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Benzodiazepine and stimulant prescriptions prior to overdose in youth

Greta Bushnell, PhD, MSPH^{a,b}, Hillary Samples, PhD, MHS^{b,c}, Tobias Gerhard, BSPHarm, PhD^{a,b,d}, Diane P. Calello, MD^e, Mark Olfson, MD, MPH^f

^aCenter for Pharmacoepidemiology and Treatment Sciences, Rutgers Institute for Health, Health Care Policy and Aging Research

^bRutgers University School of Public Health

^cCenter for Health Services Research, Rutgers Institute for Health, Health Care Policy and Aging Research

^dErnest Mario School of Pharmacy, Rutgers University

^eRutgers New Jersey Medical School

^fColumbia University Irving Medical Center, New York State Psychiatric Institute

INTRODUCTION.

In 2019, 4,777 youth died from a drug overdose in the US.¹ Seven-hundred and twenty-seven youth died from overdoses involving benzodiazepines (BZD) and 902 from overdoses involving psychostimulants.² Opioid-related overdose deaths frequently involve other substances, in youth, stimulants and BZDs are the most commonly involved substances.³ Overdoses can involve prescription drugs accessed through medical prescriptions or through illicit means. Among persons aged 18–25 years, 5.8% report past-year prescription stimulant misuse and 3.8% prescription BZD misuse.⁴

To inform overdose prevention efforts, we determined how often youth with medically treated overdoses involving BZDs and stimulants had recent BZD or stimulant prescriptions.

Corresponding author. Greta A. Bushnell, PhD, Assistant Professor, Center for Pharmacoepidemiology and Treatment Sciences, Rutgers Institute for Health, Health Care Policy and Aging Research, 112 Paterson St., Office 422, New Brunswick, NJ 08901, Phone: 484.883.5985, greta.bushnell@rutgers.edu.

Contributors' Statement Page.

Dr. Bushnell made substantial contributions to the conception and design, analysis, and interpretation of data, drafted the initial manuscript, and revised the manuscript.

Drs. Samples, Calello, Gerhard, and Olfson made substantial contributions to the design and interpretation of data and critically revised and reviewed the manuscript for important intellectual content.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Article Summary. Within a commercial claims database, this study identified how frequently youth with an overdose involving BZDs or stimulants had a recent BZD or stimulant prescription.

METHODS.

We included youth (15–24 years) from the MarketScan commercial claims database with an overdose involving stimulants or BZDs (1/1/2016–12/31/2018). MarketScan covers privately insured individuals and captures diagnoses and procedures from inpatient/outpatient visits and dispensed prescriptions.⁵ Overdose events treated in an emergency department (ED) or inpatient setting were included, defined as an ICD-10-CM code for an unintentional, intentional, or undetermined poisoning initial encounter (Table). Stimulant overdoses were limited to overdoses involving amphetamine or methylphenidate. We selected the first overdose per person and required 6 months of insurance enrollment with prescription coverage prior to the overdose.

In the 6 months prior to the overdose, we identified dispensed BZD and stimulant prescriptions and mental health diagnoses (Table). We summed the number of fills and days supply for prescriptions dispensed in the 6 months prior to the overdose. Results were stratified by intentional self-harm vs. unintentional overdoses. In a secondary analysis, class of prescription stimulant was considered with whether the overdose involved amphetamine or methylphenidate.

RESULTS.

We identified 2,986 youth with an overdose involving BZDs and 971 youth with an overdose involving stimulants (amphetamine/methylphenidate). The majority of youth had a prior mental health diagnosis; 56% of overdoses involving BZDs were intentional compared to 40% of overdoses involving stimulants (Table).

Twenty-nine percent of youth with overdoses involving BZDs had a prescription BZD dispensed in the prior 30 days and 42% in the prior 6 months (Table, Figure). Among youth with a BZD prescription in the prior 6 months, 33% received >90 days supply and 73% had an anxiety disorder diagnosis (eTable). Youth with intentional BZD overdoses were more likely to have a recent BZD prescription (51%) than unintentional overdoses (30%).

A quarter of youth with an overdose involving stimulants (amphetamine/methylphenidate) had a stimulant prescription dispensed in the prior 30 days and 39% in the prior 6 months (Table, Figure). Among youth with a stimulant prescription in the prior 6 months, 56% received >90 days supply and 71% had an ADHD diagnosis (eTable). Youth with intentional stimulant overdoses were more likely to have a recent stimulant prescription (56%) than unintentional overdoses (28%).

