was assigned per year based on date of implementation; those implemented in the fourth quarter of a calendar year were applied to state legal status during the following year.

As a sensitivity analysis, the dataset was limited to include jurisdictions that had implemented a permissive policy at any time during the study frame (Alaska, California, Colorado, District of Columbia, Illinois, Maine, Massachusetts, Michigan, Nevada, Oregon, Vermont and Washington state). In this model, we assessed numbers of exposures and their associations with policies over time by quarter (3-month periods). For this analysis, policies were further categorised as medical legal only (most restrictive), adult possession/use legal, and retail markets open (most permissive).

All analyses were conducted with Stata version 14.2 (StataCorp LB, College Station, TX). We used 0.05 as the cut-off for statistical significance.

Results

Descriptive analysis: all states

Reported synthetic cannabinoid exposures declined between 2016 and 2019; there were 2633 in 2016 and less than half as many (1117) in 2019 (see Table 1). Most of the exposures for that time period overall (56.0%) were reported by people in states with restrictive cannabis policies at the time of the exposure; 38.6% occurred among people in states with medical policies; and 5.5% occurred in states with permissive cannabis policies. Most exposures occurred in a personal residence (69.8%), and most involved only synthetic cannabinoid without other substances (66.5%).

Most exposures were experienced by men (75.3%), and the majority were between ages 21 and 54 years (62.6%). A large proportion of the exposures reported were serious, requiring medical attention (i.e., moderate, major and fatal effects combined; 4921, 64.8%), including 61 deaths.

Main policy analysis: all states

In our first model (see Table 2), state implementation of medical marijuana law was associated with 13% fewer reported annual synthetic cannabinoid exposures relative to a restrictive law (calculated as 1 minus the value of the incidence rate ratio [IRR]: 0.87, 95% confidence interval [CI]: 0.75–1.00), although the association did not reach significance ($p = 0.05$). Adoption of a permissive cannabis policy was independently and significantly associated with 37% lower reported annual synthetic exposures, relative to restrictive policies (IRR: 0.63, 95% CI: 0.50–0.79). IRRs for medical *vs.* permissive policies were significantly different from one another when formally tested, indicating that adoption of a permissive policy was associated with further reduction of synthetic cannabinoid exposures relative to a medical policy.

Table 1. Characteristics of synthetic cannabinoid exposures reported to US Poison Centres, 2016–2019.

	All states Number of exposures (%)
Total	7600 (100%)
2016	2633 (34.6)
2017	1918 (25.2)
2018	1932 (25.4)
2019	1117 (14.7)
Policy status (assigned per year)	
Restrictive (illegal or CBD/non-THC only)	4252 (56.0)
Medical	2934 (38.6)
Permissive	414 (5.5)
Exposure site	
Residence (personal or someone else's)	5305 (69.8)
Other site	2295 (30.2)
Number of substances	
Synthetic cannabis alone	5056 (66.5)
At least one additional substance	2544 (33.5)
Gender	
Male	5719 (75.3)
Female	1750 (23.0)
Pregnant	<5 (0.1)
Unknown	127 (1.7)
Age	
0–9	74 (1.0)
10–20	2042 (26.9)
21–54	4761 (62.6)
55+	324 (4.3)
Unknown	399 (5.3)
Medical outcome[a]	
Death (indirect or direct report)	61 (0.8)
Major effect	1038 (13.7)
Moderate effect	3128 (41.2)
Minor effect	1,987 (26.1)
No effect	407 (5.4)
Not followed, judged as nontoxic or minimal clinical effect	285 (3.8)
Unable to follow, judged as potentially toxic	694 (9.1)

[a]Health care intervention is generally required for medical outcomes characterised as moderate, major or death.

Table 2. Association between annual synthetic cannabinoid exposures and policy, all US states, 2016–2019.

