Trends and Risk Factors for Overlapping Stimulant and Opioid Prescriptions — Rhode Island, April 1, 2016–March 31, 2020

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ABSTRACT

OBJECTIVE: To investigate possible trends and risk factors for overlapping stimulant and opioid prescriptions in Rhode Island (RI).

METHODS: All RI residents with a stimulant prescription dispensed between April 1, 2016 and March 31, 2020 were obtained from the RI Prescription Drug Monitoring Program (PDMP). Individuals were stratified by overlapping stimulant/opioid exposure and compared by demographic and prescription characteristics.

RESULTS: While stimulant prescribing remained relatively constant, the percent of individuals with an overlapping opioid prescription declined. Individuals prescribed overlapping stimulant/opioid prescriptions differed significantly as a function of age, sex, payment method, type of stimulant prescribed, and prescriber type.

CONCLUSIONS: Among residents who were dispensed at least one stimulant prescription, individuals who were older, female, and on Medicare insurance were more likely to have an overlapping stimulant/opioid prescription. The RI PDMP can be used to identify trends and risk factors regarding prescribing patterns, which can inform future health policy and practice.

KEYWORDS: stimulant, opioid, prescription drugs, Rhode Island

INTRODUCTION

Although often overshadowed by the highly studied and publicized opioid overdose epidemic, the misuse of prescription and illicit stimulants remains a significant public health concern. Previous analyses of various drug databases and surveys have shown that prescription stimulant use doubled between 2006 and 2016,[1] with 6.8% of U.S. adults reporting prescription stimulant use in 2016.[2] Stimulants, as with other controlled substances, demonstrate a propensity for off-prescription misuse. This is particularly prevalent in school and college-age populations,[3] which in turn can be a risk factor for subsequent illicit drug use including stimulants and opioids.[4]

Recent studies have highlighted the prevalence and risk surrounding polysubstance use, particularly between opioids and stimulants, whether purposeful ("speedballing") or inadvertent (fentanyl-contaminated substances).[5-6] Hospitalization involving both opioid and amphetamine use increased by over 500% between 2003 and 2015.[7] National drug overdose death data from 2016 showed that approximately half of overdose deaths from psychostimulants with abuse potential also involved opioids[8] and about a quarter of synthetic opioid overdose deaths involved stimulant drugs including cocaine and other psychostimulants.[9]

Acknowledging the rise of polysubstance use and its associated risks, an analysis of the Rhode Island Prescription Drug Monitoring Program (PDMP) database was conducted to investigate possible trends and risk factors related to overlapping stimulant and opioid prescriptions.

METHODS

We conducted a retrospective cohort study utilizing data from the Rhode Island PDMP. All individuals who were Rhode Island residents with a stimulant prescription dispensed between April 1, 2016 and March 31, 2020 were included in our cohort.

We identified stimulant prescriptions using the American Hospital Formulary Service Pharmacologic–Therapeutic Classification Code (TCC) 28:20 associated with the National Drug Code of each medication in the IBM Micromedex RED BOOK. To identify opioid prescriptions, we included all opiate agonists (TCC 28:08.08), opiate partial agonists (TCC 28:08.12), and tramadol products (TCC 28:08.92.00.50). Buprenorphine products that were only FDA-approved for medication-assisted treatment for opioid use disorder as of July 30, 2020 were excluded from this analysis. An overlapping stimulant/opioid prescription was defined as any stimulant prescription that overlapped with an opioid prescription for at least 1 day. If an individual in either group had been dispensed multiple prescriptions, we randomly selected one for inclusion in the analysis to maintain independence of observations.

Individuals who received an overlapping stimulant/opioid prescription were compared to individuals who never received an overlapping prescription by demographic and prescription characteristics and compared with chi-square tests. Continuous variables (total number of stimulant

prescriptions dispensed during the study period and number of overlapping stimulant/opioid prescriptions dispensed) were compared using the Mann-Whitney U test.

