Trends and Regional Differences in the Diversion of Stimulants in the United States, 2015–2019

Holly E. Funk[1†‡], Susannah E. Pitt[1†‡], Alison T. Varano[1†‡], and Brian J. Piper[1]
[1]Geisinger Commonwealth School of Medicine, Scranton, PA 18509
[†]Doctor of Medicine Program
[‡]Authors contributed equally
Correspondence: spitt@som.geisinger.edu

Abstract

Background: Stimulant drugs are commonly prescribed for the treatment of attention deficit hyperactivity disorder (ADHD) in the United States (U.S.). Sympathomimetics such as amphetamine, lisdexamfetamine, and methylphenidate are classified as Schedule II substances with a high potential for misuse. Drug diversion is defined as the distribution of legal prescription medication in an unlawful way. The purpose of this study was to examine and analyze epidemiological trends in stimulant drug diversion across the U.S. for the years 2015 to 2019.

Methods: Drug data weight for the years 2015 to 2019 was obtained using StreetRx.com through a Data Use Agreement in all 50 states for the following drugs: amphetamine, lisdexamfetamine, and methylphenidate. StreetRx is a crowdsourcing public website which allows users to make submissions on the quantity, price, and location of illicit drug sales. The data set was divided into four regions, Northeast (NE), South (S), West (W), and Midwest (MW), for regional analysis. Mass of stimulants in grams was corrected for population estimates from the U.S. Census Bureau, Population Division.

Results: The total mass of diverted stimulants per population (mg/population) in the United States decreased from 2015 to 2019 for amphetamine (-31.5%), lisdexamfetamine (-51.0%), and methylphenidate (-57.0%). The percent changes varied regionally, with trends in the NE and S closely mirroring the total percent changes for most years. However, the changes in the MW and W regions were much more modest. The W stands out as having a significantly higher average value of diverted stimulants per population (mg/population) for all included years.

Conclusion: Reported diversion by StreetRx.com of stimulants on the illicit market has declined in recent years. Diversion in the W U.S. is higher than other regions. These trends do not mirror the rise in prescription distribution of amphetamine and lisdexamfetamine, nor the rise in diagnoses of ADHD over the past 10 years. Potential explanations include drug characteristics, misuser characteristics, and regional health care characteristics. This research provides health care teams with insight into the distribution of frequently prescribed stimulants in the illicit market and potentially in their communities. Further research is needed to shed light on the impact of COVID-19 on the already appreciable misuse of prescription stimulants.

Introduction

Prescription drug misuse in the United States (U.S.) is challenging to monitor and quantify. There is limited data available and illicit use often goes unreported to medical providers, health officials and law enforcement. According to the drug scheduling classification, Schedule I drugs have the highest potential for abuse, dependence, and adverse effects, while Schedule V drugs have the least potential for abuse. Stimulants, such as amphetamine, lisdexamfetamine, and methylphenidate are labeled as Schedule II drugs with high potential for abuse (1). Prescription stimulants are commonly used to treat attention deficit hyperactivity disorder (ADHD), with other indications including binge-eating disorder and narcolepsy. ADHD is the most common childhood neurodevelopmental disorder (2). Symptomology of the disorder includes inattentiveness, hyperactivity, and impulsivity in multiple settings, such as the home and in school (3). The National Institute of Drug Abuse classifies stimulant misuse as taking an inappropriate dose of prescription medication and/or in a manner other than what was prescribed to you by a physician or misusing another individual's prescription medication (4). While ADHD is commonly known as a childhood disorder, the Diagnostic and Statistical Manual (DSM) 5 criteria now addresses diagnostic issues for adult patients with ADHD, such as broadened onset age requirements and lower symptom number thresholds (5). According to the National Survey on Drug Use and Health (N=102,000), it was estimated that 6.6 % of U.S. adults used prescription stimulant drugs, 4.5% without any misuse and 2.1% with misuse (6). Abusing stimulants can lead to negative medical outcomes affecting nearly every organ system. Acute intoxication effects may include insomnia, anxiety, panic attacks, hallucinations, hypertension, tachycardia, and arrhythmias, while chronic misuse can lead to neurological, cardiovascular, pulmonary, and gastrointestinal complications. There is potential for sensitization, drug-craving and other addictive behaviors as well (7).