	IRR	95% CI	*p* Value
Time (year)	0.79	0.78–0.81	<0.001
State cannabis policy	Referent		
Restrictive			
Medical	0.87	0.75–1.00	0.05
Permissive[a]	0.63	0.50–0.79	<0.001

IRR: incidence rate ratio; CI: confidence interval.
Time (year) IRR is the average change per year in the rate of reported exposures; an IRR < 1.0 indicates declining trend, independent of policy change. Cannabis policy IRR is the reported incidence rate within states with a specific policy divided by the incidence rate among states with the referent policy, after accounting for historical time trend (time variable) and within-state correlations. An IRR < 1.0 indicates a lower rate than the referent group.
[a]Post-hoc contrast indicated significant differences between permissive and medical policies ($p < 0.001$).

Sensitivity analysis: states implementing permissive policy

Our next model (see Table 3), focused on states that implemented adult use legalisation during the period studied, which showed 22% fewer poisonings associated with

Table 3. Association between quarterly synthetic cannabinoid exposures and policy, among US states with legal adult cannabis use at any time during 2016–2019.

	IRR	95% CI	*p* Value
Time (quarters)	0.98	0.96–1.00	0.02
State cannabis policy	Referent		
Medical legalisation only			
Adult possession/use legal	0.78	0.59–1.02	0.07
Retail market open	0.64	0.46–0.90	0.01

IRR: incidence rate ratio; CI: confidence interval.
Time (quarter) IRR is the average change per quarter in the rate of reported exposures; an IRR <1.0 indicates declining trend, independent of policy change.
Cannabis policy IRR is the reported incidence rate within states with a specific policy divided by the incidence rate among states with the referent policy, after accounting for historical trend (time variable) and within-state correlations. An IRR $<$ 1.0 indicates a lower rate than the referent group.

implementation of legal adult possession/use policies *vs.* medical policies, but this association did not reach statistical significance (IRR: 0.78, 95% CI: 0.59–1.02). Opening of a legal retail market resulted in a 36% reduction in the number of synthetic cannabis exposures, relative to medical legalisation only (IRR: 0.64, 95% CI: 0.46–0.90). IRRs for adult possession/use and retail market opening were not significantly different from one another.

Discussion

Our examination of synthetic cannabinoid exposures reported in the NPDS showed that synthetic cannabis poisonings were trending downward during the 2016–2019 study period. Consistent with other studies, we also found that many exposures are among men and involve young or middle-aged adults (ages 10–54), though some patients over 55 are also victims of synthetic cannabinoid poisonings [7,14]. While exposures were trending downward, the impact on those who consumed synthetic cannabis was significant, resulting in over 4000 moderate to major effects and 61 reported deaths.

What our study adds is the finding that adoption of permissive cannabis law can be associated with significant reductions in synthetic cannabinoid exposures. While medical cannabis alone did not show a statistically significant impact on synthetic cannabinoid poisonings, the magnitude and direction of change were similar in both of our models consistent with a hypothesised dose-response relationship between more permissive cannabis law overall and fewer reported synthetic cannabinoid poisonings. Because synthetic cannabinoid use has no legitimate medical benefit, and medical cannabis markets are not readily accessible to people who may be using synthetic cannabinoids as an alternative to natural cannabis for non-medical purposes, it is not surprising that medical cannabis availability alone showed weaker association with reported cannabinoid exposures.

The effects of cannabis legalisation (especially legalisation of adult use markets) are not yet fully understood, and attention should be given to study of both direct and indirect public health outcomes that may result from this policy change. While synthetic cannabinoid use appears to be decreasing, the number of formulations and the diversity of their structure with increasing potency has led to concern about their toxicity and long-term impact [9]. This so called "fourth-generation" of synthetic cannabinoid is now being referred collectively as the Synthetic Cannabinoid Receptor Agonist (SCRA) class to acknowledge potential for differential and severe effects including neurologic and cardiac toxicity and death [9,22].

Limitations

There are inherent limitations of the NPDS database. First, NPDS data includes only data which are reported to poison centres, most likely underestimating the true number of exposures. Active reporting was reduced over the study period; this could have reflected decreases in poisonings over time for multiple reasons including variables not measured in this data such as socioeconomic status and access which have been linked in prior studies to use by adolescents [23]. Synthetic cannabinoids cannot be routinely identified in healthcare setting drug testing; therefore, the integrity of the data is reliant on accurate and complete reporting from healthcare providers and the general public. However, NPDS is the largest and only near real-time national database of exposures, and we are not aware of any reason quality of reporting would have otherwise changed associated with changes in legal status of cannabis products.

