

The CBHSQ Report

Short Report

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UPDATE: DRUG-RELATED EMERGENCY DEPARTMENT VISITS INVOLVING SYNTHETIC CANNABINOIDS

AUTHORS

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INTRODUCTION

Synthetic cannabinoids are manmade chemicals that are applied (often dissolved in a solvent and sprayed) onto plant material that is not marijuana, marketed as herbal incense products and also as a “legal high.”¹ These herbal products were originally available in 2004 in several European countries with brand names “Spice,” “Spice Diamond,” “Spice Gold,” and “Yucatan Fire.”² By late 2008, synthetic cannabinoids were identified in the United States in “Spice Diamond” and “Spice Artic Energy” products.³ Even though the caution “not for human consumption” is prominently printed on the packaging, these products are used by those seeking a legal high, with smoking as the most common route of administration.^{1,4} They are labeled “not for human consumption” to mask their intended purpose and avoid Food and Drug Administration (FDA) regulatory oversight of the manufacturing process.¹ Users claim that synthetic cannabinoids mimic the effects of delta-9-tetrahydrocannabinol (THC), the primary psychoactive ingredient in marijuana.¹

There is an incorrect assumption that synthetic cannabinoids are safe.⁴ Synthetic cannabinoids produce a combination of adverse effects that resemble intoxication from delta-9-tetrahydrocannabinol (delta-9-THC), the psychoactive component of marijuana. However, synthetic cannabinoids appear to be more potent and may stay active in the body longer than delta-9-THC.⁵ The adverse effects of synthetic cannabinoids include severe agitation, anxiety, nausea, vomiting, tachycardia (racing heartbeat), elevated blood pressure, tremors, seizures, hallucinations, paranoid behavior, and nonresponsiveness.^{1,5} After regular consumption, withdrawal signs and symptoms have been observed.⁶ Death after use of synthetic cannabinoids has also been reported.^{4,7}



In Brief

- The number of emergency department (ED) visits involving synthetic cannabinoids increased significantly from 11,406 visits in 2010 to 28,531 visits in 2011.
- The number of ED visits involving synthetic cannabinoids for patients aged 12 to 17 doubled from 3,780 visits in 2010 to 7,584 visits in 2011; for patients aged 18 to 20, visits increased fourfold from 1,881 visits in 2010 to 8,212 visits in 2011.
- Males accounted for about 79 percent (19,923 visits) of the 28,531 ED visits in 2011 involving synthetic cannabinoids; 2011 DAWN estimates indicate a threefold increase in synthetic cannabinoid-related ED visits for females.
- In 2011, synthetic cannabinoids were the only substances involved in about two-thirds of the synthetic cannabinoid-related ED visits for patients aged 12 to 20 years; for those aged 21 or older, almost half of the synthetic cannabinoid-related ED visits involved only those drugs.

Because products marketed as synthetic cannabinoids (e.g., “Spice,” “K2,” and hundreds of exotic brand names) contain various amounts of different ingredients or combinations that are different from each other, it is difficult to identify which adverse effects are caused by which synthetic cannabinoid chemicals.^{4,5,8} Additionally, it appears that the chemical structures of the psychoactive components of these products, as well as the composition of the herbal products themselves, is continually changing. There are also unpredictable contaminants in these products since they are manufactured illicitly.^{4,5} Concern about the availability and use of these products has continued to increase, as they are easily purchased online and in small retail outlets, such as “head shops” and convenience stores, without age restrictions.^{1,5}

