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Prevalence and correlates of benzodiazepine use and misuse among young adults who use prescription opioids non-medically

Benjamin A. Bouvier^a, Katherine M. Waye^a, Beth Elston^a, Scott E. Hadland^{b,c}, Traci C. Green^{a,d,e}, and Brandon D.L. Marshall^a

^aDepartment of Epidemiology, Brown University School of Public Health, 121 South Main Street, Box G-S-121-2, Providence, RI, 02912, USA

^bBoston Medical Center, Department of Pediatrics, 850 Harrison Avenue, Boston, MA, 02118

^cBoston University School of Medicine, Department of Pediatrics, Division of General Pediatrics, 88 East Newton Street, Vose Hall Room 322, Boston, MA, 02118

^dBoston Medical Center Injury Prevention Center and Boston University School of Medicine, Department of Emergency Medicine, 771 Albany Street, Room 1332, Boston, MA, 02118, USA

^eThe Warren Alpert School of Medicine of Brown University, Rhode Island Hospital, 55 Claverick Street, Providence, RI 02903, USA

Abstract

Background—Benzodiazepine use dramatically increases the risk of unintentional overdose among people who use opioids non-medically. However, little is known about the patterns of co-occurring benzodiazepine and opioid use among young adults in the United States.

Methods—The Rhode Island Young Adult Prescription Drug Study (RAPiDS) was a cross-sectional study from January 2015—February 2016. RAPiDS recruited 200 young adults aged 18–29 who reported past 30-day non-medical prescription opioid (NMPO) use. Using Wilcoxon rank sum test and Fisher’s exact test, we examined correlates associated with regular prescribed and non-medical use (defined as at least monthly) of benzodiazepines among NMPO users in Rhode Island.

Correspondence: Brandon DL Marshall, PhD, Associate Professor, Department of Epidemiology, Brown University School of Public Health, 121 South Main Street, Box G-S-121-2, Providence, RI, 02912, Telephone: 401-863-6427, Fax: 401-863-317, brandon_marshall@brown.edu.

Contributors

BAB helped conduct surveys, planned the statistical analyses, drafted the manuscript, and approved the final manuscript for submission. KMW helped draft the manuscript and approved the final manuscript for submission. BE conducted statistical analyses, and approved the final manuscript for submission. SEH, TCG, and BDLM conceived the RAPiDS study, advised on the analyses, and approved the final manuscript for submission. BDLM was the primary supervisor

Conflict of Interest

No conflict declared.

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Results—Among participants, 171 (85.5%) reported lifetime benzodiazepine use and 125 (62.5%) reported regular benzodiazepine use. Nearly all (n=121, 96.8%) reported non-medical use and 43 (34.4%) reported prescribed use. Compared to the 75 participants who did not regularly use benzodiazepines, participants who reported regular use were more likely to be white (66.3% vs. 58.0%, $p=0.03$), have ever been incarcerated (52.8% vs. 37.3%, $p=0.04$) and been diagnosed with a mood disorder (bipolar: 29.6% vs. 16.0%, $p=.04$; anxiety: 56.8 vs. 36.0%, $p=0.01$). Although the association was marginally significant, accidental overdose was higher among those who were prescribed the benzodiazepine they used most frequently compared to those who were not (41.9% vs. 24.4%, $p=.06$).

Conclusion—Benzodiazepine use and misuse are highly prevalent among young adult NMPO users. Harm reduction and prevention programs for this population are urgently needed.

Keywords

adolescent health; comorbidity; drugs; mental health; prescription drug abuse

1.0 Introduction

Benzodiazepines are a class of psychoactive drugs used for their sedative, muscle relaxant, anticonvulsant, and anxiolytic properties to treat a range of conditions (Olkkola and Ahonen, 2008; Page et al., 2002). Benzodiazepines are most often prescribed for anxiety or insomnia, but are also used for depression, obsessive-compulsive disorder (OCD), post-traumatic stress disorder (PTSD), seizures, withdrawal symptoms, and sedation prior to medical procedures (Olkkola and Ahonen, 2008; Page et al., 2002).