DISCUSSION.

A considerable fraction of youth with overdoses involving BZDs and stimulants had recent prescriptions for these drugs. Prior BZD and stimulant prescriptions were more common in youth with intentional overdoses. This underscores the importance of incorporating self-injury assessment into clinical practice for youth prescribed BZDs and stimulants and highlights the need for differing prevention efforts for intentional and unintentional youth overdoses.

The majority of youth with a BZD or stimulant prescription prior to overdose had a mental health diagnosis. These medications are prescribed for mental health problems common in youth^{6,7} and can be effective treatments. However, as these drugs are commonly misused⁴ and involved in overdoses, weighing risks and benefits at prescribing remains imperative.

Primary considerations of this research include that we cannot distinguish amphetamine overdoses related to prescription amphetamine vs. an illicit substance. We miss overdoses that did not present to the ED or hospital, including fatal overdoses occurring outside these settings, and events in which BZD or stimulant involvement was not recorded. Without comparator groups, we are unable to assess comparative overdose liability by prescription characteristics.

Given that a fourth of youth with overdoses involving these drugs have prescriptions for them in the prior month, results suggest an avenue of prevention and motivate future work examining overdose risk following prescription. Because the potential for harm with BZD and stimulants increases with selected combinations of prescription medications, alcohol, and illicit drugs, especially concurrent BZD and opioid use;^{8,9} these concerns warrant attention and discussion at prescription initiation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations.

BZD	benzodiazepine
ED	emergency department
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
ICD-10-CM	International Classification of Diseases, Tenth Revision, Clinical Modification

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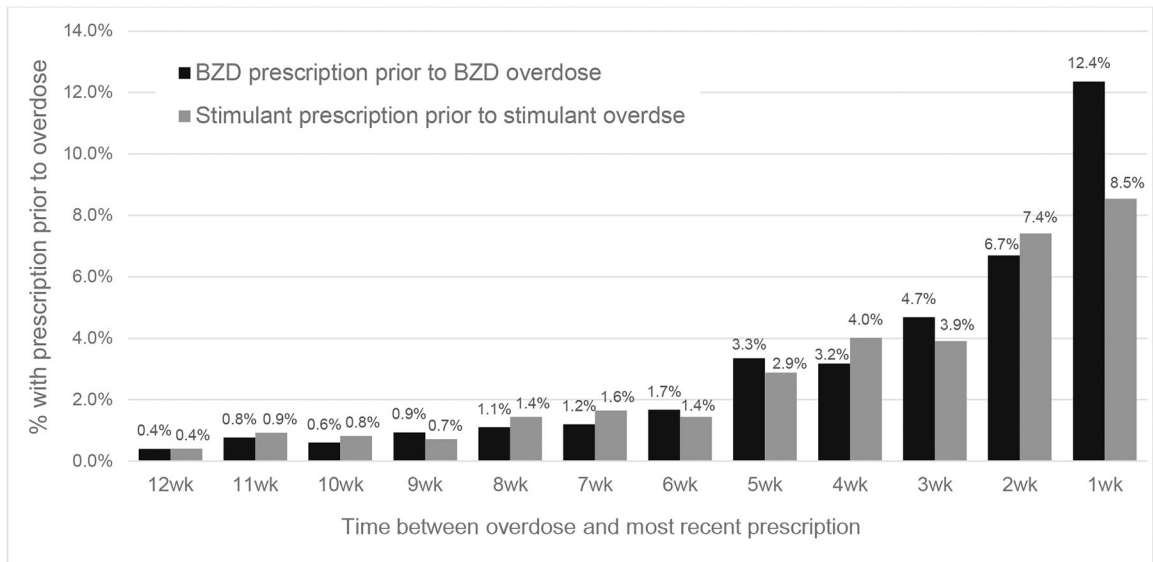


Figure.

Proportion of youth (15–24 years) with a prescription fill* prior to an overdose involving a benzodiazepine or stimulant by time between prescription and overdose

BZD: Benzodiazepine; wk: week

*Percent with BZD prescription prior to an overdose involving a BZD; Percent with stimulant prescription prior to an overdose involving amphetamine or methylphenidate

Table.