The U.S. Drug Enforcement Administration (DEA) and nearly all states have taken some degree of regulatory control over synthetic cannabinoids as they are identified.^{4,9} Manufacturers of these compounds have modified their chemical structures, sometimes only very slightly, to evade current laws and regulations to be able to continue marketing these products as “legal highs.”⁴ The ingredients are rarely clearly labeled on the packaging, and the brand names vary widely. Over the past 5 years, the DEA has identified more than 200 designer drugs, many of which are synthetic cannabinoids manufactured in China.¹⁰ Designer drugs are drugs synthesized to be chemically and pharmacologically similar to illicit drugs in order to avoid DEA scrutiny. A list of 27 synthetic cannabinoid chemicals identified in substances secured in law enforcement operations and analyzed by federal, state, and local forensic laboratories was published in a 2014 National Forensic Laboratory Information System (NFLIS) Special Report.¹¹ This special report shows that the synthetic cannabinoid chemicals identified in laboratory reports from 2010 are vastly different from those chemicals identified in 2013. Moreover, the availability of synthetic cannabinoids has surged since 2010, as indicated by the number of laboratory reports issued in January through June in 2010 (469) compared to January through June in 2013 (17,241).¹¹ As of June 2014, a number of synthetic cannabinoid chemicals have been either temporarily or permanently placed in Schedule I under the Controlled Substances Act, indicating that these are drugs with no currently accepted medical use and a high potential for abuse.¹¹ Schedule I drugs are among the most dangerous, with the potential for severe psychological or physical dependence.

Public health concerns remain heightened because synthetic cannabinoids have evolved and increased in number over time, even as regulatory action has been taken to ban specifically identified chemicals. The Centers for Disease Control and Prevention (CDC) investigated two severe illness outbreaks in 2013 that were linked to the use of synthetic cannabinoids.^{12,13} The Colorado Department of Public Health and Environment, with the assistance of the CDC, investigated 221 hospital emergency department (ED) reports of severe illness due to ingestion of synthetic cannabinoids.⁴ CDC also reported acute kidney injury associated with the use of synthetic cannabinoids in multiple states.¹⁴

Even with ongoing regulatory action and enforcement, these products continue to be marketed widely, especially to adolescents and those seeking a legal high with a desire to evade detection by current drug testing technologies.⁴ Synthetic cannabinoids are not currently identified using routine screening tests, and the creation of new synthetic cannabinoid chemicals makes it difficult to detect them in analysis of bodily fluids (e.g., blood, serum, urine).^{4,8,15,16}

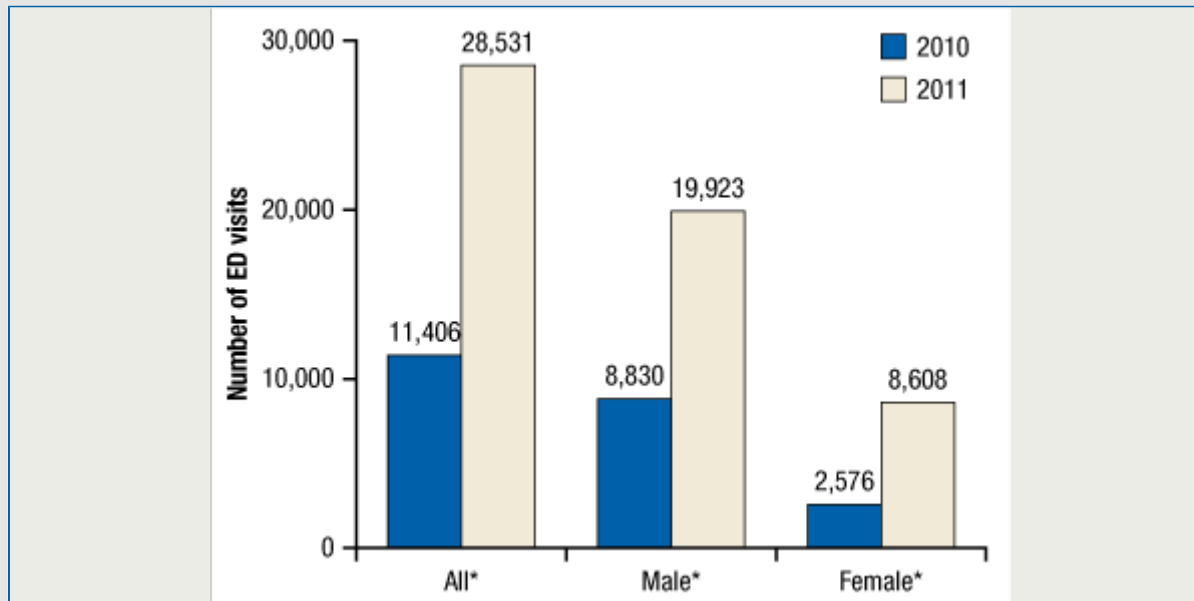
The Drug Abuse Warning Network (DAWN) was a public health surveillance system that monitored drug-related ED visits in the United States. To be a DAWN case, an ED visit must have involved a drug, either as the direct cause of the visit or as a contributing factor. DAWN first detected a measurable number of ED visits involving synthetic cannabinoids in 2010, and a report was published in 2012.^{17,18} This report presents updated data for 2011 as well as trends between 2010 and 2011.

