Characterizing Trends in Synthetic Cannabinoid Receptor Agonist Use from Patient Clinical Evaluations during Medical Toxicology Consultation

Collin Tebo MD\textsuperscript{a}, Maryann Mazer-Amirshahi PharmD, MD, MPH, PhD\textsuperscript{a,b}, Paul Wax MD\textsuperscript{a,c,d}, Sharan Campmele PhD, MPH\textsuperscript{c}, Edward Boyer MD, PhD\textsuperscript{c}, Jeffrey Brent MD, PhD\textsuperscript{c}, Amit Sheth PhD\textsuperscript{b}, and Robert Carlson PhD On behalf of the IN3 Study Group\textsuperscript{f}

\textsuperscript{a}School of Medicine, Georgetown University, Washington, DC, USA; \textsuperscript{b}Department of Emergency Medicine, MedStar Washington Hospital Center, Washington, DC, USA; \textsuperscript{c}UT Southwestern Medical School; \textsuperscript{d}American College of Medical Toxicology, Phoenix, AZ, USA; \textsuperscript{e}Department of Emergency Medicine, Brigham and Women’s Hospital, Boston, MA, USA; \textsuperscript{f}University of Colorado School of Medicine and Colorado School of Public Health, Aurora, CO, USA; \textsuperscript{g}Computer Science & Engineering, University of South Carolina, Columbia, SC, USA; \textsuperscript{h}College of Health Solution, Arizona State University, Phoenix, AZ, USA; \textsuperscript{i}Wright State University Boonshoft School of Medicine, Dayton, OH, USA

\section*{ABSTRACT}
Synthetic cannabinoid receptor agonists (SCRAs) are a new class of compounds with profound psychoactive effects and potential toxicity. This study characterizes patterns in SCRA abuse using qualitative interviews with individuals receiving medical toxicology consultation. Patients with suspected exposure to a new psychoactive substance were interviewed by medical toxicologists upon presentation for acute care. Investigators collected clinical and qualitative data including knowledge, attitudes, beliefs, and practices related to psychoactive substance use. Responses were categorized by identifying themes, and statistics were generated to describe patterns of use. Overall, 69\% (86 of the 124 cases) of novel psychoactive substance use entered into the registry were associated with exposure to SCRA. Most patients (68.8\%) had used SCRAs at least once before the presenting episode. 47.7\% considered SCRAs to be very easy to obtain, and 44.2\% reported paying for the substances while 32.6\% acquired it for free. Nearly half (48.8\%) of patients reported their primary reason for use was to get high; a small proportion used SCRAs to avoid testing positive on drug screening (6.9\%) or as an alternative to marijuana (4.6\%). Findings suggest an independent and stable culture is developing around the use of SCRAs separate from their appeal as an “undetectable” alternative to marijuana.

\section*{Introduction}
Synthetic cannabinoid receptor agonists (SCRAs) are a relatively new class of compounds that bind to cannabinoid and other receptors with often profound psychoactive and physiological effects. Over the past decade, the recreational use of these compounds has steadily risen in the United States and Europe (UNODC 2011; EMDCAA 2015). According to the United Nations Office on Drugs and Crime [UNODC], from 2017 to 18, SCRA use accounted for the greatest proportion of cases involving new psychoactive substances (UNODC 2019). While initially developed to study the endocannabinoid system for potential therapeutic applications, in the early 2000s a subset of commercial laboratories began to synthesize SCRAs for recreational use (Dresen et al. 2010). These novel compounds were combined and packaged into “herbal mixtures” colloquially referred to as “K2” or “Spice” and sold throughout Europe, Asia, and the United States as legal alternatives to marijuana. During this time, due to their widespread availability, legal ambiguity, and potent high, SCRAs have seen a tremendous growth in popularity (Dresen et al. 2010).

