HHS Public Access

Author manuscript

J Subst Abuse Treat. Author manuscript; available in PMC 2018 June 01.

Published in final edited form as:

J Subst Abuse Treat. 2017 June ; 77: 67–71. doi:10.1016/j.jsat.2017.03.002.

Beliefs about the Consequences of Using Benzodiazepines among Persons with Opioid Use Disorder

Michael D. Stein, M.D.[a,d], **Bradley J. Anderson, Ph.D.**[a], **Shannon R. Kenney, Ph.D., M.P.H.**[a,b], and **Genie L. Bailey, M.D.**[b,c]

[a]Behavioral Medicine Department, Butler Hospital, Providence, RI, 02906

[b]Warren Alpert Medical School of Brown University, Providence, RI, 02912

[c]Stanley Street Treatment and Resources, Inc., Fall River, Massachusetts 02720

[d]Boston University School of Public Health, Boston, MA 02118

Abstract

Background—Patients admitted to addiction treatment programs report high rates of concurrent opioid and benzodiazepine (BZD) use. This combination places individuals at high risk for accidental overdose and other serious consequences. However, little is known about the beliefs opioid users have about the consequences of BZD use.

Methods—We surveyed consecutive persons initiating inpatient opioid detoxification (N=476; 95.0% enrollment) and identified 245 who reported BZD use in the past 30 days and/or had a positive toxicology. We compared those who did and did not report BZD use on demographic and substance use variables, and specific beliefs about the potential effects of BZDs.

Results—Participants averaged 32.2 years of age, 71.2% were male, 86.6% used heroin, and 68.7% reported injection drug use in the past 30 days. Over half (51.5 %) used a BZD in the month prior to admission; of these, 26.2% (n = 64) reported being prescribed a BZD. Alprazolam (Xanax) was the most commonly used BZD (54%). Benzodiazepine users (versus non-users) were significantly more likely to be female and non-Hispanic White, use concurrent substances, and report past year overdose. Overall, nearly all BZD users endorsed accurate beliefs that BZDs can increase the risk of overdose and can be addictive. However, BZD users, relative to non-users, were significantly less likely to endorse some known adverse consequences of BZDs, such as risk of worsening depression and poor medication-assisted opioid treatment retention.

Conclusions—Delineating the full array of risks from combining BZDs and opioids should be a high priority in detoxification settings, given the increased risks associated with BZD misuse in this population.

Correspondence concerning this article should be addressed to: Michael D. Stein, M.D., Department of Health Law, Policy & Management, Boston University School of Public Health, 715 Albany Street, Boston, MA 02118; Pn: (617) 414-1309. mdstein@bu.edu.

Keywords

Benzodiazepines; beliefs; use; anxiety; opioids; detoxification

1.0 INTRODUCTION

Benzodiazepines (BZDs) are commonly used by patients with opioid use disorders (Brands et al., 2008; Lavie, Fatseas, Denis, & Auriacombe, 2009; SAMHSA, 2011). In our prior work, we found that 40% of patients seeking inpatient opioid detoxification had used BZDs in the past month (Stein, Kanabar, Anderson, Lembke, & Bailey, 2016), and rates of BZD use among opioid users receiving medication-assisted treatment (MAT) are reported to be as high 70% (Nielsen, Dietze, Lee, Dunlop, & Taylor, 2007). Complex opioid-BZD drug interactions (via CYP system metabolism) and hepatic dysfunction can produce increased opioid serum concentrations, exacerbating risk for overdose (Jann, Kennedy, & Lopez, 2014; White & Irvine, 1999). Benzodiazepine use is independently predictive of non-fatal overdose among injection drug users (Kerr et al., 2007) and, nationally, overdose deaths from prescribed opioid pain relievers and heroin have quadrupled from 1999 to 2014 (CDC, 2016; Volkow, Frieden, Hyde, & Cha, 2014), with nearly one-third of fatalities associated with concurrent BZD use (Chen, Hedegaard, & Warner, 2014).