TRENDS IN ED VISITS BY GENDER AND AGE]

Of the approximately 2,460,000 ED visits that involved drug misuse or abuse in 2011, synthetic cannabinoids were specifically linked to an estimated 28,531 ED visits. This was a statistically significant increase from 2010, when 11,406 visits occurred (Figure 1).

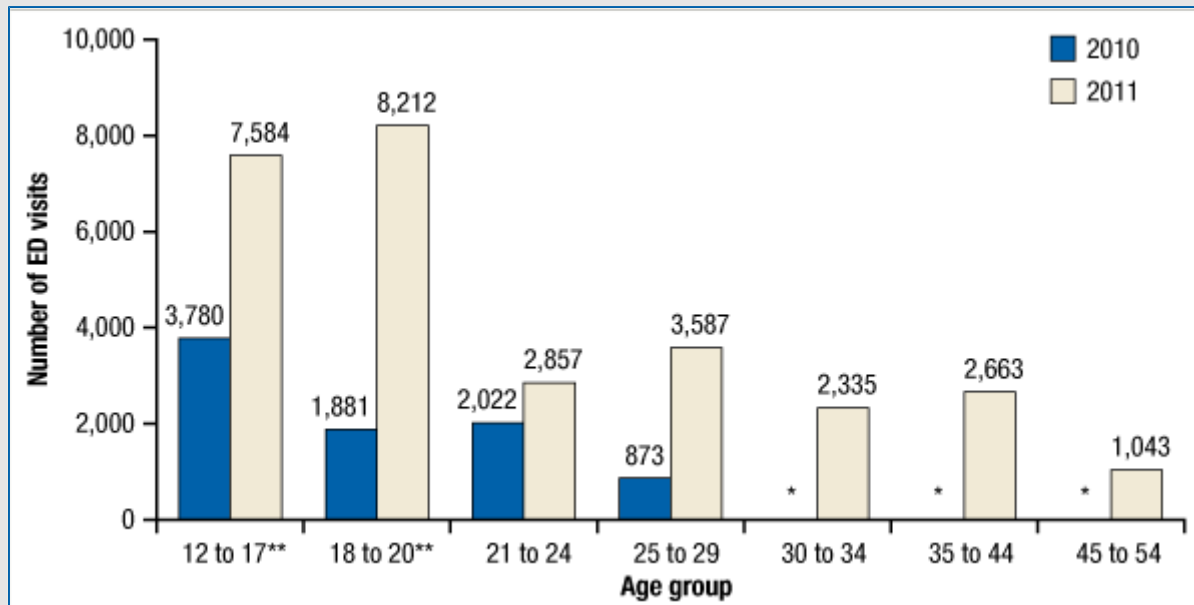
From 2010 to 2011, there were statistically significant increases for both males and females in the number of ED visits involving synthetic cannabinoids. For male patients, ED visits increased significantly from an estimated 8,830 visits in 2010 to an estimated 19,923 visits in 2011 (Figure 1). Visits for female patients tripled from 2,576 visits in 2010 to 8,608 visits in 2011.

Figure 1. Emergency department (ED) visits involving synthetic cannabinoids, by gender: 2010 and 2011



* The difference between 2010 and 2011 was statistically significant at the .05 level. Source: 2011 SAMHSA Drug Abuse Warning Network (DAWN).