Drug diversion is defined as the illegal acquirement and distribution of controlled pharmaceuticals (8). Diversion of prescription drugs may happen at any point in the supply chain course, from production to final distribution, but often occurs after the medical professional and patient interaction. The ability to effectively monitor and track the diversion of prescription drugs does not only reduce the negative health implications of prescription drug abuse but can also inform efforts to reform and improve strategies to mitigate diversion

(9). Additionally, education and training programs on the risk of misuse and diversion of prescription stimulants for healthcare providers may be necessary in order to confidently prescribe medications to patients. A national questionnaire administered to physicians (N= 826) reported that only 48% of physicians received official training on prescription drug diversion (10). It is evident that patients would benefit from programs that educated physicians and other health care providers on the prevalence, outcomes, and mitigation of stimulant drug misuse.

The Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) System is an anonymous, self-reported online platform named StreetRx.com, which allows individuals to track the price and distribution of prescription and illicit drugs across the U.S. (11). Users can make submissions that include information such as the generic name of the substance purchased, the price, raw dosage, and the geographical location of the transaction. An analysis of this platform provides valid estimates of distribution and pricing on the illicit market (12).

Researchers have used StreetRx to analyze crowdsourced reporting of illicit drug use for other substances. General opioid misuse, as well as focused oxycodone and oxymorphone cross-sectional studies have been conducted (12, 13). One study concluded that street prices were often influenced by factors such as potency and crush-resistant formulations (13). In a study focused on buprenorphine diversion, researchers found that geographic distribution and socioeconomic factors influenced the pricing and diversion through the black market (14). StreetRx data is cited in several other studies and our aim was to use similar methods to analyze the diversion of stimulants (15).

The purpose of this study was to examine trends in prescription stimulant drug diversion across the U.S. for 2015 to 2019. Previous studies have reported increases in stimulant medication use over recent years (16, 17, 18). We aimed to specifically analyze illicit use and determine if trends mirrored the increase in prescription distribution and ADHD diagnoses in recent years (16, 17, 18). Uncovering patterns of stimulant drug diversion may provide health care providers with insight regarding illicit distribution of commonly prescribed medications in their communities.

Methods

Procedures

A data use agreement between Geisinger Commonwealth School of Medicine and Rocky Mountain Poison and Drug Safety department of the Denver Health and Hospital Authority allowed access to StreetRx.com data reports. Information in the data use agreement included: generic name, drug dosage, and the date and location of submission. Drug data weight was obtained from Street Rx.com for the years 2015 to 2019 in all 50 states for the following drugs: amphetamine, lisdexamfetamine, and methylphenidate. Procedures were approved by the Geisinger Institutional Review Board.

Data analysis

The data set obtained from StreetRx.com was divided into four regions for regional analysis of distribution: Northeast (NE), South (S), West (W), and Midwest (MW). The raw dose in milligrams was totaled for each of the three drugs according to year, state, and region to determine the total quantity in milligrams of amphetamine, lisdexamfetamine and methylphenidate during the years 2015 to 2019. The mass was corrected from population estimates from the U.S. Census Bureau, Population Division for each state and region. Percent changes between each year, 2016 to 2019, were compared to 2015 for each drug. Figures were created using GraphPad Prism to plot the mean diversion distribution with standard error of mean (SEM) for each drug during the years noted. Heat maps were created using JMP Graph Builder to map the percent changes in total distribution of amphetamine, lisdexamfetamine and methylphenidate from 2015-2019.

For each drug, a paired sample t-test was completed comparing the total diversion amount for each year, 2016 to 2019, relative to 2015 values. Note that there was no methylphenidate data available for Louisiana, Montana, and North Dakota for the year 2019. The corresponding t-test paired the remaining states for the analysis, while these three were excluded. Paired sample t-tests were conducted for analysis of statistical significance of annual changes in total mass drug diversion for each region of the U.S. GraphPad Prism was utilized to perform statistical analysis. Variability was depicted as the SEM.

