



Adolescent exposures to traditional and novel psychoactive drugs, reported to National Poison Data System (NPDS), 2007–2017



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ABSTRACT

Background: Survey data on adolescent drug use trends have limitations evaluating the impact of drug use on health and may lag current trends. The objective was to describe National Poison Data System (NPDS) trends, medical outcomes, and healthcare encounters from adolescent exposures of traditional and novel psychoactive drugs.

Methods: Retrospective review of adolescent (10–18 years of age) exposure calls to all U.S. poison centers, from January 1, 2007 through December 31, 2017, using generic codes for traditional and novel psychoactive drugs. Descriptive statistics and univariate Poisson regression modeling were used for analysis.

Results: There were 49,757 exposure calls for the included psychoactive drugs. The median age was 16 years (IQR 15,17), 64% were male, and the majority were evaluated in a healthcare facility (92%). Marijuana had the most exposure calls (36.6%), followed by synthetic cannabinoids (e.g., spice; 21.3%). There were 181 (< 1%) deaths; the highest fatality rates were from fentanyl, 2C drugs (phenylethylamine derivatives), and heroin. LSD exposure calls have had the most significant increase over the past 10 years.

Conclusion: U.S. Poison Centers reported almost 50,000 exposure calls and 181 deaths over 10 years for adolescent exposures of both traditional and novel psychoactive drugs, demonstrating the significant health impact on this vulnerable population. Opioids and 2C drugs contributed to the highest mortality rates, moderate/major symptoms and healthcare utilization, and LSD had the most significant increase in calls. Multi-source surveillance methodology is critical in understanding the public health impact on drug abuse in the adolescent population.

1. Introduction

Substance abuse in the adolescent population has a significant public health burden. According to the 2017 National Survey on Drug Use and Health (NSDUH), almost 24% of adolescents have admitted to ever using an illicit drug in the past year (Substance Abuse, 2018). Death secondary to overdose and poisoning is also a leading cause of injury-related deaths in the adolescent population (Centers for Disease Control and Prevention, 2018a,b). It is critical to have close surveillance of the prevalence of drug use in adolescents, as substance abuse in this vulnerable population is associated with significant morbidity and mortality. Health impacts include drug dependence and associated use of multiple illicit drugs, poor school performance, high risk sexual behaviors and behavioral health disorders (Wang and Hoyte, 2018).

Most surveillance methods ask about current or past use (Miech et al., 2018; Substance Abuse, 2018). While these longitudinal

surveillance methods are important, they can be limited by recall bias, fear of repercussions, and may lag behind current trends in drug use. There is also limited information on medical outcomes, impacts on the healthcare system, and epidemiology pertaining to novel psychoactive drugs. Novel psychoactive drugs or drugs of abuse are considered newer synthetic drugs of abuse, analogs of known drugs of abuse, new illicit use of an older existing drug, or naturally occurring substances that do not fit the typical pharmacological or behavioral profile of traditional illicit substances (Rech et al., 2015; Vandrey et al., 2013; Wang and Hoyte, 2019). Some of these xenobiotics are readily available online or in gas stations and convenience stores, labeled as other substances such as “incense” or “bath salts” and “not for human consumption.” Examples of novel psychoactive drugs include synthetic cannabinoids (e.g., spice) and synthetic cathinones (e.g., bath salts), fentanyl analogs (e.g., carfentanyl), PCP and LSD analogs, and phenylethylamine analogs (2C compounds and NBOMBe). Other emerging psychoactive drugs, not

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necessarily novel synthetic drugs, include kratom and loperamide. Epidemiologic data and medical outcomes of these substances are challenging to collect, as specific analogues, popularity and availability of these drugs are constantly changing. Detection and confirmation of these drugs are difficult, as standard drug tests do not detect these xenobiotics (Drug Enforcement Administration, 2017; Rech et al., 2015; Vandrey et al., 2013).

Poison centers collect surveillance information on psychoactive drugs from the drug users themselves, bystanders, and healthcare facilities and practitioners. Trends in poison center exposure calls can help detect recent changes in use patterns, epidemiologic outbreaks, and the appearance of novel drugs and associated clinical effects. These data can help supplement surveillance trends in prevalence of admitted use. The objective of this study was to use the American Association of Poison Control Centers (AAPCC) National Poison Data System (NPDS) data to describe trends in poison center calls for reported adolescent exposures to traditional and novel psychoactive drugs. Secondary objectives were to describe healthcare encounters and associated medical outcomes.