From 2002 to 2014, the number of people prescribed benzodiazepines in the United States increased by 31%, and the proportion of co-prescribed opioids and benzodiazepines increased from 6.8% to 9.6% (Hwang et al., 2016). Among people who use opioids, benzodiazepine use has been associated with several adverse outcomes, including increased risk for overdose (Curtin et al., 2017; Stein et al., 2017a), poorer retention in opioid treatment (Franklyn et al., 2017), more emergency department visits (Jones and McAninch, 2015; Sun et al., 2017; Herbert et al., 2017), heroin use (Darke et al., 2010), HIV infection (Ickowicz et al., 2015), and hepatitis C virus infection (Bach et al., 2016).

For those who misuse opioids, benzodiazepine use has been associated with being white (Cropsey et al., 2015; Tucker et al., 2016); being female (Cropsey et al., 2015; Stein et al., 2017b); older age (Stein et al., 2017b); and incarceration history (Tucker et al., 2016). Non-medical benzodiazepine use has been associated with screening positive for anxiety, depression, and other mental health concerns in this population (Chen et al., 2011; Lavie et al., 2009). Research has found that concurrent non-medical benzodiazepine and other opioid use can be motivated by desires to create a greater “high” as well as decrease symptoms of opiate withdrawal (Chen et al., 2011; Stein et al., 2016). Finally, when pain conditions and anxiety co-occur, some clinicians may prescribe both opioids and benzodiazepines despite the increased risk for overdose (Park et al., 2015). Thus, concurrent, non-medical use of these medications may have iatrogenic origins.

While benzodiazepine use and misuse have been studied among people prescribed opioids (Dasgupta et al., 2016), patients on methadone treatment for opioid use disorder (Chen et al., 2011), and people who use heroin (Darke et al., 2010), very few studies have examined the prevalence and correlates of benzodiazepine use among young adults who use prescription opioids non-medically. Among the general population of young adults aged 18 to 25, 3.6 million (one in ten) reported any benzodiazepine use in the past year, 1.8 million (half) of whom reported non-medical benzodiazepine use in the past year (SAMHSA, 2015). More research is needed to understand the patterns of co-occurring benzodiazepine use among young adults who engage in non-medical prescription opioid (NMPO) use in order to inform overdose prevention, treatment, and harm reduction strategies.

Our analysis uses data from the Rhode Island Young Adult Prescription Drug Study (RAPiDS), which recruited individuals aged 18 to 29 in Rhode Island who reported recent NMPO use. We sought to determine the prevalence and correlates of regular benzodiazepine use and misuse among this sample. We also explored the prevalence, correlates, and chronology of medical and non-medical benzodiazepine use among participants with regular benzodiazepine use.

2.0 Methods

2.1 Participants

Young adults (18–29 years) who reported 30-day NMPO use (using prescription opioids without a prescription or not as a doctor directed) were invited to participate in RAPiDS between January 2015 and February 2016. RAPiDS was approved by the Brown University Institutional Review Board. More detailed methods regarding recruitment and inclusion criteria can be found in previously published papers (Evans et al., 2016; Liebling et al., 2016).

2.2 Primary Measures

Participants were shown a card with pictures of the following benzodiazepines: Klonopin (clonazepam), Xanax (alprazolam)/Ativan (lorazepam), Valium (diazepam), Librium, Limbitrol, Rohypnol, Serax, and Tranxene. Participants who indicated ever using benzodiazepines then identified which on the card they used most regularly (defined as more than once a month), as well as other benzodiazepines they had ever used. Specifically, these participants were asked if a doctor, dentist, or nurse had ever prescribed this benzodiazepine to them and the age they were first prescribed. Participants were also asked if they had ever used the benzodiazepine non-medically, what age they first took it non-medically, and how often they have used it in the last six months (daily vs. weekly vs. monthly).

2.3 Statistical Analyses

Through Wilcoxon rank sum test and Fisher's exact test, we explored factors associated with regular benzodiazepine use, comparing participants who did not regularly use benzodiazepines vs. participants who regularly used benzodiazepines, both non-medically and medically. Additionally, we examined the factors associated with ever being prescribed the benzodiazepine used most regularly. Variable selection was guided by previous research

on opioid use, benzodiazepine use, and overdose (Riley et al., 2016). All analyses were conducted in SAS version 9.3. *P*-values were two-sided; *p*-values<0.05 were considered significant.