Figure 2. Emergency department (ED) visits involving synthetic cannabinoids, by age group: 2010 and 2011



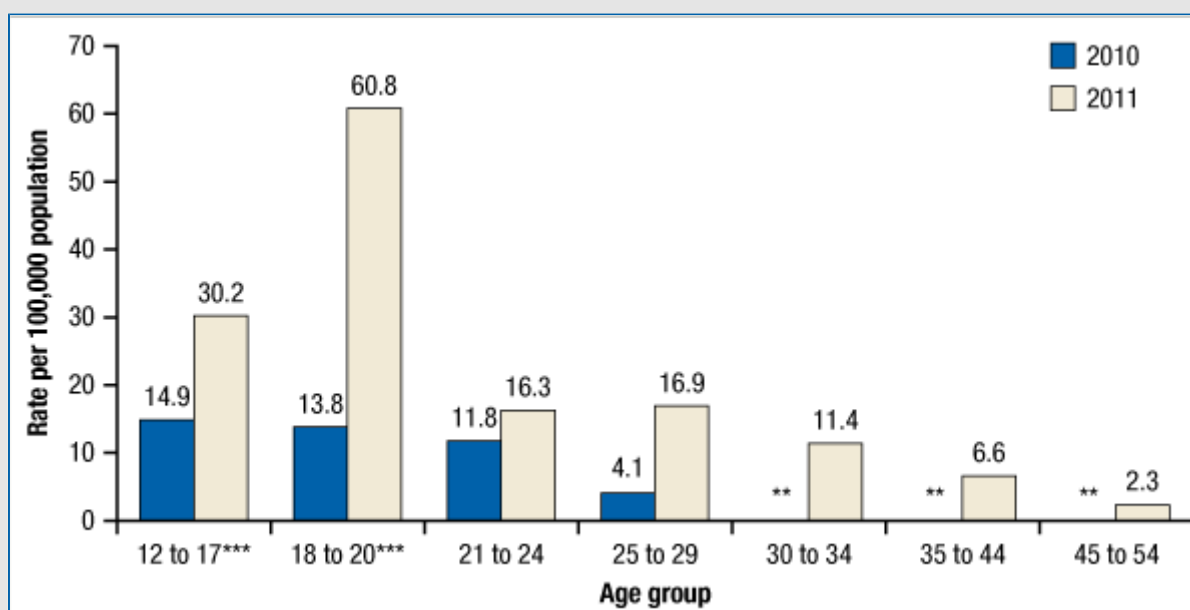
* Low precision; no estimate reported.

** The difference between 2010 and 2011 was statistically significant at the .05 level. Source: 2010 and 2011 SAMHSA Drug Abuse Warning Network (DAWN).

When looking at visits made to the ED involving synthetic cannabinoids by age, the number of visits for patients aged 12 to 17 had a statistically significant doubling from 3,780 visits in 2010 to 7,584 visits in 2011 (Figure 2). For patients aged 18 to 20, visits increased fourfold, from 1,881 visits in 2010 to 8,212 visits in 2011. Although the number of visits appears to have increased for patients aged 21 to 24 and aged 25 to 29 between 2010 and 2011, the difference was not statistically significant. For older age groups, 2011 was the first year that visits involving synthetic cannabinoids reached a measurable level. There were 2,335 ED visits involving synthetic cannabinoids by patients aged 30 to 34, 2,663 visits made by patients 35 to 44, and 1,043 visits made by patients aged 45 to 54 (Figure 2).

The rate of ED visits involving synthetic cannabinoids per 100,000 population was calculated in order to compare age groups of different sizes. In 2011, the rate was highest among persons aged 18 to 20, with 60.8 visits per 100,000 population (Figure 3).

Figure 3. Emergency department (ED) visits involving synthetic cannabinoids, rate per 100,000 population,* by age group: 2010 and 2011



* Rates take into consideration the population size of each group; therefore, groups of different sizes may have varying numbers of ED visits but have similar population rates.