Similar to natural cannabinoids such as cannabidiol and tetrahydrocannabinol (THC), SCRAs are agonists at CB1 and CB2 receptors (Castaneto et al. 2014). The desired effects of SCRAs are similar to those of THC including euphoria, relaxation, and analgesia (Castaneto et al. 2014). Due to their significantly enhanced activity at CB1, CB2 receptors and other receptors, however, SCRAs have been associated with more severe toxicity than natural cannabis (Castaneto et al. 2014; Fantegrossi et al. 2014; Forrester et al. 2012). A number of case reports have been published describing patients with acute complications of SCRA use including alterations in mood and perception, psychosis, prolonged seizures, rhabdomyolysis, acute kidney injury, and myocardial infarction (Bernson-Leung, Leung, and Kumar 2014;
Bhanushali et al. 2013; Koethe et al. 2006; Mir et al. 2011). The incidence of SCRA toxicity peaked in 2015 with 7,797 cases reported by the American Association of Poison Control Centers (Hassoun 2019). More recently, toxicity from SCRA products contaminated with anticoagulants has been reported. From March 10 to April 5th 2018, 63 previously healthy SCRA users presented to emergency departments (EDs) in Illinois, Missouri, Maryland, Indiana, and Wisconsin for severe unexpected bleeding with no history of anticoagulant use. Response to treatment and subsequent diagnostic evaluation indicated exposure to vitamin K antagonists, which were contaminants of SCRA containing products (CDC 2018). An additional case series identified 34 patients with suspected SCRA associated coagulopathy and found that nearly half tested positive for the anticoagulant brodifacoum with other patients testing positive for difenacoum, bromadiolone, or warfarin (Kelkar et al. 2018).

Given their growth in popularity and potential for severe toxicity, SCRAs have become a topic of great interest for public health officials and medical toxicologists. However, most of the current data regarding SCRAs are from case reports and case series. To date, few studies have been published which contain data from a substantial clinical sample regarding subjective experiences with SCRAs and the behaviors/practices surrounding their use. The present collaborative study involving the Toxicology Investigators Consortium (ToxIC), Wright State University, and the University of Massachusetts sought to elucidate knowledge, attitudes, practices, beliefs, and clinical effects related to patients’ use of SCRAs via standardized clinical evaluations in a sample of individuals who received medical toxicology consultation with acute psychoactive drug intoxication.

Methods

Study design

The data for the present study were gathered by members of ToxIC, a national network of medical toxicologists, when patients presented for acute care and a medical toxicology consultation was obtained. ToxIC members routinely provide direct patient consultation at the bedside and are uniquely trained at recognizing, evaluating, and treating toxicologic disease, including events involving novel psychoactive substances. The consortium currently has 48 sites throughout the United States; however, this study comprises data received from 10 sentinel sites selected for this project because of their robust patient volume and special expertise. The 10 sentinel sites were located in: Worcester, MA; Rochester, NY; Philadelphia, PA; Atlanta, GA; Indianapolis, IN; Dallas, TX; St. Louis, MO; Denver, CO; Phoenix, AZ; and Portland, OR.

At the 10 ToxIC sites participating in the current study, expanded clinical qualitative data were recorded in addition to usual clinical data that are recorded by all 48 ToxIC sites. Data were recorded on knowledge, attitudes, practices, beliefs, and clinical effects related to patient’s use of novel psychoactive substances. Short answer qualitative data were collected at the bedside and entered into the study’s dedicated web-based registry from October 2014 through early 2016. Because data were collected in the context of a routine clinical evaluation, interviews were not audio-recorded and patients were not compensated. Responses to the interviews presented below are in part paraphrased answers provided by the consulting medical toxicologists. Drugs used were largely based on patient self-report.

Cases entered into the study-specific sub-registry were reviewed for data quality and completeness by ToxIC’s staff. Completed cases were then forwarded for review to one medical toxicologist co-investigator. Cases with any initial missing or incomplete data were sent to the individual sentinel site via written query for data completion.

Patient responses were analyzed by identifying categories and themes and applying them consistently across all patient responses recorded in the database. Descriptive statistics were calculated to quantitatively describe: (i) characteristics of the sample, (ii) patient knowledge, (iii) their experiences related to synthetic cannabinoid use.

This project was supported by a grant from the National Institute on Drug Abuse.

Inclusion and exclusion criteria

All patients consulted on by medical toxicologists with a history of synthetic cannabinoid use were included. Only those for whom it was not possible to obtain a routine clinical history, for example if the patient was too ill, were excluded.