There are complexities in correlating policy change with patient outcomes. Our study tested the effects of both medical and recreational substitution law changes on consumption of synthetics which we attempted to measure precisely, however, variations in policy take time to both implement and note effects, making precision less attainable. Further, we generalised changes in law very broadly, including combining states that had legalised adult use and markets with those had legalised but not yet begun to allow retail sales, and similarly combining states that allow medical use by individuals without regard to whether they allow medical purchasing, or what restrictions they place on criteria for being recognised as a medical patient. This approach was conservative because it measured progressive policy changes sensitively by not requiring full implementation when maximum effect would be anticipated.

Additionally, we applied a legal status designation for an entire year, when in fact that policy might not have been passed until mid-year depending on legislative sessions. We justified this approach as conservative for modelling because it also included some unaffected time periods within the "policy change" periods. We tested this by applying a sensitivity analysis using a more focused parameterisation of time and policy, and the results were similar, which suggested robust findings.

Finally, we cannot account for other factors that may be affecting synthetic cannabinoid poisonings. These might include delayed effect of the federal policy from 2012, public education campaigns, gradual denormalisation of synthetic cannabinoid use, or normalisation of plant-based cannabis use which might reduce motivation to use synthetic varieties.

Nonetheless, we do not believe these potential contributors to general trends could explain the patterns of the policy-specific observations we observed, although it is possible, they could have affected the true magnitude of the effects measured.

Conclusion

The gradual reduction of prohibitions against plant-based cannabis offers an opportunity to study use of cannabis and powerful synthetic analogues that may have been used as natural cannabis substitutes. Our study identified an association between more liberal policies (legalisation) for natural cannabis and declines in reported synthetic cannabinoid poisonings. This finding suggests a potential effect of policy change on substance use behaviours that may have long-term public health implications [24].

Disclosure statement

ELL: Senior Editorial Board: ToxED, online point of care toxicology resource; Elsevier Publishing; paid annual honorarium $2500.00. Up to Date: online clinical information resource; author of "Acute Iron Poisoning"; paid annual Royalty from Wolters-Kluwer Publishing. JMG: Board of Directors of the nonprofit Washington State Poison Center. JAD and TAK have no disclosures. The American Association of Poison Control Centers (AAPCC; http://www.aapcc.org/) maintains the national database of information logged by the country's poison centers (PCs). Case records in this database are from self-reported calls: they reflect only information provided when the public or healthcare professionals report an actual or potential exposure to a substance (e.g., an ingestion, inhalation, or topical exposure, etc.), or request information/educational materials. Exposures do not necessarily represent poisoning or overdose. The AAPCC is not able to completely verify the accuracy of every report made to member centers. Additional exposures may go unreported to PCs and data referenced from the AAPCC should not be construed to represent the complete incidence of national exposures to any substance(s).

Funding

This investigation was supported in part by funds provided for medical and biological research by the State of Washington Initiative Measure No. 171.

References

[1] Loeffler G, Delaney E, Hann M. International trends in spice use: prevalence, motivation for use, relationship to other substances, and perception of use and safety for synthetic cannabinoids. Brain Res Bull. 2016;126(Pt 1):8–28.

[2] Palamar JJ, Barratt MJ, Coney L, et al. Synthetic cannabinoid use among high school seniors. Pediatrics. 2017;140(4):e20171330.

[3] Tamama K, Lynch MJ. Newly emerging drugs of abuse. Handb Exp Pharmacol. 2020;258:463–502.

[4] Winstock AR, Barratt MJ. Synthetic cannabis: a comparison of patterns of use and effect profile with natural cannabis in a large global sample. Drug Alcohol Depend. 2013;131(1–2):106–111.

[5] Ninnemann AL, Lechner WV, Borges A, et al. Synthetic cannabinoids to avoid urine drug screens: implications for contingency management and other treatments for drug dependence. Addict Behav. 2016;63:72–73.