2. Methods

This was a retrospective review of adolescent (10–18 years of age) exposure calls to all U.S. regional poison centers from January 1, 2007 through December 31, 2017. We queried the AAPCC NPDS using generic codes for methamphetamine (0201127), marijuana (0083000), cocaine (0113000), heroin (0037702), synthetic cathinone (310140), loperamide (550000), fentanyl and analogs (200628), LSD and analogs (027000), phenylethylamine analogs (including 2C and NBOMe compounds, 310143), khat (097000), phencyclidine (0071000), synthetic cannabinoids (200617), and hallucinogenic amphetamines (0201126). Information is systematically collected by trained specialists in poison information, and cases are followed until outcomes can be determined. Historical generic code mappings were included for those categories with new generic codes.

Data were abstracted into a standardized dataset and included age, sex, management site, reason, route, medical outcomes, and clinical effects. Further details on NPDS data field and medical outcome definitions are available in the appendix of the AAPCC 2017 annual report of the NPDS (Gummin et al., 2017). Descriptive statistics were performed on demographic data, management site, and medical outcomes. The data were a mix of both single substance and polysubstance exposures; however, the number of single substance exposures and the number of deaths due to a single substance were specifically reported. Total number of NPDS calls for adolescents 10–18 years was used to account for overall volume of poison center calls. Univariate Poisson Regression modeling was used to determine rate ratios (RR) evaluating the overall change in rate of calls per annual poison center calls. The study was exempt from our local Institutional Review Board.

3. Results

From 2007–2017, there were 49,757 exposure calls for the included psychoactive drugs. Overall, the median age was 16 years (IQR 15,17), and 64% (31,644) were male. Most calls involving traditional psychoactive drugs involved polysubstance drug exposures, while novel psychoactive drugs were mostly single substance exposures (Table 1). In regard to the total number of exposure calls, most were for marijuana (18,216; 36.6%) followed by calls for synthetic cannabinoids (10,586; 21.3%). Among novel psychoactive drugs, most calls were for synthetic cannabinoids. With the exception of khat (82, 32%) and loperamide (631, 69%), most exposures were evaluated in a healthcare facility (90–97%). Psychoactive drugs that had at least half of exposures with reported moderate and major effects were 2C drugs (436, 70%), LSD (1,881; 65%), synthetic cathinones (840, 59%), heroin (1,047; 54%), and fentanyl (274, 51%). Overall, deaths were rare ($n = 181$; < 1%).

Of the 181 deaths, 36 (20%) occurred in adolescents exposed to a single substance, and 145 (80%) were exposed to more than one substance. Drug categories contributing to the highest fatality rates were fentanyl (16, 3%), 2C drugs (12, 2%), and heroin (23, 1%) (Table 1).

All categories of psychoactive drugs, with the exception of loperamide and synthetic cathinones, had significant changes in exposure calls per 100,000 annual NPDS calls from 2007 through 2017 (Table 1). Marijuana exposure calls have had a steady and significant increase over the 10-year period, from 647 to 1,187 calls per 100,000 annual calls (RR 1.06, 95% CI 1.05–1.07), while the rate of synthetic cannabinoid exposure calls per 100,000 NPDS calls peaked in 2011 (1,533 per 100,000 exposure calls) and have declined through 2017 (RR 1.07, 95% CI 1.06, 1.08) (Table 1, Fig. 1a). The rate of LSD exposure calls has had the most significant increase in the past 10 years, rising from 63 calls per 100,000 to 256 exposure calls per 100,000 (1.19, 95% CI 1.17, 1.21) (Table 1, Fig. 1b).

4. Discussion

With almost 50,000 poison center calls and near 200 deaths reported in a 10-year period, adolescent exposures to both traditional and novel psychoactive drugs have a significant health impact on the adolescent population. The majority of exposure calls required healthcare evaluations and caused moderate to major effects, further demonstrating the severity of disease both traditional and novel psychoactive drugs have on this vulnerable population. Traditional psychoactive drugs and overall reported deaths were associated with more polysubstance exposures, while novel drugs were more commonly reported with single use exposures. The higher rates of deaths reported with fentanyl and heroin illustrate how the opioid epidemic has also reached this population. These NPDS surveillance data reveal the majority of these drug exposures continue to increase, demonstrating the importance of continued development of surveillance and prevention methods in combatting both traditional and novel psychoactive drugs in this vulnerable population.