Additional factors explored were age; sex at birth (male vs. female); race (white vs. non-white); Hispanic or Latino descent; ever experiencing homelessness (defined as not having a regular place to stay, living in a shelter because of nowhere to go, or living in a place not ordinarily used for sleeping); experiencing homelessness in the last six months; ever being incarcerated; ever overdosing by accident; using NMPOs to feel less depressed or anxious; screening positive for depressive symptomology, using a cut-off of 10 on the Center for Epidemiologic Studies Depression Short Scale (CES-D10) (Andresen et al., 2013); ever being diagnosed with Attention-Deficit Disorder (ADD)/Attention-Deficit Hyperactivity Disorder (ADHD), a depressive disorder, bipolar disorder, or anxiety disorder, and screening positive for unhealthy alcohol use (a score 3 for women and 4 for men), based on the Brief Alcohol Use Disorders Identification Test (AUDIT-C) (Bradley et al., 2007).

3.0 Results

Among 200 participants, the median age was 25 (IQR=22–28), 131 (65.5%) were male, and 123 (61.5%) were white. A total of 171 (85.5%) reported lifetime benzodiazepine use. Table 1 summarizes the characteristics of those reporting regular benzodiazepine use (n=125, 62.5%) versus those who did not report regular benzodiazepine use (n=75, 36.5%). Among the former group, 121 (96.8%) reported non-medical benzodiazepine use, while only 43 (34.4%) reported ever being prescribed the benzodiazepine they use most regularly. Table 2 summarizes the correlates by those who have or have not been prescribed the benzodiazepine they use most frequently.

Xanax (alprazolam)/Ativan (lorazepam) were the mostly commonly used benzodiazepines, where 151 (88.3%) reported Xanax (alprazolam)/Ativan (lorazepam) use in their lifetime. Klonopin (clonazepam) and Valium (diazepam) were the second and third most commonly used benzodiazepines in one's lifetime, endorsed by 126 (73.7%) and 106 (62.0%), respectively. Among the 43 participants who had ever been prescribed the benzodiazepine they used most regularly, the age (in years) of first prescribed ranged from 12 to 27, with a median of 19 (IQR=18–23). Among the 121 participants who had ever engaged in non-medical use of the benzodiazepine they used most regularly, the age of first non-medical use ranged from 9 to 28, with a median of 19 (IQR=17–22). Among 39 participants who reported both prescribed and non-medical use, the median age of first prescribed use was 19 (IQR=18–23), and the median age of first non-medical use was 18 (IQR=17–22). Of these 39 participants, 16 (41.0%) used the benzodiazepine non-medically before being prescribed it, 12 (30.8%) were prescribed it before using it non-medically, and 11 (28.2%) were first prescribed it and used it non-medically at the same age. Further, persons prescribed the benzodiazepine they used regularly were more likely to use NMPOs to feel less depressed or anxious (64.8% vs. 40.0%, *p*=0.002) and were marginally more likely to report a history of overdose (41.9% vs. 24.4%, *p* = 0.06).

4.0 Discussion

Our study illustrates a high prevalence and lifetime rate of initiation of benzodiazepine use among young adults who use NMPOs. We observed a number of correlates with co-occurring benzodiazepine and NMPO use that have been identified in previous research, including being of white race/ethnicity (Cropsey et al., 2015; Tucker et al., 2016); having a history of incarceration (Tucker et al., 2016); and co-occurring anxiety and mood disorders (McHugh et al., 2017; Vogel et al., 2013). We also found correlates of regular benzodiazepine use that we believe have not yet been identified, including a specific motivation for NMPO use (i.e., to feel less depressed or anxious).

The study's findings offer important clinical ramifications. Research has indicated that individuals tend to be prescribed benzodiazepines more frequently by non-psychiatrist doctors (Simon et al., 2001; Young et al., 2001). One study found that approximately 55% of benzodiazepine prescriptions in the US were prescribed by family care physicians, whereas only 16% by psychiatrists (Cascade and Kalali, 2008). Primary care physicians prescribing benzodiazepines should be cognizant of populations at risk for benzodiazepine misuse, especially NMPO-using youth, where benzodiazepine use started as young as 9 years of age in this study (3.31% were 12 years or younger in this study). Physicians should delay the onset of benzodiazepine prescribing among youth, advise non-pharmacological treatment methods, and screen for substance use disorders (Maxwell, 2011; Okie, 2010). Additionally, as suggested by the Centers for Disease Control, prescribers can utilize the prescription drug monitoring program (PDMP) when patients either initiate or continue opioid therapies or other benzodiazepine treatments—allowing physicians to develop risk mitigation plans and ensure the patient is not receiving unsafe drug combinations (Dowell et al., 2016).