Although persons with opioid use disorders use BZDs for intended anxiolytic reasons (Fatseas, Lavie, Denis, & Auriacombe, 2009) and as a sleep aid (Gelkopf, Bleich, Hayward, Bodner, & Adelson, 1999; Posternak & Mueller, 2001; Vogel et al., 2013), BZDs are commonly used in conjunction with opioids to enhance their rewarding effects or “high” (Chen et al., 2011; Fatseas et al., 2009; for review see Jones, Mogali, & Comer, 2012) or to decrease the effects of opiate withdrawal (Stein et al., 2016). Not surprisingly, BZD use among opioid dependent persons is associated with heightened risk. Benzodiazepine users tend to report a longer history of opioid use and prior detoxifications; use higher doses of opioids; have a higher frequency of injection drug use, needle sharing, co-occurring use of alcohol and cocaine; and report greater criminal activity (Darke et al., 2010; Rooney, Kelly, Bamford, Sloan, & O’Connor, 1999; Ross & Darke, 2000). In addition to increasing overdose risk, BZD misuse among opioid dependent persons has pronounced adverse effects on physical and psychological health, and quality of life (Lavie et al., 2009). Benzodiazepine-related side effects include mental and physical fatigue (Longo & Johnson, 2000) and heightened risk for motor vehicle accidents (Rapoport et al., 2009). Long-term BZD use is associated with impaired cognitive functioning (see Barker, Greenwood, Jackson, & Crowe, 2004 for meta-analysis), increased depressive symptomatology (Manthey et al., 2010; Nordfjaern, 2012), and BZD addiction (O’Brien C, 2005). Additionally, BZD use among patients receiving MAT predicts poorer treatment outcomes (e.g., withdrawal, health, legal problems, alcohol misuse; B Brands et al., 2008; Eiroa-Orosa et al., 2010).

Persons with opioid use disorders tend to underestimate their risk of opioid-related overdose (Frank et al., 2015; Wilder et al., 2016), and those opioid users who also use BZDs further underestimate their risk for overdose (i.e., present optimistic bias) (Rowe, Santos, Behar, & Coffin, 2016). Perceptions of risk are a key driver of behavior and thus represent an

important target for prevention strategies (for review see Clark, Wilder, & Winstanley, 2014).

The current study is the first to examine how perceptions of a range of BZD-related risks may differ by BZD use status among opioid dependent persons entering short-term inpatient medical detoxification. Particularly because opioid detoxification is a common initial step for treatment-seeking persons with opioid use disorders (Bailey, Herman, & Stein, 2013; Carrier et al., 2011; Mark, Dilonardo, Chalk, & Coffey, 2002; Stein, Anderson, Thurmond, & Bailey, 2015; Substance Abuse and Mental Health Services Administration, 2004), insight into perceptions that may influence drug use behaviors could be used to guide clinical discussions.

2.0 MATERIALS AND METHODS

2.1 Recruitment

Data for the current study were collected between May 2015 and December 2015 at the Stanley Street Treatment Addiction and Recovery, Inc. (SSTAR) in Fall River, Massachusetts. Persons seeking opioid detoxification were approached within their first 24 hours of their inpatient stay to participate in a survey research study and were interviewed immediately upon consent. SSTAR has 38 beds and is a 24-hour medically supervised treatment facility that utilizes a methadone protocol and provides evaluation, withdrawal management, individual and group counseling, and case management. On average, patients stay for 4.9 days.

During the recruitment period, 501 opioid users who were admitted to SSTAR met Butler Hospital Institutional Review Board-approved study criteria: 18 years or older, English-speaking, and able to provide verbal informed consent. In all, 25 patients refused study participation or were discharged before interviews could be performed and 476 persons completed a non-incentivized 15-minute face-to-face interview with a non-treating research staff member. Each respondent received medication and therefore was physically comfortable and not in acute withdrawal when interviewed. Persons were defined as BZD users if they responded to the question, “How many days in the last 30 have you used benzos (for instance, Ativan, Klonopin, Librium, Xanax, Valium)?” by reporting at least one day of use, or if they were positive for BZD on urine toxicological testing at entry to detoxification. All toxicological testing was done by enzyme immunoassay and confirmation testing by liquid chromatography, mass spectrometry.

2.2 Measures

Assessed demographic measures included age, gender, race/ethnicity, employment (part-or full-time vs. unemployed), and years of education. We also asked participants if they had ever received opioid detoxification in the past, or had ever been prescribed methadone or buprenorphine. Participants also reported on their past 30-day drug use behaviors, including cocaine, stimulant use (Adderall or Ritalin) without a prescription, methamphetamine use, and alcohol use (frequency and usual quantity). Hazardous drinking was defined as more than 7 drinks per week for females or 14 drinks per week for males in the past month

(National Institute on Alcohol Abuse and Alcoholism, 2005). Respondents were provided the following definition of overdose (on any drug): “you were unarousable (couldn’t be woken) with shaking or calling your name because of the drugs you consumed” and asked how many times they had overdosed in the past year.