Data extraction

Data were collected, entered into an excel database and analyzed based on numerical and categorical predictors. Counts of pre-coded scaled variables were calculated.

Data analysis

Because this was an exploratory analysis no formal data validation process was possible. However, all data in the
ToxIC Registry is subject to formal quality control by review of the ToxIC staff and inquires back to the entering medical toxicologist to clarify missing or contradictory data.

**Ethical approval**

This study was deemed to be exempt by both the Wright State University and Western Institutional Review Boards because the data were de-identified and were collected in the context of routine clinical evaluations.

**Results**

Overall, 124 consecutive cases of novel psychoactive substance use were entered into the ToxIC registry during the study period. The majority of cases were associated with exposure to SCRAs (N = 86), which is the focus of this report.

**Demographics**

Most of the SCRA users were male (80, 93%) with a mean age of 31. The majority of patients were white (39, 45.3%), followed by African American (37, 43.0%). Nearly half of patients had an incomplete high school or secondary school education (41, 47.7%). Most patients were single (62, 72.1%), a substantial proportion self-identified as “homeless” (16, 18.6%), and small minority reported prior or current military service (4, 4.7%) (Table 1).

**Other illicit drug use**

Nearly one-third of patients had a history of substance abuse treatment (25, 29.1%), and the majority reported other psychoactive drug use in the past 30 days, most commonly marijuana (37, 43.0%), followed by cocaine (15, 17.4%), heroin (7, 8.1%), and methamphetamine (6, 7.0%) (Table 2). About a third of patients had a history of alcohol misuse (28, 32.6%). Approximately one-fourth had a history of taking prescription drugs for the purposes of getting high (23, 26.7%), and approximately one-fifth reported prior injection drug use (17, 19.8%).

**Psychiatric history**

Over half of the SCRA users reported at least one psychiatric comorbidity (50, 58.1%). The most common was depression (14, 16.3%), followed by anxiety (13, 15.1%), bipolar disorder (11, 12.8%), schizophrenia, or schizoaffective disorder (11, 12.8%), other (7, 8.1%), and post-traumatic stress disorder (4, 4.7%). Data on psychiatric comorbidity were missing in seven cases as these patients refused to provide answers on this topic.

**Previous synthetic cannabinoid receptor agonist use**

A majority of the patients used SCRAs before the present episode (59, 68.6%). Among these, a proportion of patients gave reports suggesting daily use (12, 14.0%), while a minority of participants described using SCRAs between 1 and 4 times previously. Patients described their use in the following ways.

“Smoked a blunt of it a day for five months”

“I have taken small amounts of it a lot over the past two years.”

“Yes, daily, I smoke it once a day”

Most of those individuals who reported having used SCRAs prior to their current presentation described regular use.
Circumstances of SCRA use

Patients were evenly split between using SCRAs with friends (35, 40.7%) and alone (36, 41.9%); three reported using with relatives and one with acquaintances at a shelter. Over half of the patients took no other drug with SCRAs (45, 52.3%). The most common concomitantly used drugs were alcohol (9, 10.5%) and marijuana (7, 8.1%). Data on concomitant use was missing in 10 cases as these patients refused to provide answers on this topic.

Source of synthetic cannabinoid receptor agonists

The most common sources of SCRAs were “from friends” (34, 39.5%), purchase at a gas station/head shop/convenience store (often using a “code/under the counter”) (19, 22.1%), buying from a friend (7, 8.1%), or a dealer (6, 7.0%). Two patients mentioned purchasing at school (2, 2.3%), and two mentioned ordering online on the DarkWeb (2, 2.3%). Ten patients refused to provide answers on this topic (Table 3). Nearly half (41, 47.7%) of patients believed SCRAs were very easy to obtain. Only two patients reported finding them very difficult to obtain. Nineteen patients refused to provide answers on this topic.

Acquaintance use of synthetic cannabinoid receptor agonists

When asked about the number of people patients knew who used SCRAs, responses ranged considerably from “none” to “everyone/many.” For example, some patients explained,

“Several people with substance abuse issues on probation; all using SCRAs to get around drug tests.”