** Low precision; no estimate reported.

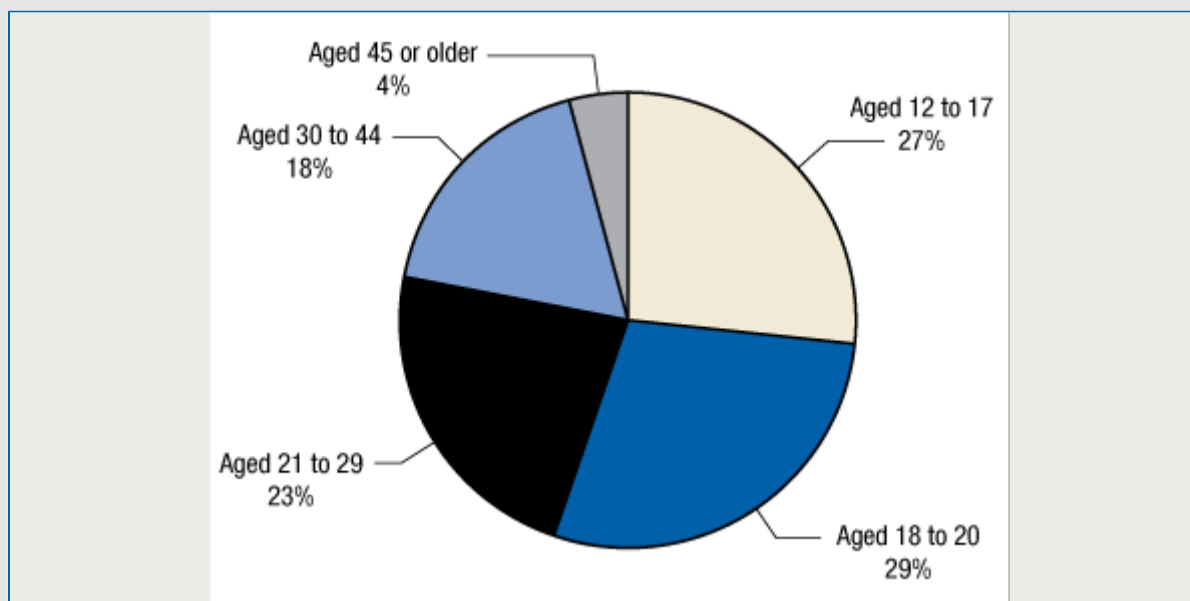
*** The difference between 2010 and 2011 was statistically significant at the .05 level.

Source: 2010 and 2011 SAMHSA Drug Abuse Warning Network (DAWN).

This rate was double the rate among persons aged 12 to 17 (30.2 visits per 100,000 population) and higher than the rate among persons aged 21 or older. Between 2010 and 2011, the rate of ED visits involving synthetic cannabinoids had a statistically significant doubling for patients aged 12 to 17, from 14.9 visits per 100,000 population in 2010 to 30.2 visits per 100,000 population in 2011. The rate per 100,000 population for those aged 18 to 20 had a statistically significant increase of more than four times, from 13.8 visits per 100,000 population in 2010 to 60.8 visits per 100,000 population in 2011. The rate of ED visits involving synthetic cannabinoids did not increase significantly for patients aged 21 or older (Figure 3).

The age distribution of the estimated 28,531 ED visits involving synthetic cannabinoids in 2011 is shown in Figure 4. Approximately a quarter of all visits were made by patients aged 12 to 17 (7,584 visits, or 27 percent), and 29 percent of visits were made by patients aged 18 to 20 (8,212). Summed together, patients aged 12 to 20 made 55 percent (15,796 visits) of all ED visits involving synthetic cannabinoids in 2011. An additional 41 percent of ED visits involving synthetic cannabinoids were made by patients aged 21 to 44. The remaining 4 percent of visits were made by those aged 45 or older (1,090 visits).

Figure 4. Emergency department (ED) visits involving synthetic cannabinoids, by age group*: 2011



*Percentages may not sum to 100 due to rounding.
Source: 2010 and 2011 SAMHSA Drug Abuse Warning Network (DAWN).

DRUGS INVOLVED IN ED VISITS

Among patients aged 20 or younger, no other substances were combined with synthetic cannabinoids in about two-thirds (65 percent) of ED visits related to their use; among patients aged 21 or older, 47 percent of visits involved synthetic cannabinoids only (Table 1).

Table 1. Emergency department (ED) visits involving synthetic cannabinoids only or in combination with other substances, by age group: 2011

Drug combination	Aged 20 or younger		Aged 21 or older	
	Number of ED visits*	Percent of ED visits*	Number of ED visits*	Percent of ED visits*
Total	15,998	100	12,533	100
Synthetic cannabinoids only	10,335	65	5,886	47
Synthetic cannabinoids in combination	5,664	35	6,646	53
Illicit drugs	3,404	21	3,335	27
Other marijuana	2,708	17	**	**
Stimulants***	**	**	1,018	8
Pharmaceuticals	2,531	16	3,243	26
Alcohol	2,438	15	1,368	11

*Because multiple drugs may be involved in each visit, estimates of visits by drug may add to more than the total, and percentages may add to more than 100 percent.