There has been a significant increase in poison center exposures from marijuana use in adolescents. Despite this observation, most surveillance methodologies such as NSDUH and Monitoring the Future (MTF) study do not demonstrate an increase in admitted adolescent use (Miech et al., 2018; Substance Abuse, 2018). These conflicting trends are in the setting of increasing state marijuana legalization for medical indications and recreational use (State Marijuana Laws, 2018). These findings demonstrate that perhaps legalization does not increase overall prevalence of use but may further negatively impact the health of adolescents who already use or are at risk for marijuana use. With legalization, the industry brings higher potency products such as edibles, waxes, dabs, budders and other vaporization products which contain high concentrations of tetrahydrocannabinol (THC). California has reported a high percentage use of non-traditional forms, including edible products and vaporization products, among the adolescent population (Peters et al., 2018). These higher potency marijuana products can lead to more psychosis, agitation and adverse events (Di Forti et al., 2009; Ford et al., 2017; Spindle et al., 2018). There have also been reports of increasing emergency department visits in Colorado associated with marijuana use, a state that has legalized marijuana medically and recreationally, despite lack of increase in prevalence of use (Monte et al., 2019). Most of these visits were observed mainly in the behavioral health population (Wang et al., 2018; Monte et al., 2019). Despite our observation, we did not perform state-level analysis to specifically evaluate the impact of state legalization.

On the contrary, synthetic marijuana (“Spice” or “K2”) and synthetic cathinones (“bath salts” or “plant food”) have seen a decline in poison center exposure calls in the past 5 years (2012 through 2017). These drugs first appeared in convenience stores in the mid-2000’s, and rates of emergency room visits peaked in the early 2010’s, mirroring the peak in NPDS exposure calls in adolescents (Substance Abuse, 2011).

Table 1
Characteristics of adolescent psychoactive drug abuse.

TRADITIONAL PSYCHOACTIVE DRUGS	Marijuana (n = 18216, 36.6%)	Cocaine (n = 3291, 6.6%)	Heroin (n = 1922, 3.9%)	LSD and Analogs (n = 2906, 5.8%)	PCP and Analogs (n = 787, 1.6%)	Methamphetamine (n = 2641, 5.3%)	
Median Age, years (IQR)	16 (15-17)	17 (16-18)	17 (16-18)	17 (16.17)	16 (15,17)	17 (15-18)	
Male	11470 (63%)	2001 (61%)	1070 (56%)	2086 (72%)	504 (64%)	1441 (55%)	
Single Substance Exposures	5870 (32%)	1070 (33%)	1015 (53%)	1839 (63%)	363 (46%)	1386 (52%)	
Management Site							
Enroute/Referred to HCF	16606 (91%)	3110 (95%)	1858 (97%)	2766 (95%)	735 (93%)	2386 (90%)	
Not Referred to HCF	1299 (7%)	140 (4%)	41 (2%)	104 (4%)	40 (5%)	199 (8%)	
Other/Unknown	311 (2%)	41 (1%)	23 (1%)	36 (1%)	12 (2%)	56 (2%)	
Medical Outcomes							
No effect	1442 (8%)	447 (14%)	148 (8%)	110 (4%)	47 (6%)	412 (16%)	
Minor effect	6076 (33%)	816 (25%)	405 (21%)	564 (19%)	198 (25%)	558 (21%)	
Moderate effect	6428 (35%)	1093 (33%)	694 (36%)	1689 (58%)	351 (45%)	874 (33%)	
Major effect	772 (4%)	279 (8%)	353 (18%)	192 (7%)	58 (7%)	157 (6%)	
Total Deaths (including indirect) [†]	42 (< 1%)	20 (< 1%)	23 (1%)	5 (< 1%)	2 (< 1%)	18 (< 1%)	
Single Substance Deaths	0 (0%)	3 (< 1%)	5 (< 1%)	2 (< 1%)	0 (0%)	3 (< 1%)	
Exposures per 100,000							
Poison Center Calls							
2007	647	315	65	63	50	69	
2017	1187	152	86	256	20	153	
**Rate Ratio (95% CI)	1.06 (1.05-1.07)	0.93 (0.92, 0.95)	1.05 (1.03, 1.07)	1.19 (1.17, 1.21)	0.92 (0.89, 0.95)	1.1 (1.08, 1.11)	
NOVEL PSYCHOACTIVE DRUGS	2C Drugs (n = 625, 1.3%)	*Synthetic Cannabinoids (n = 10586, 21.3%)	*Synthetic Cathinones (n = 1434, 2.9%)	Fentanyl and Analogs (n = 537, 1.1%)	Hallucinogenic Amphetamines (n = 5649, 11.4%)	Khat (n = 255, 0.5%)	Loperamide (n = 908, 1.8%)
Median Age, years (IQR)	17(16,18)	16 (15,17)	17(16,18)	17(16,18)	17(15,18)	14(11,16)	15(13,17)
Male	457 (73%)	7795 (74%)	978 (68%)	348 (65%)	2970 (53%)	171 (67%)	353 (39%)
Single Substance Exposures	470 (75%)	8341 (79%)	920 (64%)	320 (60%)	3084 (55%)	234 (92%)	431 (47%)
Management Site							
Enroute/Referred to HCF	608 (97%)	10040 (95%)	1366 (95%)	484 (90%)	5292 (94%)	82 (32%)	631 (69%)
Not Referred to HCF	16 (3%)	431 (4%)	48 (3%)	44 (8%)	273 (5%)	166 (65%)	254 (28%)
Other/Unknown	1 (< 1%)	115 (1%)	20 (1%)	4 (< 1%)	84 (1%)	7 (3%)	23 (3%)
Medical Outcomes							
No effect	22 (4%)	469 (4%)	44 (3%)	38 (7%)	335 (6%)	84 (33%)	232 (26%)
Minor effect	101 (16%)	3513 (33%)	289 (20%)	102 (19%)	1371 (24%)	31 (12%)	216 (24%)
Moderate effect	369 (59%)	4588 (43%)	699 (49%)	166(31%)	2383 (42%)	19 (7%)	130 (14%)
Major effect	67 (11%)	569 (5%)	141 (10%)	108 (20%)	343 (6%)	2 (< 1%)	17 (2%)
Total Death (including indirect) [†]	12 (2%)	15 (< 1%)	3 (< 1%)	16 (3%)	23 (< 1%)	0 (0%)	2 (< 1%)
Single Substance Deaths	7 (1%)	2 (< 1%)	1 (< 1%)	9 (2%)	3 (< 1%)	0 (0%)	1 (< 1%)
Exposures per 100,000							
Poison Center Calls							
2007	3	3	18	34	276	3	45
2017	13	184	23	28	152	16	52
**Rate Ratio (95% CI)	1.13 (1.09, 1.17)	1.07 (1.06, 1.08)	1.02 (0.99, 1.04)	0.95 (0.91, 0.98)	0.93 (0.92, 0.95)	1.1 (1.04, 1.16)	1.03 (0.99, 1.06)