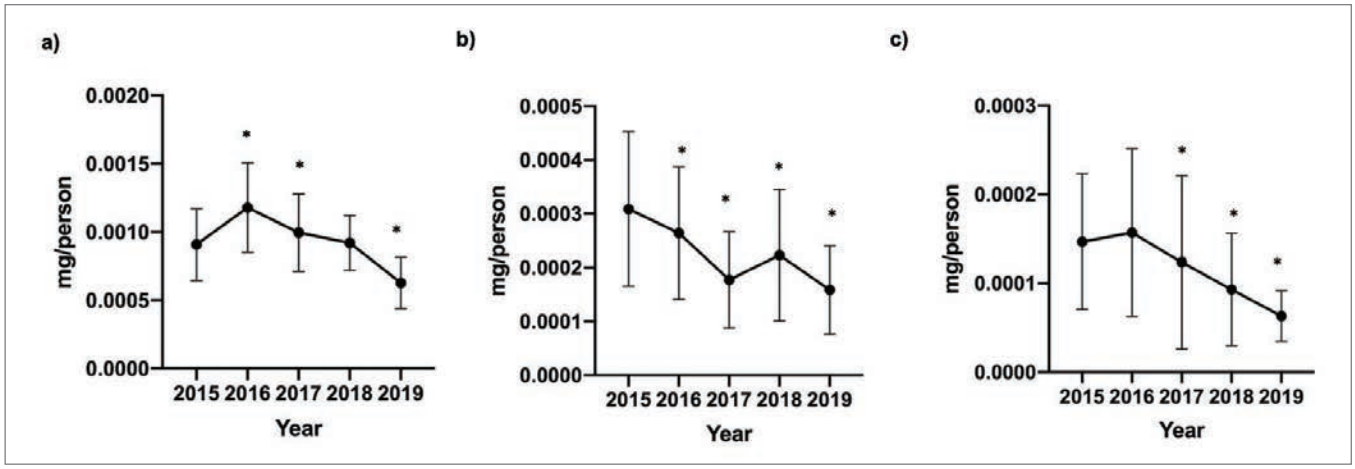

Figure 1. Total diversion in milligrams per person of amphetamine (A), lisdexamfetamine (B), and methylphenidate (C) for all 50 states from 2015 to 2019 as reported by StreetRx and corrected for population.

Results

Total mass diversion distribution

Diverted amphetamine distribution decreased by an average of -31.54% across all 50 states from 2015 to 2019 (Figure 1A). Diverted lisdexamfetamine distribution decreased by an average of -50.97% (Figure 1B). Diverted methylphenidate distribution decreased by an average of -57.03% (Figure 1C). The percent change trends in the NE and S were relatively similar to the total percent changes for lisdexamfetamine and methylphenidate, while the percent changes in NE for amphetamine and the MW and W for all three stimulants were relatively modest. Specific percent change values for each drug according to region are summarized in Table 1. Paired t-tests comparing the total mass of distribution for illicit stimulants showed varying significance through the years 2015 to 2019. For amphetamine, the percent changes showed statistical significance between the years 2015 and 2016, 2017, and 2019, while 2018 did not show a statistically significant change relative to 2015 ($P < 0.05$). For lisdexamfetamine, the percent changes showed statistical significance between all years relative to 2015 ($P < 0.05$). For methylphenidate, the percent changes showed statistical significance between the years 2015 and 2017, 2018, and 2019 with only 2016 showing an insignificant change relative to 2015 ($P < 0.05$). Statistical analysis for total distribution for the three stimulants is summarized in Table 2.

Drug and Region	2015-2016	2015-2017	2015-2018	2015-2019
Amphetamine				
Total	28.4453129	8.198745229	0.737128322	-31.54165813
NE	31.863679	10.739925	9.07858599	-0.557449018
South	27.117521	7.6340232	1.86205719	-36.42499951
MW	-0.01741395	-0.1644597	-1.006049953	-1.351972268
West	-0.415700155	-0.813303709	-7.30561E-08	-1.659781534
Lisdexamfetamine				
Total	-14.88263178	-45.73224181	-31.13649708	-50.97419456
NE	-19.66623644	-35.91231259	-33.30168268	-59.29691055
South	-16.23468413	-35.27792792	-25.77770481	-54.19633153
MW	-0.10155561	-0.20836658	-1.03630734	-1.29574174
West	-0.45542736	-0.833224182	-1.345503073	-1.631178517
Methylphenidate				
Total	3.06501973	-25.40854204	-36.07713342	-57.0329104
NE	4.663978405	-20.20863043	-40.21391058	-56.20222024
South	7.330996953	-29.1013914	-42.04674584	-58.21407168
MW	-0.0901446	-0.2008862	-1.0391369	-1.2915368
West	-0.449951851	-0.829631965	-1.346760752	-1.629102703