Depression and anxiety were measured via the Patient Health Questionnaire (PHQ-4) which is comprised of the PHQ-2 depression scale (Kroenke, Spitzer, Williams, & Lowe, 2009) and the GAD-2 anxiety scale (Kroenke, Spitzer, Williams, Monahan, & Lowe, 2007). Participants provided answers to the question: “Over the past two weeks, how often have you been bothered by the following problems.” Two items assessed depressive symptoms (e.g., “little interest or pleasure in doing things”) and two items assessed anxiety symptoms (e.g., “feeling nervous, anxious or on edge”). For each item, the possible responses were: “not at all=0”, “several days=1”, “more than half the days=2”, and “nearly every day=3,” resulting in a summed score ranging from ‘0’ to ‘6’ for each two-item scale. The validated cut point for positive screens for clinically significant depression or anxiety—scores of at least 3—were used in the current study (Kroenke, Spitzer, & Williams, 2003).

We asked, “Which is the benzo you use most often?” Responses included Klonopin, Librium, Xanax, Valium, and ‘I don’t know.’ We also asked, “Where were you most likely to get the benzos that you used in the last 30 days?” Responses included: “bought them from someone else such as a dealer or on the street,” “bought or borrowed from a friend,” and “prescribed to you by a physician.” BZD severity was measured using the Severity of Dependence Scale (de las Cuevas, Sanz, de la Fuente, Padilla, & Berenguer, 2000). This 5-item scale (each with a potential range 0–3) had high internal consistency reliability (alpha = .89). A score of ≥ 7 is considered the cut-off for psychological dependence.

We created a series of belief statements about BZD effects with “true or false” response options. Respondents also had the option of not responding; non-responses were coded as “false” or incorrect responses on any given item. The veracity of each statement was derived from past outcome studies of BZD use (Lavie et al., 2009; Schuman-Olivier et al., 2013). These statements included the following: “Benzos can make depression worse;” “Benzos can increase the risk of overdosing from opiates;” “Benzos can fog a person’s thinking;” “Benzos can be addictive;” “Benzos can make you feel overtired during the day;” “Benzos can increase the risk of a driving accident;” “Benzos can cause withdrawal if you stop suddenly;” and “Benzos can cause problems staying in methadone or buprenorphine treatment.”

2.3 Analytical Methods

We report descriptive statistics to summarize the characteristics of the sample. We used the χ^2-test of independence to statistically compare recent BZD users and non-users with respect to beliefs about BZDs. Percentages are reported to describe the substantive differences between groups. Using these same methods, we conducted an auxiliary analysis among persons who were BZD positive evaluating the association of mental health (depression and anxiety) and baseline BZD dependence severity with beliefs that BZD use can make depression worse, and with the belief that BZD use can cause problems staying in methadone or buprenorphine treatment.

3.0 RESULTS

The 476 participants (95.0% of eligible) averaged 32.2 (± 8.6) years of age, 71.2% were male, and 42 (8.8%) were Hispanic. About 86.6% identified their race as White, 5.5% as Black, and 10.1% identified other racial origins (Table 1). Race/Ethnicity was dichotomized to contrast non-Hispanic Whites (82.4%) to all racial or ethnic minorities in subsequent analyses. Mean educational attainment was 11.8 (± 1.9) years. Most (86.6%) reported that heroin was the primary drug from which they were detoxifying and 68.7% reported injection drug use within past 30 days. About 41.4% and 7.8% had recently used cocaine and stimulants or methamphetamines, respectively. One hundred fifteen (24.2%) met NIAAA criteria for hazardous use of alcohol and 25.1% had overdosed within the past 12 months. Just over half (51.5%) had used BZDs in the last month; of these, 94.3% self-reported BZD use and an additional 14 persons (5.7%) were identified by a positive urine toxicology test without self-reporting use. Among BZD users, mean scores on the Severity of Dependence Scale were 3.42 (± 4.51); 108 (47.0%) of current BZD users in this sample had severity of dependence scores of 0, and 54 (23.5%) had scores ≥ 7.