** Low precision; no estimate reported.

*** Includes amphetamines and methamphetamine.

Source: 2011 SAMHSA Drug Abuse Warning Network (DAWN).

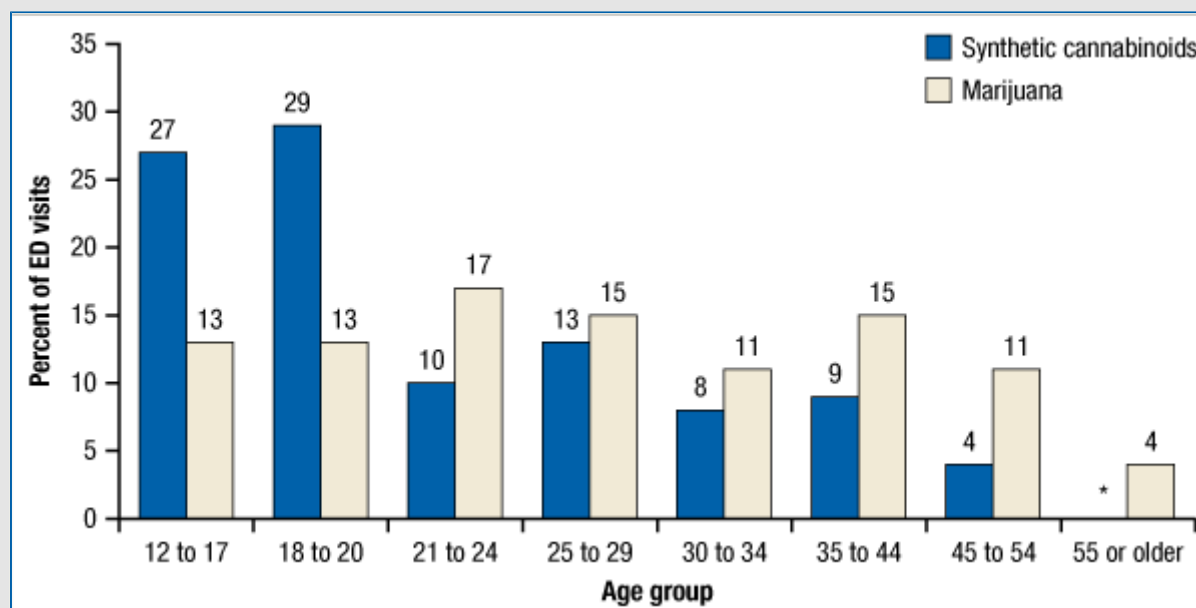
Synthetic cannabinoids were combined with illicit drugs in 21 percent of visits among patients aged 20 or younger and in 27 percent of visits among patients aged 21 or older.

In 2011, synthetic cannabinoids were combined with pharmaceuticals in 16 percent of visits among patients aged 12 to 20 and in 26 percent of visits among patients aged 21 or older.

SYNTHETIC CANNABINOIDS COMPARED WITH MARIJUANA-RELATED ED VISITS

Because synthetic cannabinoids have been marketed as a legal alternative to marijuana, this section will provide a brief comparison of the patient characteristics between ED visits for marijuana and those for synthetic cannabinoids. In 2011, marijuana-related ED visits outnumbered synthetic cannabinoid-related visits (455,668 and 28,531 visits, respectively). The average patient age for marijuana-related visits was 30 years of age, and the average patient age for synthetic cannabinoid-related visits was 23 years of age (data not shown). The age distribution also differed between the two drugs (Figure 5). More than half of synthetic cannabinoid-related visits (55 percent) were made by patients aged 12 to 20, with 27 percent aged 12 to 17. In comparison, 26 percent of marijuana-related visits involved patients aged 12 to 20, with 13 percent aged 12 to 17.

Figure 5. Age distribution of synthetic cannabinoid and marijuana-related emergency department (ED) visits: 2011



* Low precision; no estimate reported.