Table 1. Total and regional percent change values relative to 2015

Drug Name	Years Compared	95% Confidence Interval	Mean of Differences	P-Value	Significance (Yes/No)
Amphetamine	2015 vs 2016	0.0002261 to 0.0003161	0.0002711	<0.0001	Yes
	2015 vs 2017	3.967e-005 to 0.0001328	8.625e-005	0.0005	Yes
	2015 vs 2018	-2.746e-005 to 5.136e-005	1.195e-005	0.5452	No
	2015 vs 2019	-0.0003327 to -0.0002310	-0.0002818	<0.0001	Yes
Lisdexamfetamine	2015 vs 2016	-7.022e-005 to -1.904e-005	-4.463e-005	0.0010	Yes
	2015 vs 2017	-0.0001709 to -9.261e-005	-0.0001318	<0.0001	Yes
	2015 vs 2018	-0.0001167 to -5.529e-005	-8.598e-005	<0.0001	Yes
	2015 vs 2019	-0.0001860 to -0.0001148	-0.0001504	<0.0001	Yes
Methylphenidate	2015 vs 2016	-1.002e-005 to 3.005e-005	1.001e-005	0.3201	No
	2015 vs 2017	-4.253e-005 to -4.331e-006	-2.343e-005	0.0172	Yes
	2015 vs 2018	-6.999e-005 to -3.809e-005	-5.404e-005	<0.0001	Yes
	2015 vs 2019	-0.0001013 to -6.431e-005	-8.279e-005	<0.0001	Yes

Table 2. T-test results comparing StreetRx total diversion between years

Regional differences in drug diversion

Average mass per population for each year was plotted to show regional differences in non-medical prescription stimulant reporting (Figure 2). Heat maps of 2015 to 2019 percent changes showed varying degrees of both positive and negative percent changes by state (Figures 3-5). Paired t-tests comparing the regional data showed no statistical significance among intraregional averages for any year relative to 2015 ($P < 0.05$).

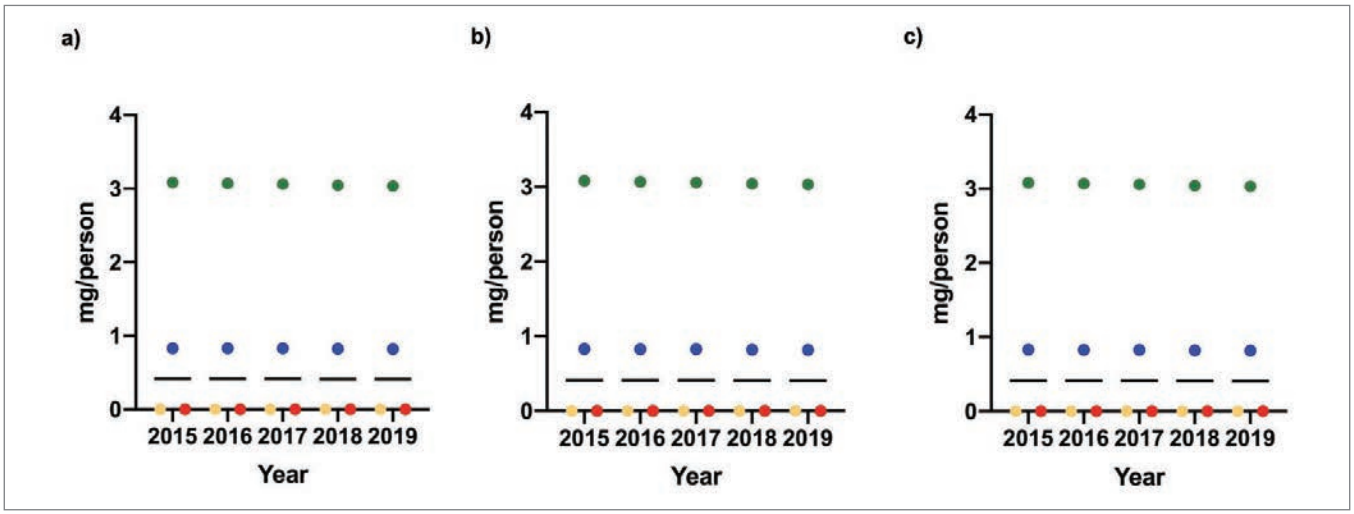

Figure 2. Average values in milligrams per person of amphetamine (A), lisdexamfetamine (B), and methylphenidate (C) by region from 2015 to 2019 as reported by StreetRx and corrected for population. Green represents W, blue represents MW, red represents S, and yellow represents NE.