BZD users were significantly less likely to be male ($\chi^2 = 7.62$, p = .006) and significantly less likely ($\chi^2 = 9.67$, p = .002) to be of Hispanic origin than non-users (Table 1). Race was not associated significantly with BZD use. Benzodiazepine users were significantly ($\chi^2 = 4.67$, p = .031) more likely to report recent use of cocaine ($\chi^2 = 4.67$, p = .031), recent use of stimulants or methamphetamines ($\chi^2 = 4.16$, p = .041), and meet NIAAA guidelines for hazardous use of alcohol ($\chi^2 = 6.40$, p = .011). They were also considerably (32.4% v 17.3%) more likely to report overdosing within the past 12-months ($\chi^2 = 14.33$, p < .001). Although not statistically significant at conventionally accepted levels, BZD users also tended ($\chi^2 = 3.67$, p = .055) to be more likely to report injection drug use.

Mean days of BZD use reported by current users was 13.2 (± 10.9, Median = 10) days in the month prior to data collection. Just over half (51.3%) of the recent users said buying from someone on the street was their most likely source of BZDs in the past 30-days; 20.9% said they had bought or borrowed BZDs from a friend or family member, and 27.8% said they had been prescribed by a doctor. Alprazolam was used by 54.2% of the BZD users, Clonazepam by 26.7%, Lorazepam by 5.2%, Diazepam by 3.6%, Chloradizepoxide by 0.8%, and 9.6% said they did not know which BZD they used most often.

Recent BZD users were significantly ($\chi^2 = 15.24$, p <.001) less likely (64.5% v 80.5%) than non-users to believe BZD use could make depression worse (Table 2). They were also significantly ($\chi 2 = 4.56$, p = .033) less likely (79.2% v 86.6%) to believe BZD use can cause problems staying in methadone or buprenorphine treatment programs. Recent BZD users and non-users did not differ significantly with respect to the belief that BZDs can fog a person’s thinking, increase the risk of overdose, that BZDs can be addictive, can make people feel overly tired during the day, can increase the risk of accident, or that they can cause withdrawal.

In auxiliary analyses restricted to persons who were BZD positive, the association of meeting screening criteria for depression (PHQ-2 ≥ 3) was not associated significantly with

the belief that BZD use can make depression worse ($\chi^2 = 0.29$, p = .593) or with the belief that BZD use could cause problems staying in MAT programs ($\chi^2 = 0.08$, p < .930). Similarly, meeting screening criteria for anxiety (GAD-2 ≥ 3) was not associated with the belief that BZD use could make depression worse ($\chi^2 = 2.11$, p = .146) or with the belief that BZD use could cause problems staying in treatment ($\chi^2 = 0.37$, p = .545). Benzodiazepine dependence severity was associated significantly ($\chi^2 = 4.96$, p < .026) with the belief that BZD use can make depression worse; 79.3% of persons with BZD severity scores ≥ 7 said that statement was true, compared with 62.7% of persons with less severe BZD dependence. Benzodiazepine dependence severity was not associated significantly ($\chi^2 = 0.71$, p < .402) with the belief that BZD use could cause problems staying in treatment programs.

4.0 DISCUSSION

The goal of this study was to explore whether recent BZD users had different beliefs about the negative effects of BZDs than non-users in a cohort of opioid users entering inpatient detoxification. Our findings are important because of the high rate of BZD misuse among persons with opioid use disorder and for raising the possibility that misuse may be augmented by false beliefs. Study participants were nearly universally aware that BZDs can be addictive, muddle one's thinking, cause fatigue and driving accidents, contribute to overdose risk, and if halted, produce withdrawal symptoms. That is, BZD users, overall, held accurate perceptions about BZDs' major adverse effects. However, BZD users, relative to non-users, were less likely to believe that BZD use was associated with two important adverse consequences: worsening depressive symptoms and poorer MAT outcomes.

Despite their similarities in beliefs about the effects of BZDs, users differed from non-users in terms of personal characteristics. Consistent with large-scale surveillance studies showing that females exhibit consistently higher BZD prescribing rates than males (e.g., Paulozzi et al., 2015) women in this sample were more likely to be BZD users than men. Benzodiazepine users were also more likely to be non-Hispanic. White women represent a growing subpopulation at risk for concurrent opioid-BZD use and associated consequences. From 1999 to 2014, annual opioid overdose fatalities increased four-fold among middle-aged White women, with BZDs involved in an increasing percentage of the deaths during this time (Kindy & Keating, 2016). In the current sample, BZD users were also more likely to report using other substances. As in other studies (Vogel et al., 2013), BZDs may be used to mitigate the negative effects of cocaine, alcohol, and stimulants (Ross & Darke, 2000). Users were also more likely to report having overdosed in the past year, supporting studies demonstrating the increased overdose risk of concurrent opioid-BZD use. The ongoing use of BZDs, despite nearly one-third having overdosed, suggests that many users may be heavy users of BZDs (in this sample, nearly one-quarter were "dependent") and would have difficulty quitting, likely fearing withdrawal symptoms (Jones et al., 2012).