Source: 2011 SAMHSA Drug Abuse Warning Network (DAWN).

DISPOSITION OF ED VISITS

Among the 28,531 ED visits involving synthetic cannabinoids in 2011, about 3,510 (12 percent) resulted in admission to the hospital or transfer to another health care facility (Table 2).

Among patients who were admitted or transferred, 21 percent were aged 12 to 17, and 23 percent were aged 18 to 20. Patients aged 21 to 29 and those aged 30 to 44 each made up about one-fifth of visits resulting in admission or transfer (20 and 22 percent, respectively). Of patients

that received follow-up care (e.g., patients who were referred to detoxification/treatment, admitted to the hospital (any unit), or transferred), approximately one-half involved synthetic cannabinoids only and no other substance (54 percent; data not shown).

Table 2. Disposition of emergency department (ED) visits involving synthetic cannabinoids, by age group: 2011

Drug combination	Treated and released		Admitted or transferred	
	Number of ED visits	Percent of ED visits	Number of ED visits	Percent of ED visits
Total ED visits	22,938	100	3,510	100
Aged 12 to 17	6,824	30	745	21
Aged 18 to 20	6,547	29	822*	23*
Aged 21 to 29	4,948	22	702	20
Aged 30 to 44	3,792	17	777	22
Aged 45 or older	**	**	**	**

*Estimate may be unreliable due to low precision.

**Low precision; no estimate reported.

Source: 2011 SAMHSA Drug Abuse Warning Network (DAWN).

DISCUSSION

As synthetic cannabinoids have become more available, the estimated number of ED visits involving synthetic cannabinoids has increased threefold from 2010 to 2011.¹⁹ Most of the estimated 28,531 ED visits in 2011 involving synthetic cannabinoids were made by males (79 percent). This is consistent with information published in a summarized review of adverse events, medical treatments and outcomes.²⁰ Additionally, 2011 DAWN data indicate a threefold increase in ED visits made by females compared to 2010.

For those aged 12 to 17, the rates of ED visits involving synthetic cannabinoids more than doubled from 14.9 per 100,000 in 2010 to 30.2 per 100,000 in 2011. For patients aged 18 to 20, the rates of ED visits involving synthetic cannabinoids increased more than fourfold from 13.8 per 100,000 in 2010 to 60.8 per 100,000 in 2011. These significant increases in rates of ED visits involving synthetic cannabinoids, especially among adolescents, are of great concern to health care professionals, public health officials, and law enforcement.^{4,5} To date, only acute adverse effects of synthetic cannabinoid use have been reported. There is little information about the health effects and toxicity following chronic use of synthetic cannabinoids, but several cases of new-onset psychosis after multiple uses of synthetic cannabinoids have recently been reported.^{5,21}

Concern is not limited to synthetic cannabinoid use by adolescents and young adults. The substantial number of ED visits involving synthetic cannabinoids in 2011 allowed for statistical analysis and reporting of patients in more age ranges, including patients in the 45 to 54 age range. Reports in scientific literature indicate a wider appeal of synthetic cannabinoids among those not only seeking what is advertised as a legal high, but also by those in parole and probation situations and by those in workplaces that require drug testing.^{4,5,15} This may be because of ease of access to products containing synthetic cannabinoids and the inability to easily test for synthetic cannabinoids using current clinical tests, parole and probation drug tests, and routinely used military and civilian workplace drug tests.^{4,5,15,16} There are several published reports describing the presentation, treatment, and outcome of ED patients who have ingested synthetic cannabinoids. The patients described in these reports range in age from 13 to 59.^{8,22,23,24} For all of the aforementioned reasons, it has been suggested that clinicians, especially in the ED, be constantly on the alert for synthetic cannabinoid toxicity symptoms, even if drug screen results are negative.⁵

Education about the dangers of synthetic cannabinoids needs to be provided to the general public, the medical community, and retailers.¹⁹ Educators can help prevent use of synthetic cannabinoids by addressing use of these substances in programs designed to prevent illicit drug use, such as the White House Office of National Drug Control Policy's Drug-Free Communities Program.¹⁹ Parents can also

discuss the dangers of these drugs with their children and use parental controls for online purchases. Recent survey results show that such interventions may have already resulted in teens being less likely to use “synthetic marijuana” because past year use among 12th graders dropped from 11.3 percent in 2012 to 7.9 percent in 2013.²⁵ However, it is important to note that this same survey indicates that 8th, 10th and 12th graders report a low level of perceived risk of using synthetic cannabinoids once or twice.²⁵ Because most synthetic cannabinoid-related ED visits result in discharge, a patient's time in the ED is a valuable opportunity for intervention and education.