“Everybody, there is not one person in my crew that doesn’t use. Like over 30 people.”

“When I was in prison I bet 1/2 of the people there used it. Everyone in work release uses it. I can’t give you a number but it would be in the in hundreds.”

Table 3. Sources of SCRAs.

<table>
<thead>
<tr>
<th>Sources of SCRAs</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free from friend or acquaintance</td>
<td>34 (39.5%)</td>
</tr>
<tr>
<td>Purchased from gas station/tobacco shop/ convenience store</td>
<td>19 (22.1%)</td>
</tr>
<tr>
<td>Purchased from friend</td>
<td>7 (8.1%)</td>
</tr>
<tr>
<td>Purchased from drug dealer</td>
<td>6 (7.0%)</td>
</tr>
<tr>
<td>Found it</td>
<td>3 (3.5%)</td>
</tr>
<tr>
<td>“At school”</td>
<td>2 (2.3%)</td>
</tr>
<tr>
<td>Ordered online</td>
<td>2 (2.3%)</td>
</tr>
<tr>
<td>Given by relative</td>
<td>2 (2.3%)</td>
</tr>
<tr>
<td>Traded for prescription drug</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>Patients refused to answer</td>
<td>10 (11.6%)</td>
</tr>
</tbody>
</table>

The above table lists the sources which patients described acquiring SCRA products from.

Patients evaluating experience as generally positive or negative

When asked to characterize their experience with SCRAs in terms of it being generally positive or negative, patients most commonly described their experiences as generally positive (30, 34.9%). Smaller subsets of patients evaluated their experience as being overall negative (21, 24.4%), or mixed with regards to containing both positive and negative elements (17, 19.8%). As patients commented:

There are some good types and bad types of spice. I like the good types and the relaxed feeling it gives me.

There are bad types and those are not to be [messed] with. They lead to bad trips like climbing on the floor and punching the wall. I don’t like these trips and losing control of my mind and body.

It was “very addictive” very pleasurable (body); it took the place of heroin. He felt it was too easy to OD on; his hearing loss wasn’t anticipated. Felt it was “dangerous” and more prone to binges than heroin.

It gets me high, but doesn’t show up in a urine drug screen for prison or a job. It makes you high, but you don’t have to worry about losing your job. [Don’t like] how it makes you feel when it wears off. You have no appetite, nausea, stomacher pains, can’t sleep. It also makes me have diarrhea and feel drowsy and forgetful.

Likes that it feels very similar to marijuana; doesn’t like that it seems to change (potency). “Sometimes it’s not right.

He did not like panic anxiety, chest pain. He knew he got agitated, “I’m never going to do this [stuff] again!”

Of the remaining patients, one was indifferent saying he neither liked nor disliked SCRAs, and four patients gave answers that were unclear and difficult to decipher. Data were missing in 13 cases as these patients refused to provide answers on this topic.

Reasons for use

Nearly half of the patients interviewed (42, 48.8%) reported that they used SCRAs primarily for the effect achieved when consuming them, while only six patients (6.9%) reported using them to avoid testing positive on drug tests. Less common themes uncovered were used due to being addicted to SCRAs, as a substitute for marijuana, or due to curiosity and/or boredom. Ten patients refused to provide answers regarding this topic (Table 4).

Attempt at self-harm

Three SCRA users indicated an attempt at self-harm. One patient was a 27-year-old white male with bipolar
disorder who was single and had some high school education. He presented to the ED with delirium/toxic psychosis. On the day he came into the ED, he had smoked a synthetic cannabinoid joint that had been dipped in phencyclidine. A second patient who expressed an attempt at self-harm was an 18-year-old white male in high school who was found confused and falling. His clinical effects included coma/central nervous system depression. His friends gave him an SCRA called, “Toochi,” that “people take to trip out.” The third patient who attempted self-harm was a single white male, age 21, who had smoked an SCRA called “Sexy Monkey,” and had injected the drug 2 C (a phenethylamine similar in structure to MDMA, Ecstasy). On the day he presented to the ED, he had also reported using heroin, cocaine, and hydroxyzine, reporting that he was attempting suicide. The effects of the drugs “felt great and [I] realized I did not want to die,” he said.