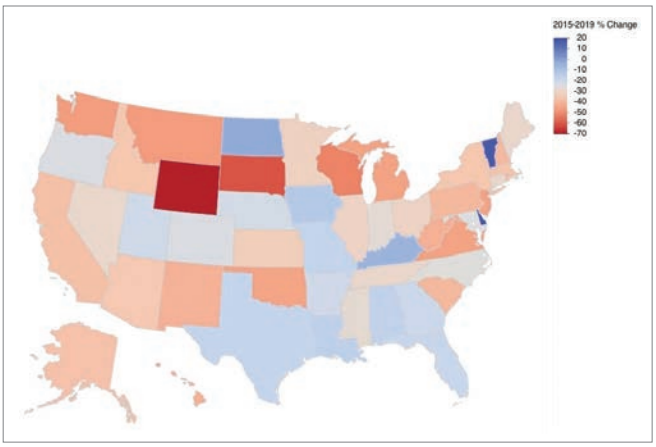

Figure 3. 2015 to 2019 percent changes in amphetamine distribution for 2015 to 2019. The total grams of amphetamine diversion as reported by StreetRx has been corrected for population.

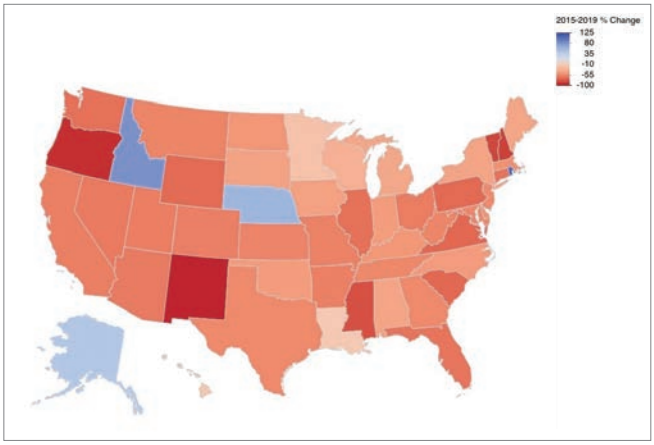

Figure 4. 2015 to 2019 percent changes in lisdexamfetamine distribution for 2015 to 2019. The total grams of lisdexamfetamine diversion as reported by StreetRx has been corrected for population.

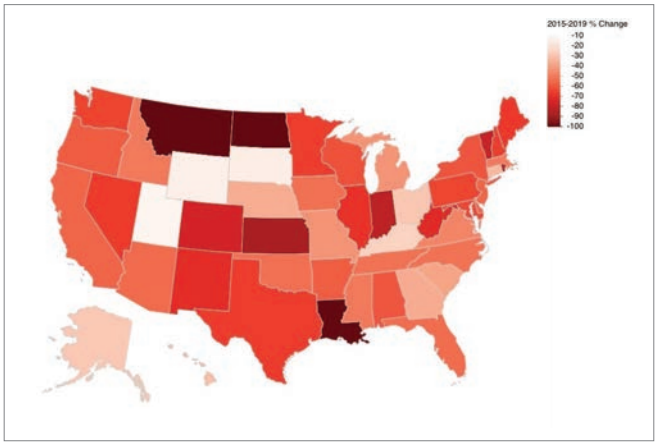

Figure 5. 2015 to 2019 percent changes in methylphenidate distribution for 2015 to 2019. The total grams of methylphenidate diversion as reported by StreetRx has been corrected for population.

Discussion

Across all 50 states, reported diversion by StreetRx.com of all three stimulants decreased. Amphetamine reporting by raw number comprised greater than half of total submissions. The average mass per population for each year was significantly higher in the W and MW than in the NE and S regions, with the W showing the greatest value. The differences within each region by year were not statistically significant and are very modest compared to the interregional differences. While the overall percent changes for each drug from 2015 to 2019 were negative, some states showed positive percent changes from 2015 to 2019 for amphetamine and lisdexamfetamine, while all states showed negative percent changes from 2015 to 2019 for methylphenidate. The West is thus an interesting area of study in terms of stimulant drug distribution, both prescription and illicit (17).