Nearly three-quarters of participants believed that BZDs can make depression worse. However, persons who did not use BZDs were more likely to perceive the depressogenic effects of BZDs, and perhaps this perception contributes, in part, to individuals' choice not to use BZDs. Among BZD users in this sample, depression and anxiety status did not

influence these same beliefs. It is plausible that BZD users experience some anxiety symptom relief and, generalizing from this positive effect, perceive that BZDs improve depressive symptoms as well. However, the finding that among BZD users, those with BZD dependence were more likely to believe that BZDs can make depression worse contributes to research showing that heroin users physically dependent on BZDs (versus not) report greater use of anti-depressants and poorer general psychiatric health (Darke et al., 2010; Eiroa-Orosa et al., 2010). More research is needed to better understand how escalated risk perceptions may be leveraged for treatment purposes in this high-risk subgroup of patients with co-occurring opioid and BZD dependence.

Although most (79.2%) of respondents accurately perceived that BZD use may impede the effectiveness of MAT, BZD users were less likely to endorse this belief than non-BZD users. These findings are concerning given public health goals focused on linking opioid dependent persons in inpatient detoxification treatment with outpatient MAT, and given that many aftercare maintenance treatment programs will not accept patients who are misusing BZDs (K. W. Chen et al., 2011). Because BZD use is a marker for psychiatric symptoms and both mental health and addiction severity (B Brands et al., 2008; Eiroa-Orosa et al., 2010), BZD users entering MAT, particularly those with untreated mental health issues, are susceptible to poor retention and overall treatment failure. However, among BZD users, those screening positive for anxiety, depression, or BZD dependence did not differ from other respondents in their perceptions that BZD use interferes with MAT. Thus, it appears that depressed, anxious or BZD dependent patients in detoxification may benefit from brief interventions that raise awareness about their heightened risk for MAT-related complications and teach strategies that minimize MAT withdrawal so as to augment aftercare treatment.

This study has limitations. First, although the high recruitment rate (95%) obtained in this study is a strength, its focus on individuals seeking inpatient opioid detoxification limits the generalizability of findings. Second, participants were recruited from a single location and were primarily Non-Hispanic White and male. Although the mean age and gender composition found in the present sample are similar to national samples of detoxifying patients (e.g., Wu et al., 2010), the current results cannot be generalized to other regions. Third, we don’t know if those defined as non-users in this study ever used BZDs; some may have halted use. Fourth, most BZD use in this cohort was misuse, that is use without a prescription, but we did not confirm that those who reported being prescribed BZDs in fact had prescriptions or were using BZDs as prescribed. Indeed, as the number of adults filling BZD prescriptions has risen in the past fifteen years, opioid users have increasingly obtained diverted BZD (Bachhuber, Hennessy, Cunningham, & Starrels, 2016). While it is less likely that opioid users receive prescriptions from medical providers who are aware of their increased risk of overdose and development of BZD use disorder, it is nonetheless important to assess this occurrence. Fifth, we did not collect data on doses or duration of BZDs used. Finally, we do not know motivations for BZD use.

5.0 CONCLUSIONS

BZD use among patients undergoing inpatient opioid detoxification is common and places those returning to the community at high risk for overdose and death, as well as higher risk

of poor treatment outcomes after entering MAT (Brands et al., 2008; Eiroa-Orosa et al., 2010). Our findings suggest that detoxification programs may be well positioned to implement screening to identify and intervene with patients reporting BZD misuse. Patients appear to understand the risks associated with concurrent opioid-BZD use—the vast majority of concurrent users in this sample recognized risk for overdose (92.7%), dependence (97.6%), and withdrawal (95.1%)—but may lack the motivation and strategies needed to quit BZD use or prevent future consequences. Distributing pamphlets or educational materials during detoxification about BZD-related risks may be a cost-effective way to raise awareness among BZD users with misperceptions. Further, educating patients misusing BZDs about alternatives to ongoing use (e.g. other medications or non-pharmacological means to address mood or withdrawal symptoms) is a critical component of the care of persons with opioid use disorders during detoxification as well as the aftercare period.