Benzodiazepine involvement in opioid overdoses has increased over the last two decades. From 2004–2011, the rate of overdose deaths involving benzodiazepines and opioids increased from 11.0 to 34.2 per 100,000 (Jones and McAninch, 2015). The high percentage who have ever overdosed (30.4%) among participants who regularly use benzodiazepine is a cause for concern. Additionally, a history of overdose was more common among those who were ever prescribed the benzodiazepine they use most regularly. This relationship is surprising and requires future research. However, the small sample precluded multivariable analysis, and we cannot rule out the fact that this association may be due to confounding. Nevertheless, our results emphasize the need for greater public health interventions that educate individuals about increased overdose risk with polysubstance use, especially in the context of combined benzodiazepine and NMPO use.

Overdose and other harm reduction interventions in clinical settings can be influential access points to leverage at risk and hard to reach populations (Mueller et al., 2015; Coffin et al., 2016). For example, Project Lazarus in Western North Carolina trained physicians in identifying and providing naloxone to patients at risk; decreasing overdose death rates from 46.6 to 29.0 per 100,000 (Albert et al., 2011). Additionally, Frank et al. found that young adult NMPO users (aged 18–32) are not usually aware of overdose risks, especially in relation to polysubstance use (2015). Harm reduction materials that provide information on the risks of concurrent benzodiazepine and prescription opioid use would be beneficial.

Our study has multiple limitations. A sample of 200 participants is small and prevented us from conducting multivariable analyses. Observed associations are subject to confounding and only represent crude associations. Although we recruited participants through diverse methods, our findings may not be generalizable to all young adults who use NMPOs. When we assessed regular benzodiazepine use, we asked participants to endorse the benzodiazepine they used most regularly but did not ask them to report all benzodiazepines they use regularly. Therefore, we were not able to report or identify the multiple benzodiazepines used regularly. We did not ascertain who (i.e., a doctor, nurse, dentist, etc.) prescribed the benzodiazepine participants used regularly and how those who used non-medically received their benzodiazepines. Further, this study did not analyze other motivations for benzodiazepine use.

5.0 Conclusion

In summary, this study is among the first to explore benzodiazepine prevalence and correlates among young adult NMPO users. These results indicate the need to research the effects of psychopathology and other sociodemographic factors on the development of co-occurring benzodiazepine use and misuse among NMPO-using youth. Our results should inform practices surrounding prescribing and co-prescribing of opioids and benzodiazepines to young adults, as well as enhance current harm reduction interventions for young adults who report NMPO use.

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Highlights

- Studied benzodiazepine use among young adults using nonmedical prescription opioids
- Benzodiazepine use associated with white race, incarceration and mood disorders
- Among study sample, 86% reported lifetime benzodiazepine use
- Age of first non-medical benzodiazepine use between 9 to 28 years
- Accidental overdose higher among those prescribed their frequented benzodiazepine

Table 1

Factors associated with regular benzodiazepine use among young adults who use prescription opioids non-medically in Rhode Island (N = 200)

	Total n (%) n=200	No regular benzodiazepine use n (%) n=75	Regular benzodiazepine use n (%) n=125	p – value *
Age (median, IQR) **	25 (22–28)	24 (22–27)	25 (22–28)	0.20
Sex at birth				
Male	131 (65.5)	50 (66.7)	81 (64.8)	0.88
Female	69 (34.5)	25 (33.3)	44 (35.2)	
Race				
White	123 (61.5)	39 (52.0)	84 (67.2)	0.03
Non-White	74 (37.0)	35 (46.7)	39 (31.2)	
Hispanic or Latino descent				
Yes	28 (14.0)	13 (17.3)	15 (12.0)	0.30
No	172 (86.0)	62 (82.7)	110 (88.0)	
Ever been homeless				
Yes	109 (54.5)	35 (46.7)	74 (59.2)	0.11
No	91 (45.5)	40 (53.3)	51 (40.8)	
Been homeless in the last 6 months				
Yes	50 (25.0)	15 (20.0)	35 (28.0)	0.24
No	150 (75.0)	60 (80.0)	90 (72.0)	
Ever incarcerated				
Yes	94 (47.0)	28 (37.3)	66 (52.8)	0.04
No	106 (53.0)	47 (62.7)	59 (47.2)	
Ever overdosed by accident				
Yes	53 (26.5)	15 (20.0)	38 (30.4)	0.14
No	147 (73.5)	60 (80.0)	87 (69.6)	
Screened positive for depressive symptomology (CES-D 10)				
Yes	119 (59.5)	39 (52.0)	80 (64.0)	0.14
No	80 (40.0)	35 (46.7)	45 (36.0)	
Ever been diagnosed with a depressive disorder				
Yes	95 (47.5)	30 (40.0)	65 (52.0)	0.14
No	102 (51.0)	43 (57.3)	59 (47.2)	
Ever been diagnosed with a bipolar disorder				
Yes	49 (24.5)	12 (16.0)	37 (29.6)	0.04
No	148 (74.0)	61 (81.3)	87 (69.6)	
Ever been diagnosed with an anxiety disorder				
Yes	98 (49.0)	27 (36.0)	71 (56.8)	<0.01
No	99 (49.5)	46 (61.3)	53 (42.4)	
Ever been diagnosed with ADHD or ADD				
Yes	78 (39.0)	27 (36.0)	51 (40.8)	0.65
No	119 (59.5)	46 (61.3)	73 (58.4)	