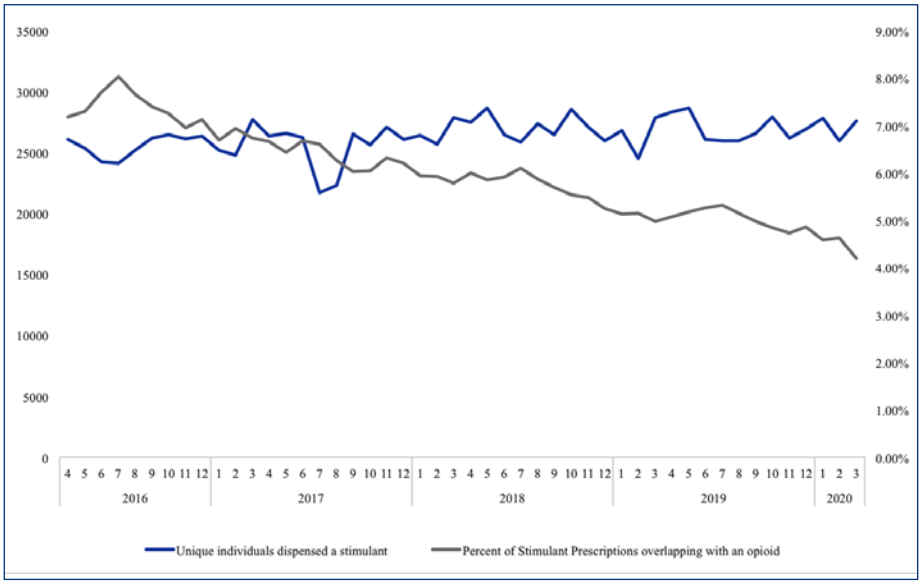
This study was part of RIDOH's response to the opioid overdose epidemic in Rhode Island and did not require institutional review board approval. All analyses were conducted in SAS 9.4 (Cary, North Carolina).

RESULTS

From April 1, 2016–March 31, 2020, 1,557,849 stimulant prescriptions were dispensed to 79,737 unique Rhode Island residents, with 15,073 individuals dispensed at least one overlapping stimulant and opioid prescription (18.9%). While the number of unique individuals dispensed stimulant prescriptions each per month remained relatively constant over the study period (April 2016: 26,064; March 2020: 27,596), the percent of individuals with an overlapping opioid prescription declined over the study period from 7.18% of stimulant prescriptions dispensed in April of 2016 to 4.19% of stimulant prescriptions dispensed in March of 2020 (**Figure 1**). As illustrated in **Table 1**, the prevalence of individuals ever prescribed stimulants who also ever received an overlapping stimulant/opioid prescription differed significantly as a function of multiple factors including age, sex, payment method, type of stimulant prescribed, and prescriber type (all $p < 0.0001$).

When looking at demographic factors, the proportion of stimulant-prescribed patients who received overlapping stimulant/opioid prescriptions increased significantly as age increased, ranging from approximately 4.1% amongst those in the age 0–18 year bracket to 39.1% in the age 65+ bracket. Furthermore, while the percent of individuals dispensed an overlapping opioid and stimulant prescription declined over time, this stratification pattern remained consistent across the entire study period. Females had a higher rate of overlapping prescriptions (22.5% compared to 14.6% in males), which also remained consistent from April 2016 through March 2020. The proportion of overlapping prescription varied by payment type, ranging from 16.5% (Medicaid payments) to 43% (Medicare payments). Additionally, while the median number of stimulant prescriptions dispensed was 12 (inter-quartile range (IQR): 4-30), this was substantially higher among individuals who received at least one overlapping stimulant/opioid prescription (median: 28; IQR: 13–44), when compared to individuals who never received an overlapping stimulant/opioid prescription (median: 9; IQR: 3–25).

Figure 1. The number of unique RI Residents dispensed an opioid, and the percent of stimulant prescriptions overlapping for at least 1 day with an opioid prescription, April 1, 2016–March 31, 2020.



DISCUSSION

While the number of stimulant prescriptions dispensed per month has remained relatively constant in Rhode Island during the study period, the percent of prescriptions dispensed with an overlapping opioid prescription has declined from 2016–2020. Overall, among Rhode Island residents who were dispensed at least one stimulant prescription, individuals who were older, female, and on Medicare insurance were more likely to have an overlapping stimulant/opioid prescription.

Although the proportion of stimulant prescriptions generally decreased as age increased, complimenting patterns found from nationwide data[2], the highest proportion of overlapping stimulant/opioid prescription were found in the oldest age group, with rates nearly 10 times that of the youngest age group. This is interesting when paired with the results showing Medicare as the payer group with the highest proportion of overlapping prescriptions, prompting future investigation into the prevalence of polysubstance prescriptions under Medicare.

Rhode Island is currently experiencing an increase in accidental fatal opioid overdoses that involve stimulants; however, the risk factors for a fatal overdose (younger, male) appear to differ from the risk factors for overlapping opioid/stimulant prescriptions (older, female) which is promising.[10] However, a sizable portion of younger/male individuals were prescribed overlapping stimulant/opioid prescriptions in this cohort, and future work will look to identify previous co-prescription exposure among individuals who died of an accidental stimulant/opioid overdose. Such analyses, in turn, could inform future public health policy and intervention efforts, including reducing exposure to potentially harmful drug combinations.