Acknowledgments

This study was funded by the National Institute on Drug Abuse (RO1 DA034261). Trial registered at clinicaltrials.gov; Clinical Trial # NCT01751789.

6.0 REFERENCES

Bachhuber MA, Hennessy S, Cunningham CO, Starrels JL. Increasing Benzodiazepine Prescriptions and Overdose Mortality in the United States, 1996–2013. American Journal of Public Health. 2016; 106(4):686–688. DOI: 10.2105/AJPH.2016.303061 [PubMed: 26890165]

Bailey GL, Herman DS, Stein MD. Perceived relapse risk and desire for medication assisted treatment among persons seeking inpatient opiate detoxification. Journal of Substance Abuse Treatment. 2013; 45(3):302–305. DOI: 10.1016/j.jsat.2013.04.002 [PubMed: 23786852]

Barker MJ, Greenwood KM, Jackson M, Crowe SF. Persistence of cognitive effects after withdrawal from long-term benzodiazepine use: a meta-analysis. Arch Clin Neuropsychol. 2004; 19(3):437–454. DOI: 10.1016/S0887-6177(03)00096-9 [PubMed: 15033227]

Brands B, Blake J, Marsh DC, Sproule B, Jeyapalan R, Li S. The impact of benzodiazepine use on methadone maintenance treatment outcomes. Journal of Addictive Diseases. 2008; 27(3):37–48. DOI: 10.1080/10550880802122620

Carrier E, McNeely J, Lobach I, Tay S, Gourevitch MN, Raven MC. Factors associated with frequent utilization of crisis substance use detoxification services. Journal of Addictive Diseases. 2011; 30(2):116–122. DOI: 10.1080/10550887.2011.554776 [PubMed: 21491293]

CDC. Centers for Disease Control and Prevention-ranging online data for epidemiologic research (WONDER). Atlant, GA: National Center for Health Statistics; 2016.

Chen KW, Berger CC, Forde DP, D'Adamo C, Weintraub E, Gandhi D. Benzodiazepine use and misuse among patients in a methadone program. BMC Psychiatry. 2011; 11:90.doi: 10.1186/1471-244X-11-90 [PubMed: 21595945]

Chen LH, Hedegaard H, Warner M. Drug-poisoning Deaths Involving Opioid Analgesics: United States, 1999–2011. NCHS Data Brief. 2014; (166):1–8.

Clark AK, Wilder CM, Winstanley EL. A systematic review of community opioid overdose prevention and naloxone distribution programs. Journal of Addiction Medicine. 2014; 8(3):153–163. DOI: 10.1097/ADM.0000000000000034 [PubMed: 24874759]

Darke S, Ross J, Mills K, Teesson M, Williamson A, Havard A. Benzodiazepine use among heroin users: baseline use, current use and clinical outcome. Drug and Alcohol Review. 2010; 29(3):250–255. DOI: 10.1111/j.1465-3362.2009.00101.x [PubMed: 20565516]

de las Cuevas C, Sanz EJ, de la Fuente JA, Padilla J, Berenguer JC. The Severity of Dependence Scale (SDS) as screening test for benzodiazepine dependence: SDS validation study. Addiction. 2000; 95(2):245–250. [PubMed: 10723853]

Eiroa-Orosa FJ, Haasen C, Verthein U, Dilg C, Schafer I, Reimer J. Benzodiazepine use among patients in heroin-assisted vs. methadone maintenance treatment: findings of the German randomized controlled trial. Drug and Alcohol Dependence. 2010; 112(3):226–233. DOI: 10.1016/j.drugalcdep.2010.06.013 [PubMed: 20708349]

Fatseas M, Lavie E, Denis C, Auriacombe M. Self-perceived motivation for benzodiazepine use and behavior related to benzodiazepine use among opiate-dependent patients. Journal of Substance Abuse Treatment. 2009; 37(4):407–411. DOI: 10.1016/j.jsat.2009.03.006 [PubMed: 19339146]

Frank D, Mateu-Gelabert P, Guarino H, Bennett A, Wendel T, Jessell L, Teper A. High risk and little knowledge: overdose experiences and knowledge among young adult nonmedical prescription opioid users. Int J Drug Policy. 2015; 26(1):84–91. DOI: 10.1016/j.drugpo.2014.07.013 [PubMed: 25151334]