Cost

When asked about the cost of SCRAs, nearly half of patients responded that they paid in some form (38, 44.1%). Price paid was inconsistent as some patients reported paying as much as 100 USD for a single gram while others reported paying as little as 8-10 USD for a whole ounce. Other patients reported paying various prices “per hit” but did not report the exact amount. Of the remaining patients, approximately one-third (28, 32.5%) reported acquiring SCRAs for free while three reported bartering for prescription drugs, marijuana, or tobacco. In 17 cases, patients refused to answer questions regarding the cost of SCRAs.

Discussion

The majority of patients in the present study were white males with incomplete secondary school education, a history of psychiatric comorbidity and/or previous substance abuse. Male predominance is an established feature of SCRA use with former studies reporting users to be between 62% and 81.0% male (Bonar, Ashrafion, and Ilgen 2014; Gunderson et al. 2014; Palomar and Acosta 2015). Two additional studies based on ToxIC national data similarly found 83–84.0% of SCRA users were male (Monte et al. 2017; Riederer et al. 2016). While we found 18.1% of patients were homeless, another study among SCRA users admitted for drug treatment in Texas found that the percentage of participants who were homeless ranged from 45.5% in 2012 to 66.7% in 2011 (Maxwell 2018). Consistent with previous research, we found a majority of SCRA users were white. For example, one study surveyed members of a residential substance abuse treatment center and found that, of 150 self-reported SCRA users, 81.0% were white with the remainder consisting of various ethnicities (Bonar, Ashrafion, and Ilgen 2014). Similar to our findings, one study found that among 110 SCRA users presenting to an urban ED, 32.2% had more than one psychiatric comorbidity; 71.0% had a past psychiatric visit to a hospital, and 63.0% had a history of comorbid substance use/abuse (Manseau et al. 2017).

The majority of patients interviewed (68.6%) reported prior use of SCRAs, and most of these patients reported extensive prior use. One study reported that most SCRA users, when asked about their frequency of use, reported having taken the drug two or more times in the past 12 months with 21.0% reporting taking it up to 40 times during this period (Bonar, Ashrafion, and Ilgen 2014). These results suggest that a growing number of SCRA users have a habitual relationship with the drug.

Few previous studies have reported on whether it is more common for SCRAs to be used alone or in groups. The present study found that it is equally likely to use SCRAs alone as it is to use with friends or acquaintances. It is possible that individuals who take the drug alone represent more habitual users while those who use with friends may represent individuals who are experimenting or social users.

The majority of patients in the present study reported that SCRAs were the only drug taken the day they presented to the ED. Of those that did use other drugs, marijuana and alcohol were most commonly reported, consistent with previous research (Maxwell 2018). These data accord with a previous study of 132 patients with suspected SCRA intoxication, which found that, of 72 patients who tested positive for an SCRA, 55.6% were negative for other substances. Among the remaining patients in this study who tested positive for other drugs, the most common substance detected was also THC (Tebo et al. 2018). This is consistent with a web-

<table>
<thead>
<tr>
<th>Reasons for Use</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects achieved upon use</td>
<td>42 (48.8%)</td>
</tr>
<tr>
<td>Evade drug tests</td>
<td>6 (6.9%)</td>
</tr>
<tr>
<td>Currently “addicted”</td>
<td>5 (5.8%)</td>
</tr>
<tr>
<td>Substitute for marijuana</td>
<td>4 (4.7%)</td>
</tr>
<tr>
<td>Curiosity/experimentation</td>
<td>4 (4.7%)</td>
</tr>
<tr>
<td>Boredom</td>
<td>3 (3.5%)</td>
</tr>
<tr>
<td>Mistook for marijuana</td>
<td>2 (2.3%)</td>
</tr>
<tr>
<td>Treat anxiety or addiction to other drug</td>
<td>2 (2.3%)</td>
</tr>
<tr>
<td>Self Harm</td>
<td>3 (3.5%)</td>
</tr>
<tr>
<td>Cheap price/easy availability</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>Other</td>
<td>11 (12.8%)</td>
</tr>
<tr>
<td>Refused to answer</td>
<td>10 (11.6%)</td>
</tr>
</tbody>
</table>

The above table lists reasons given by patients for using SCRAs. Total exceeds 86, as some patients gave more than one answer.
based survey conducted among college student athletes which found that current alcohol use and use of marijuana were most commonly associated with use of SCRAs (Egan et al. 2016).