Prior prescriptions in youth (15–24 years) with a medically-treated overdose involving a BZD or stimulant, 2016–2018^{a,b}

Overdoses involving BZDs	N=2,986	Intent of overdoses involving BZDs ^f		p-value
		Intentional N=1,664	Unintentional N=1,160	
Age at overdose, Median (IQR)	20 (17–22)	20 (18–22)	20 (18–22)	
Female	1,556 (52.1%)	1,045 (62.8%)	447 (38.5%)	<0.001
Mental health diagnosis in prior 6 months ^c	2,232 (74.7)	1,300 (78.1)	813 (70.1)	<0.001
Prior BZD prescription ^d				
0–1 month	854 (28.6%)	590 (35.5%)	234 (20.2%)	<0.001
0–6 months	1,243 (41.6%)	850 (51.1%)	348 (30.0%)	<0.001
Days from overdose to most recent prescription, Median (IQR)	16 (5–39)	16 (5–37)	15 (4–40)	
Subset with BZD prescription(s) in prior 6 months	N=1,243	N=850	N=348	
Number of BZD fills, Median (IQR)	3 (1–5)	2 (1–4)	3 (1–5)	
>3 fills dispensed	470 (37.8%)	300 (35.3%)	156 (44.8%)	0.002
Total BZD days supplied, Median (IQR)	60 (30–120)	60 (30–120)	73 (30–136)	
>90 days dispensed	413 (33.2%)	267 (31.4%)	134 (38.5%)	0.018
Mental health diagnosis in prior 6 months ^c	1,153 (92.8)	785 (92.4)	324 (93.1)	0.653
Overdoses involving stimulants (amphetamine or methylphenidate)	N=971	Intent of overdoses involving stimulants ^f		p-value
		Intentional N=388	Unintentional N=524	
Age at overdose, Median (IQR)	19 (17–22)	18 (16–20)	20 (18–22)	
Female	415 (42.7%)	213 (54.9%)	179 (34.2%)	<0.001
Mental health diagnosis in prior 6 months	634 (65.3)	299 (77.1)	299 (57.1)	<0.001
Prior stimulant prescription ^e				
0–1 month	239 (24.6%)	137 (35.3%)	93 (17.7%)	<0.001
0–6 months	380 (39.1%) ^g	219 (56.4%)	147 (28.1%)	<0.001
Days from overdose to most recent prescription, Median (IQR)	20 (8–47)	21 (9–47)	14 (5–46)	
Subset with stimulant prescription in prior 6 months	N=380	N=219	N=147	
Number of stimulant fills, Median (IQR)	4 (2–5)	3 (2–5)	4 (2–6)	
>3 fills dispensed	191 (50.3%)	102 (46.6%)	83 (56.5%)	0.064
Total stimulant days supplied, Median (IQR)	120 (60–180)	117 (60–150)	120 (90–180)	
>90 days dispensed	213 (56.1%)	112 (51.1%)	95 (64.6%)	0.011
Mental health diagnosis in prior 6 months	335 (88.2)	199 (90.9)	123 (83.7)	0.038

BZD: Benzodiazepine; IQR: Interquartile range

^aICD-10-CM overdose definitions: Overdose involving BZD: T42.4X1A, T42.4X2A, T42.4X4A; Overdose involving stimulant: amphetamine (T43.621A, T43.622A, T43.624A) and methylphenidate (T43.631A, T43.632A, T43.634A)

^bPrior prescriptions identified through records of dispensed prescriptions before overdose event. **BZDs**: alprazolam, chlordiazepoxide, clobazam, clonazepam, clorazepate, diazepam, estazolam, flurazepam, lorazepam, midazolam, oxazepam, quazepam, temazepam, triazolam;

Stimulants: Amphetamines (amphetamine, dextroamphetamine, lisdexamfetamine, methamphetamine) and methylphenidates (methylphenidate, dexmethylphenidate)

^c Mental health diagnoses identified in 6months prior to overdose event (excluding date of overdose event): ICD-9-CM: 290–319; ICD-10-CM: F01-F99; See supplement for specific diagnoses

^d Prescription anytime in prior 0–12months: Overall: 1,380 (46.2%), intentional: 923 (55.5%), unintentional: 407 (35.1%)

^e Prescription anytime in prior 0–12months: Overall: 416 (42.8%), intentional: 238 (61.3%), unintentional: 162 (30.9%)

^f Undetermined overdose events not displayed (BZD: N=162, stimulant: N=59); if multiple overdose codes were recorded with differing intents (intentional, unintentional, undetermined), precedence in classification was given to intentional then unintentional

^g Overdose by type: Overdose involving amphetamine (n=833), 31.8% have amphetamine prescription in prior 6mo; Overdose involving methylphenidate (n=146), 64.4% have methylphenidate prescription in prior 6mo