	Total n (%) n=200	No regular benzodiazepine use n (%) n=75	Regular benzodiazepine use n (%) n=125	p – value *
Use prescription opioids non-medically to feel less depressed or anxious				
Yes	111 (55.5)	30 (40.0)	81 (64.8)	<0.01
No	87 (43.5)	43 (57.3)	44 (35.2)	
Unhealthy Alcohol Use ***				
Yes	127 (63.5)	42 (56.0)	85 (68.0)	0.10
No	73 (36.5)	33 (44.0)	40 (32.0)	

Not all columns add to 100% due to missing values

Abbreviations: ADD, Attention-Deficit Disorder; ADHD, Attention-Deficit Hyperactivity Disorder

* Fisher's exact test used to estimate p-values, unless otherwise noted

** Wilcoxon rank sum used to compare age differences

*** Based on the AUDIT-C Brief Alcohol Screen for unhealthy alcohol use

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Table 2

Factors associated with ever being prescribed the benzodiazepine used most regularly among young adult non-medical prescription opioid users in Rhode Island who use benzodiazepines regularly (N = 125)

	Total n (%) n=125	Never been prescribed the benzodiazepine they use most regularly n (%) n=82	Have been prescribed the benzodiazepine they use most regularly n (%) n=43	p – value *
Age (median, IQR) **	25 (28–22)	25 (28–22)	25 (27–22)	0.50
Sex at birth				
Male	81 (64.8)	55 (67.1)	26 (60.5)	0.55
Female	44 (35.2)	27 (32.9)	17 (39.5)	
Ever overdosed by accident				
Yes	38 (30.4)	20 (24.4)	18 (41.9)	0.06
No	87 (69.6)	62 (75.6)	25 (58.1)	
Screened positive for depressive symptomology (CES-D 10)				
Yes	80 (64.0)	54 (65.9)	26 (60.5)	0.56
No	45 (36.0)	28 (34.2)	17 (39.5)	
Ever been diagnosed with a depressive disorder				
Yes	65 (52.0)	37 (45.1)	28 (65.1)	0.04
No	59 (47.2)	45 (54.9)	14 (32.6)	
Ever been diagnosed with a bipolar disorder				
Yes	37 (24.5)	20 (24.4)	17 (39.5)	0.10
No	87 (74.0)	62 (75.6)	25 (58.1)	
Ever been diagnosed with an anxiety disorder				
Yes	71 (56.8)	38 (46.3)	33 (76.7)	<0.01
No	53 (42.4)	44 (53.7)	9 (20.9)	
Ever been diagnosed with ADHD or ADD				
Yes	51	29 (35.4)	22 (47.6)	0.08
No	73	53 (64.6)	20 (52.4)	
Use prescription opioids non-medically to feel less depressed or anxious				
Yes	81 (64.8)	55 (67.1)	26 (60.5)	0.55
No	44 (35.2)	27 (32.9)	17 (39.5)	
Unhealthy Alcohol Use ***				
Yes	85	63 (76.8)	22 (51.2)	<0.01
No	40	19 (23.2)	21 (48.8)	

Not all columns add to 100% due to missing values

* Fisher's exact test used to estimate p-values, unless otherwise noted

** Wilcoxon rank sum used to compare age differences

*** Based on the AUDIT-C Brief Alcohol Screen for unhealthy alcohol use