Most patients considered SCRAs very easy to obtain with the top three sources being “from friends,” a store (“head shop” or gas station), or a drug dealer. One study similarly reported that 76.0% of surveyed SCRA users had acquired them from a friend at some point, while 57.0% and 19.0% had acquired SCRAs from a retailer or a drug dealer, respectively (Gunderson et al. 2014). These data suggest that SCRA use may reach individuals via their social networks. It is also clear that SCRAs are still commonly acquired from stores suggesting that current regulations and their enforcement have not been adequate to deter retailers from selling them as they may have been with other illegal drugs. Conversely, retailers may be selling newer SCRA products containing molecules that are not currently banned. Unlike other drugs of abuse, the acquisition of SCRAs from drug dealers appears to be less common. Patients who reported obtaining SCRAs from friends were not questioned further regarding where their friends had acquired them.

Over one-third of patients (34.9%) enjoyed their experience with SCRAs while a smaller proportion found it primarily negative or indicated mixed feelings. The unpredictable effects of the drug was a common theme in patients’ responses. One study utilized structured interviews with individuals with problematic SCRA use who had entered a rehabilitative treatment program. A large proportion of those interviewed similarly noted that the effects of SCRAs were unpredictable, often rapidly changing from pleasant to unpleasant with little warning (Kasai et al. 2017). An additional study conducted interviews with self-reported cannabis users who had tried SCRAs. Unlike the current study, the majority of participants (56.4%) in that study reported disliking the effects. This discrepancy is likely attributable to differences in study populations or possibly different chemical constituents of SCRA products. The majority of patients in the current study were frequent SCRA users while the majority of users in this study were cannabis users who had used SCRAs only once before, with a very small minority (6.6%) reporting frequent use (Cooper 2016). A web-forum-based study found that the mention of negative effects associated with SCRA use increased from 2008 to 2015. Additionally, the mention of positive effects such as “high” and “euphoria” steadily decreased over this period. The authors of this study proposed that these trends were due to recent bans in SCRAs prompting the introduction of new, more harmful compounds by manufacturers attempting to evade regulatory efforts (Lamy et al. 2017).

A small number of studies has asked users about their motives for taking SCRAs. Between 67 and 91.0% of participants in these studies indicated that their primary motivation was curiosity or to “try a new high”, while only 4.7% of our population indicated this as a motivation. Additionally, between 57% and 71.0% of participants in these studies mentioned the avoidance of a positive drug screening as a reason to use SCRAs while only 6.9% of the individuals in the current report gave this response (Bonar, Ashrafioun, and Ilgen 2014; Gunderson et al. 2014). These differences may be attributable to a number of factors. First, these studies were published between two and 3 years prior to the collection of our data and trends may have shifted toward SCRA use as an end in itself rather than for experimentation or to replace another drug. Second, our population was comprised of more frequent users than those examined in these studies and it may be inferred that frequent users pursue SCRAs primarily because they enjoy the effects. Our data further support this hypothesis as the most common motivation elicited from patients in the present study was to achieve the high associated with SCRAs.

Our study found that most patients paid for SCRAs. The mean price was difficult to determine as amount purchased and price per amount were inconsistently reported. Many patients reported prices for various non-standardized units of the drug. Some patients were able to supply the price for a specific amount but answers varied substantially from 100 dollars for a single gram to 10 dollars for a 4-ounce bag. Previous reports were more successful at obtaining an average price by specifically asking about money spent per week on SCRAs, finding the median to be 17.50 USD with a range of 0-40 USD (Gunderson et al. 2014).