Not all management sites or medical outcomes were documented.

* Synthetic cannabinoids were reported 2009–2017, Synthetic Cathinones were reported 2010–2017.

** Rate Ratios represent the average change for every one year during the study period.

[†] per NPDS: an indirect death report are deaths that the poison center acquired from medical examiner or media, but did not manage nor answer any questions about the death.

This may be due to a decrease in use but also may be attributed to familiarity amongst healthcare providers of this novel psychoactive drug. The MTF Study also noted a decline of admitted synthetic cannabinoid use (11.4% in 2011 to 3.7% in 2017 amongst 12th graders) and partially attributed this decline to increased Drug Enforcement Agency (DEA) regulation, thus reducing availability (Miech et al., 2018). This noted decline is welcome news, as synthetic cannabinoid use in adolescents has been associated with morbidity, mortality, behavioral health disorders and other substance use (Ninnemann et al., 2017; Palamar et al., 2017). However, given that synthetic cannabinoids and synthetic cathinones remain readily available, with a wide variety of products to choose from, outbreaks continue to be reported and continued vigilance is critical (Centers for Disease Control and Prevention 2018b).

There was a resurgence in LSD as demonstrated in a significant increase in LSD exposure calls, with the majority reporting moderate or

major effects and 95% seeking healthcare evaluation. Although LSD has been abused for its hallucinogenic properties for decades, there have been several recent reports of use of LSD analogs and its increased frequency in use (Brandt et al., 2018; Coney et al., 2017). This is in contrast to MTF survey data which describes a low and steady prevalence of LSD use (Miech et al., 2018). More data on specific LSD compounds and reported clinical effects and details on abuse patterns are needed to understand this recent observation.