Most importantly, medical professionals need to understand the effects of synthetic cannabinoids, so that supportive care and treatment can be provided to patients who experience their adverse effects. Suggested treatment recommendations include intravenous fluids, administration of benzodiazepine medications, and possibly antipsychotic medication if symptoms are severe.²⁶ With new drugs of abuse, it is difficult to disseminate information about their effects when they have only recently been identified and their effects have not yet been studied in a comprehensive way. Furthermore, the changing composition of products containing synthetic cannabinoids, and the inability of routinely used clinical laboratory tests to detect these substances, makes it difficult for treating physicians to make a clear diagnosis and establish a treatment plan for the intoxicated patient. Health professionals in the ED can seek information from other sources, such as medical toxicologists or poison control center staff, who may be better informed about new designer drugs.²⁷

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SUMMARY

Background: Synthetic cannabinoids are dangerous products which are sold as a legal high and marketed towards youth with names such as “Spice,” and “K2.” Although regulatory agencies have attempted to stop the distribution of these products, manufacturers continually change their chemical structures to evade current laws and regulations. **Methods:** Data from 2010 and 2011 Drug Abuse Warning Network (DAWN) were analyzed. **Results:** The estimated number of visits made to emergency departments (EDs) that involved synthetic cannabinoids more than doubled between 2010 (11,406 visits) and 2011 (28,531 visits). When stratified by age, the rate of ED visits increased more than fourfold for those aged 18 to 20 (from 13.8 visits per 100,000 population in 2010 to 60.8 visits per 100,000 population in 2011) and doubled for those aged 12 to 17 (from 14.9 visits per 100,000 population in 2010 to 30.2 visits per 100,000 population in 2011). In 2011, synthetic cannabinoids were the only substance involved in 65 percent of ED visits by those aged 20 or younger. **Conclusion:** These results demonstrate the harmful effects of synthetic cannabinoids, especially on youth. Education continues to be needed for parents, the medical community and to retailers who sell such products.

Keywords: synthetic cannabinoids, synthetic marijuana, spice, marijuana, Drug Abuse Warning Network, DAWN

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KEYWORDS

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The Substance Abuse and Mental Health Services Administration (SAMHSA) is the agency within the U.S. Department of Health and Human Services that leads public health efforts to advance the behavioral health of the nation. SAMHSA's mission is to reduce the impact of substance abuse and mental illness on America's communities.

The Drug Abuse Warning Network (DAWN) was a public health surveillance system that monitored drug-related morbidity and mortality. DAWN used a probability sample of hospitals to produce estimates of drug-related emergency department (ED) visits for the United States and selected metropolitan areas annually. DAWN also produced annual profiles of drug-related deaths reviewed by medical examiners or coroners in selected metropolitan areas and States.

Any ED visit related to recent drug use was included in DAWN. All types of drugs - licit and illicit - were covered. Alcohol involvement was documented for patients of all ages if it occurred with another drug. Alcohol was considered an illicit drug for minors and was documented even if no other drug was involved. The classification of drugs used in DAWN is derived from the Multum Lexicon, copyright 2012 Lexi-Comp, Inc., and/or Cerner Multum, Inc. The Multum Licensing Agreement governing use of the Lexicon can be found at <http://www.samhsa.gov/data/emergency-department-data-dawn>.

DAWN is one of three major surveys conducted by SAMHSA's Center for Behavioral Health Statistics and Quality (CBHSQ). For more information on other CBHSQ surveys, go to <http://www.samhsa.gov/data/>. SAMHSA contracted with Westat (Rockville, MD) and RTI International (Research Triangle Park, NC) to operate the DAWN system and produce publications.

For publications and additional information about DAWN, go to <http://www.samhsa.gov/data/emergency-department-data-dawn>.



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