Hypothesized etiologies of these patterns can be summarized in three broad categories: drug characteristics, misuser characteristics, and regional health care characteristics. First, drug characteristics may include differences in efficacy, abuse potential, and availability of certain stimulants. For example, lisdexamfetamine may carry a lower abuse potential than other stimulants due to certain pharmacodynamic and route of administration parameters (19, 20). This could lead to decreasing misuse of this particular stimulant across the U.S. Second, misuser characteristics may include varying popularity of stimulants, pricing preferences, and demographics of misusers. For example, research shows that white college-aged students that self-report symptoms of ADHD are more likely to abuse stimulants, often to improve concentration or alertness (21). Additionally, misusers may prefer amphetamine over other stimulants due to perceived higher efficacy, greater availability, and higher rates of prescribing, leading to overall higher reporting of misuse (22). Third, regional healthcare factors may include differences in ADHD diagnoses, prescriber preferences, and number of prescribers per population. For instance, the median number of psychiatrists in the U.S. has continued to decline in recent years (23). There are pronounced differences in the availability of psychiatrists and mental health resources in certain areas of the U.S, particularly poverty-stricken rural areas (24). This could lead to differences in absolute distribution, as well as perceived need to obtain illicit substances if patients cannot access proper health care.

As research moves forward, delineating the data into specific states and cities of interest may further elucidate potential etiologies. Focusing on Pennsylvania as an example, approximately 65% of the StreetRx.com entries included the city of purchase. From these, approximately 32.7% of the self-reported purchases were made in Philadelphia, 16.1% in Pittsburgh, and 3.4% in the Scranton/Wilkes-Barre area. It is noteworthy that Philadelphia makes up roughly 12.4% of Pennsylvania's population, yet almost one-third of data points collected were from Philadelphia. Moving forward, this type of analysis could identify particular cities and counties that could benefit from community level interventions.

Understanding illicit drug use patterns is important to community health, specifically during times of global crisis. While it is difficult to fully capture trends in illicit drugs as compared to legal use, analysis is still necessary. Some of the

trends found in illicit stimulant use in this study can potentially be explained by the trends in prescription stimulant use. Elucidating socioeconomic factors that contribute to regional variations in stimulant misuse will require further investigation.

Limitations

An important limitation to note in our study is the data obtained from StreetRx.com is dependent on user submissions, therefore our study is not able to represent a complete understanding of all illicit drug use and distribution. Since submissions were self-reported, there is the potential for individuals to input information inaccurately and inconsistently. There is also the possibility that individuals did not want to self-report illicit drug use due to fear of self-incrimination or negative societal views. Furthermore, socioeconomic factors such as a lack of access to the internet could lessen use of the platform in some communities. Lack of awareness of the platform's existence may also influence data, potentially influencing regional differences in reporting. This limitation can be diminished by correlating trends found in this study to other databases and resources. This research team and others analyzed pharmacoepidemiological trends in both prescription and illicit stimulant distribution of these drugs in the U.S. over similar time periods. The prescription data can be obtained from the Automation of Reports and Consolidated Orders System (ARCOS) retail drug summary reports (16). Future efforts to analyze potential correlations or differences among studies and databases may potentially solidify regional and nationwide patterns.

Conclusion

Over the past 5 years, reported diversion by StreetRx.com of stimulants on the illicit market has declined. Diversion in the W of the U.S. is higher than other regions. We hypothesized that trends in stimulant misuse would mirror trends in stimulant prescription distribution, yet this relationship was not found for every drug, year, and region. Potential contributing factors to explain these trends include differences in drug, user, and regional health care characteristics.

While states have some commonalities in regulations regarding controlled substances such as stimulants, the specific guidelines of each state may vary. Additionally, existing individual state and community-level programs may influence the use and distribution of stimulants in different regions. It is important to analyze data surrounding the efficacy of intervention and treatment programs in decreasing illicit stimulant use and distribution in order help future policymakers address the issue and allocate appropriate funding. Future research will focus on these state and community-level programs to further characterize regional trends.

Future research exploring the trends of drug diversion through StreetRx.com may unveil additional patterns. Although our study looked at stimulant drug distribution including amphetamine, lisdexamfetamine and methylphenidate, broadening the Date Use Agreement to receive data on all drugs reported to StreetRx.com would allow for comparison of stimulant drug diversion to other drug classes, such as opioids and benzodiazepines.

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Disclosures

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