The current study was successful in demonstrating trends and patterns in the use and use behaviors relating to SCRAs. However, there were a number of limitations in the present study. First, lack of routine laboratory testing for SCRAs prevented biological confirmation in most patients interviewed as well as identification of SCRA type. Additionally, clinical data obtained during consultations were subject to patient recall and clinician documentation bias. The high number of missing values is primarily due to patient refusal to answer which may have been influenced by state of mind at the time of interview. The psychiatric history of patients described in this study were obtained by asking patients about previous mental health diagnoses. These diagnoses were merely reported by the patients and not confirmed by further assessment or chart review.

Patients were interviewed during medical toxicology consultation after recent exposure to SCRAs and in
some cases other drugs. The questions asked of these patients in many cases required recall and insight, both of which may have been impacted by recent intoxication. Additionally, patients in the study received medical toxicology consultation, which might bias our population to those with more severe toxicity.

The open-ended style of questioning was subject to some limitations as well. While this format allowed for answers that were not biased by questioning, most patients only supplied a single answer to questions asked. It is possible that for some questions, a single patient may have had more than one answer. Conversely, a survey format that allows patients to check or mark multiple answers to a question might be able to more accurately account for the distribution of answers to a specific question. Additionally, it is possible that results may have been improved through a modified open-ended format supplemented by a structured prompt protocol or some additional guidance by the interviewers. This preliminary study used non-traditional innovative approaches to qualitative data collection in the ED setting. Digital recording of interviews, as is often used in qualitative research, would have allowed transcription and analysis using qualitative data management software.

Finally, all participants in the present study had used SCRAs in such a way as to cause them to present to the ED. It is possible that our population comprises a small subset of users whose relationship with the drug is more extensive than the average user. Additionally, the current data were acquired from patients at 10 hospitals, mainly clustered in the Midwest and East coast regions of the United States. It is possible that these results may not accurately describe the behavior of users in other regions.

Our exploratory study has implications for future research. First, our study indicates that conducting open-ended interviews with SCRA users in the context of a clinical toxicological evaluation is feasible. It also suggests ways in which qualitative data collection among people who have used SCRAs presenting to EDs could be improved by including digital recordings to more accurately capture patient responses. Second, large-scale mixed-methods studies are needed to better understand drug use behaviors, and psychiatric comorbidity among SCRA users who present to the ED. Systematic, longitudinal knowledge of the drug use practices among this group is currently lacking.

**Conclusions**

To our knowledge, this study is one of the first to examine SCRA use from a qualitative data obtained through clinical evaluation by medical toxicologists. Of reported SCRA exposures, most patients reported having used it extensively prior to presentation and using it primarily for the subjective effects associated with the drug. These results support the view that an independent and stable culture is developing around the use of SCRAs separate from their appeal as an "undetectable" alternative to marijuana.

**Acknowledgments**

We would like to acknowledge and thank the following IN3 Study Group investigators who collected the data: Robert Hendrickson, MD, Oregon Health and Science University Hospital; Kurt Kleinschmidt, MD, Parkland Memorial Hospital; Alex Manini, MD, Mount Sinai Medical Center; Alex Monte, MD, Denver Health, Adam Pomerleau, MD, Grady Memorial Hospital; Anne-Michelle Ruha, MD, Banner Good Samaritan Medical Center; Daniel Rusyniak, MD, IU Health University Hospital; Evan Schwarz, MD, Washington University School of Medicine; David Yerrarid, MD, Hahnemann University Hospital; Timothy Wiegand, MD, University of Rochester Medical Center. A previous version of this paper was presented as an abstract poster at the North American Congress of Clinical Toxicology, 2019, Nashville TN.

**Disclosure statement**

The authors have no financial relationships relevant to this article to disclose.

**Funding**

This study was supported by the National Institute on Drug Abuse Grant Number: R56DA03866, "IN3 An Innovative Approach." The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute on Drug Abuse or the National Institutes of Health.

**References**


Castaneto, M. S., D. A. Gorelick, N. A. Desrosiers, R. L. Hartman, S. Pirard, and M. A. Huestis. 2014. Synthetic cannabinoids: Epidemiology, pharmacodynamics,
and clinical implications. Drug and Alcohol Dependence 144:12–41. doi:10.1016/j.drugalcdep.2014.08.005.