Table 1. Characteristics of Rhode Island Residents Dispensed Overlapping Stimulants compared to those dispensed overlapping Stimulants and Opioid Prescriptions, April 1, 2016–March 31, 2020*

	Ever Prescribed Stimulants	Ever Prescribed Overlapping Stimulants & Opioids		
		Yes	No	
Characteristic	**N=79,737 n (%)†**	**N=15,073 n (%)†**	**N=64,664 n (%)†**	**P-value†**
Patient				
Age				
0–18	20,915 (26.2)	853 (5.7)	20,062 (31.0)	<0.0001
18–24	10,406 (13.0)	1,317 (8.7)	9,089 (14.1)	
25–34	15,271 (19.2)	2,857 (19.0)	12,414 (19.2)	
35–44	12,365 (15.5)	3,202 (21.2)	9,163 (14.2)	
45–54	10,473 (13.1)	3,161 (21.0)	7,312 (11.3)	
55–64	6,918 (8.7)	2,358 (15.6)	4,560 (7.0)	
65+	3,389 (4.2)	1,325 (8.8)	2,064 (3.2)	
Sex				
Female	43,817 (55.0)	9,838 (65.3)	33,979 (55.6)	<0.0001
Male	35,913 (45.0)	5,234 (34.7)	30,679 (47.4)	
Unknown	7 (0.0)	<5	6 (0.0)	
Payment method				
Private insurance	53,118 (66.6)	9,689 (64.3)	43,429 (67.2)	<0.0001
Medicaid	13,787 (17.3)	2,272 (15.1)	11,515 (17.8)	
Medicare	3,205 (4.0)	1,379 (9.2)	1,826 (2.8)	
Cash	8,968 (11.2)	1,538 (10.2)	7,430 (11.5)	
Military	445 (0.6)	110 (0.7)	335 (0.5)	
Workers' compensation	12 (0.0)	5 (0.0)	7 (0.0)	
Unknown	202 (0.2)	80 (0.5)	122 (0.2)	
Prescription				
Stimulant type				
Amphetamine & Comb.	38,791 (46.6)	8,904 (59.1)	29,887 (46.2)	<0.0001
Armodafinil	472 (0.6)	153 (1.0)	319 (0.5)	
Benzphetamine	<5	<5	<5	
Dexmethylphenidate	2,494 (3.1)	181 (1.2)	2,313 (3.6)	
Dextroamphetamine	1,358 (1.7)	333 (2.2)	1,025 (1.6)	
Diethylpropion	49 (0.1)	10 (0.1)	39 (0.1)	
Lisdexamfetamine	6,390 (8.0)	1,125 (7.5)	5,265 (8.1)	
Methamphetamine	5 (0.1)	<5	<5	
Methylphenidate	16,511 (20.7)	2,050 (13.6)	14,461 (22.4)	
Modafinil	1,088 (1.4)	340 (2.3)	748 (1.2)	
Phendimetrazine	1,529 (1.9)	175 (1.2)	1,354 (2.1)	
Phentermine & Comb.	11,035 (13.8)	1,796 (11.9)	9,239 (14.3)	
Solriamfetol	13 (0.0)	<5	10 (0.0)	
Prescriber Type				
Physician	53,319 (66.9)	9,500 (63.0)	43,819 (67.8)	<0.0001
PA	2,355 (3.0)	546 (3.6)	1,809 (2.8)	
Adv Nurse	12,747 (16.0)	2,821 (18.7)	9,926 (15.4)	
Unknown	11,316 (14.2)	2,206 (14.6)	9,107 (14.1)	
Medication Info				
Total number of stimulant prescriptions‡	12 (4, 30)	28 (13,44)	9 (3,25)	<0.0001
Number of overlapping prescriptions‡	2 (1, 4)	2 (1, 4)	—	—
Quantity prescribed‡	30 (30, 60)	30 (30, 60)	30 (30, 56)	<0.0001
Stimulant supply(days)‡	30 (30, 30)	30 (30, 30)	30 (30, 30)	<0.0001

*For patients with >1 overlapping stimulant opioid prescription or >1 stimulant prescription, we randomly selected one for inclusion in this analysis. † Unless otherwise specified. ‡ Median (IQR). § This analysis excluded buprenorphine products only FDA-approved for medication assisted treatment of opioid use disorder.

Additionally, as of January of 2020, Rhode Island required International Classification of Disease (ICD-10) codes for every controlled substance prescription. Leveraging this diagnostic information will allow future investigation into why individuals may be co-prescribed specific drug combinations, and these insights could be translated into a safer and more gestalt prescribing framework.

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Ethics Statement

This study was part of RIDOH's response to the opioid overdose epidemic in Rhode Island and did not require institutional review board approval. This analysis is limited to prescriptions dispensed vs. prescribed, and overlap was assumed based on the dispensed date and day supply, which may inaccurately represent prescribing practices. All authors approve this work, and we have no conflicts of interest to disclose.

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Disclaimer

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