[6] 112th United States Congress (2011–2012). S.3190. Synthetic drug abuse prevention act of 2012 (Introduced version). 2012. Available from: https://www.congress.gov/bill/112th-congress/senate-bill/3190/

[7] National Poison Data System, American Association of Poison Control Centers. Synthetic cannabinoids. 2022. Available from: https://aapcc.org/track/synthetic-cannabinoids

[8] Zaurova M, Hoffman RS, Vlahov D, et al. Clinical effects of synthetic cannabinoid receptor agonists compared with marijuana in emergency department patients with acute drug overdose. J Med Toxicol. 2016;12(4):335–340.

[9] Malaca S, Tini A, Ronchi U. F. Fourth generation of synthetic cannabinoid receptor agonists: a summary on the latest insights. Acta Biomed. 2022;92(6):e2021546.

[10] Le Boisselier R, Alexandre J, Lelong-Boulouard V, et al. Focus on cannabinoids and synthetic cannabinoids. Clin Pharmacol Ther. 2017;101(2):220–229.

[11] Gunderson EW, Haughey HM, Ait-Daoud N, et al. Spice" and "K2" herbal highs: a case series and systematic review of the clinical effects and biopsychosocial implications of synthetic cannabinoid use in humans. Am J Addict. 2012;21(4):320–326.

[12] Adamowicz P, Meissner E, Maślanka M. Fatal intoxication with new synthetic cannabinoids AMB-FUBINACA and EMB-FUBINACA. Clin Toxicol (Phila). 2019;57(11):1103–1108.

[13] Riederer AM, Campleman SL, Carlson RG, et al. Acute poisonings from synthetic cannabinoids - 50 US toxicology investigators consortium registry sites, 2010–2015. MMWR Morb Mortal Wkly Rep. 2016;65(27):692–695.

[14] Choi NG, Marti CN, DiNitto DM, et al. Cannabis and synthetic cannabinoid poison control center cases among adults aged 50+, 2009-2019. Clin Toxicol (Phila). 2021;59(4):334–342.

[15] Roehler DR, Hoots BE, Vivolo-Kantor AM. Regional trends in suspected synthetic cannabinoid exposure from January 2016 to September 2019 in the United States. Drug Alcohol Depend. 2020;207:107810.

[16] Carpenter JE, Chang AS, Bronstein AC, et al. Identifying incidents of public health significance using the national poison data system, 2013–2018. Am J Public Health. 2020;110(10):1528–1531.

[17] Gummin DD, Mowry JB, Beuhler MC, et al. 2019 Annual report of the American association of poison control centers' national poison data system (NPDS): 37th annual report. Clin Toxicol (Phila). 2020;58(12):1360–1541.

[18] Tait RJ, Caldicott D, Mountain D, et al. A systematic review of adverse events arising from the use of synthetic cannabinoids and their associated treatment. Clin Toxicol (Phila). 2016;54(1):1–13.

[19] Lake S, Assaf RD, Gorbach PM, et al. Selective changes in medical cannabis use early in the COVID-19 pandemic: findings from a Web-Based sample of adults in the United States. Cannabis Cannabinoid Res. 2022. DOI:10.1089/can.2021.0115

[20] National Conference of State Legislatures. Cannabis overview. 2022. Available from: https://www.ncsl.org/research/civil-and-criminal-justice/marijuana-overview.aspx

[21] Americans for Safe Access. State of the states report 2015–2020. Available from: https://www.safeaccessnow.org/reports_archive

[22] Darke S, Banister S, Farrell M, et al. Synthetic cannabis': a dangerous misnomer. Int J Drug Policy. 2021;98:103396.

[23] Keyes KM, Rutherford C, Hamilton A, et al. Age, period, and cohort effects in synthetic cannabinoid use among US adolescents, 2011–2015. Drug Alcohol Depend. 2016;166:159–167.

[24] Pacula RL, Jacobson M, Maksabedian EJ. In the weeds: a baseline view of cannabis use among legalizing states and their neighbours. Addiction. 2016;111(6):973–980.