4.1. Limitations

NPDS reports national regional poison center exposure call trends; however, NPDS data relies on self-reporting by individuals or healthcare providers. Although the data is systematically collected, not all data fields may be obtained due to the information needed to provide time-sensitive medical care. The study period was chosen due to lack of

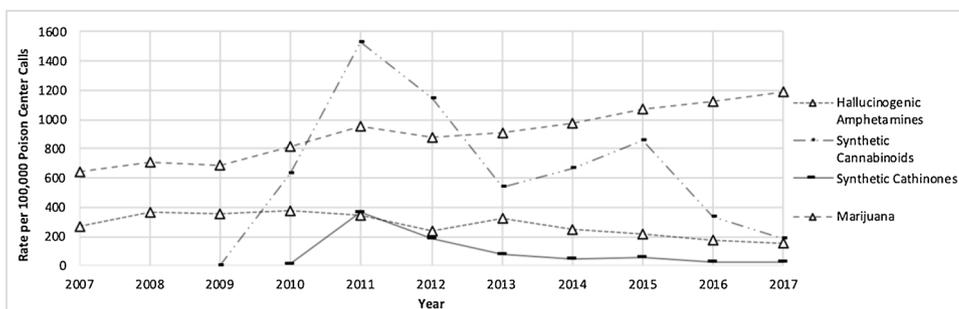
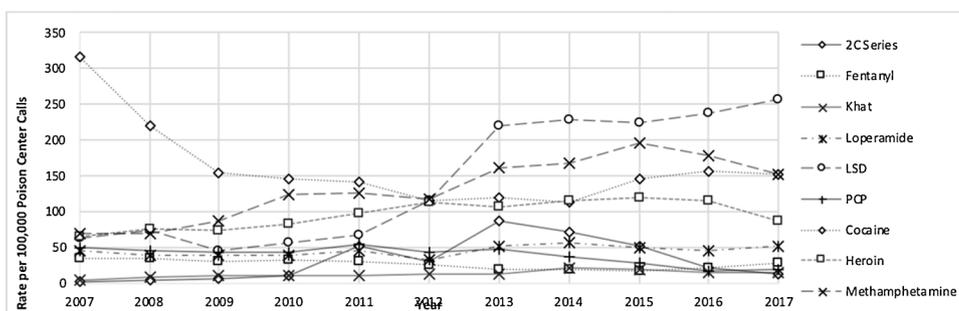


Fig. 1. a. Adolescent drug exposure rate per 100,000 poison center calls among 10–18 years, 2007–2017 (Hallucinogenic amphetamines, Synthetic cannabinoids, Synthetic cathinones, and Marijuana). **b.** Adolescent center drug exposure rate per 100,000 poison center calls among 10–18 years, 2007–2017 (2C, Fentanyl, Khat, Loperamide, LSD, PCP, Cocaine, Heroin, and Methamphetamine).



several drug codes that did not exist or have complete data in NPDS prior to 2007. Thus, we cannot comment on trends prior to 2007; this is particularly true for more recent drugs of abuse. Confirmatory assays are not available for many psychoactive drugs, especially novel psychoactive drugs, limiting verification of suspected exposures reported. There may be an underestimation in exposure rates and deaths using poison center calls. This may be due to several reasons: clinical under-recognition due to poor detection methods, novel drugs adulterating common drugs, healthcare provider unfamiliarity with novel drugs, or healthcare providers not calling poison centers for deceased patients and deaths on the scene. Further, there may be other factors contributing to the trends identified using NPDS data that are not accounted for. For example, synthetic cannabinoid calls may be decreasing partially secondary to provider familiarity with the exposure, thus not prompting a call to the poison center. Some deaths may have been reported in multiple categories if they involved multiple drugs.

5. Conclusion

U.S. Poison Centers reported almost 50,000 exposure calls and 181 deaths over 10 years for adolescent use of both traditional and novel psychoactive drugs, demonstrating a significant health impact on this vulnerable population. Fentanyl, heroin, and 2C drugs accounted for the highest mortality rates, moderate/major symptoms and healthcare utilization. Although synthetic cannabinoid and cathinone exposure calls have been decreasing, marijuana, methamphetamine and LSD exposure calls are increasing from 2007 through 2017. Multi-source surveillance methodology is critical in understanding the public health impact on drug abuse in the adolescent population.

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Contributors

Dr. Ng participated in manuscript draft development and data interpretation. Dr. Banerji participated in data collection, draft development and data interpretation. Dr. Graham participate in manuscript draft development and data interpretation. Ms. Leonard participated in data analysis and manuscript development. Dr. Wang participated in

research development, manuscript draft development and data interpretation. All authors contributed to and approved of the final version of the manuscript.

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