Gelkopf M, Bleich A, Hayward R, Bodner G, Adelson M. Characteristics of benzodiazepine abuse in methadone maintenance treatment patients: a 1 year prospective study in an Israeli clinic. Drug and Alcohol Dependence. 1999; 55(1–2):63–68. [PubMed: 10402150]

Jann M, Kennedy WK, Lopez G. Benzodiazepines: a major component in unintentional prescription drug overdoses with opioid analgesics. J Pharm Pract. 2014; 27(1):5–16. DOI: 10.1177/0897190013515001 [PubMed: 24436437]

Jones JD, Mogali S, Comer SD. Polydrug abuse: a review of opioid and benzodiazepine combination use. Drug and Alcohol Dependence. 2012; 125(1–2):8–18. DOI: 10.1016/j.drugalcdep.2012.07.004 [PubMed: 22857878]

Kerr T, Fairbairn N, Tyndall M, Marsh D, Li K, Montaner J, Wood E. Predictors of non-fatal overdose among a cohort of polysubstance-using injection drug users. Drug and Alcohol Dependence. 2007; 87(1):39–45. DOI: 10.1016/j.drugalcdep.2006.07.009 [PubMed: 16959438]

Kindy K, Keating D. Risky along, deadly together. The Washington Post. 2016 Aug 31.

Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire-2: validity of a two-item depression screener. Med Care. 2003; 41(11):1284–1292. DOI: 10.1097/01.MLR.0000093487.78664.3C [PubMed: 14583691]

Kroenke K, Spitzer RL, Williams JB, Lowe B. An ultra-brief screening scale for anxiety and depression: the PHQ-4. Psychosomatics. 2009; 50(6):613–621. DOI: 10.1176/appi.psy.50.6.613 [PubMed: 19996233]

Kroenke K, Spitzer RL, Williams JB, Monahan PO, Lowe B. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. Annals of Internal Medicine. 2007; 146(5):317–325. [PubMed: 17339617]

Lavie E, Fatseas M, Denis C, Auriacombe M. Benzodiazepine use among opiate-dependent subjects in buprenorphine maintenance treatment: correlates of use, abuse and dependence. Drug and Alcohol Dependence. 2009; 99(1–3):338–344. DOI: 10.1016/j.drugalcdep.2008.07.017 [PubMed: 18824311]

Longo LP, Johnson B. Addiction: Part 1. Benzodiazepines-Side effects, abuse risk and alternatives. American Family Physician. 2000; 61(7):2121–2128. [PubMed: 10779253]

Manthey C, Mern DS, Gutmann A, Zielinski AJ, Herz C, Lassmann S, Hasskarl J. Elevated endogenous expression of the dominant negative basic helix-loop-helix protein ID1 correlates with significant centrosome abnormalities in human tumor cells. BMC Cell Biol. 2010; 11:2.doi: 10.1186/1471-2121-11-2 [PubMed: 20070914]

Mark TL, Dilonardo JD, Chalk M, Coffey RM. Trends in inpatient detoxification services, 1992–1997. Journal of Substance Abuse Treatment. 2002; 23(4):253–260. S0740547202002714 [pii]. [PubMed: 12495787]

National Institute on Alcohol Abuse and Alcoholism. Helping Patients Who Drink Too Much: A Clinician's Guide. NIH Publication No. 07–3769. Rockville, MD: National Institutes of Health; 2005.

Nielsen S, Dietze P, Lee N, Dunlop A, Taylor D. Concurrent buprenorphine and benzodiazepines use and self-reported opioid toxicity in opioid substitution treatment. Addiction. 2007; 102(4):616–622. DOI: 10.1111/j.1360-0443.2006.01731.x [PubMed: 17286641]

Nordfjaern T. A population-based cohort study of anxiety, depression, sleep and alcohol outcomes among benzodiazepine and z-hypnotic users. Addictive Behaviors. 2012; 37(10):1151–1157. DOI: 10.1016/j.addbeh.2012.05.017 [PubMed: 22704915]

O'Brien CP. Benzodiazepine use, abuse, and dependence. J Clin Psychiatry. 2005; 66(Suppl 2):28–33.

Paulozzi LJ, Strickler GK, Kreiner PW, Koris CM. Centers for Disease C., & Prevention. Controlled Substance Prescribing Patterns--Prescription Behavior Surveillance System, Eight States, 2013. MMWR Surveill Summ. 2015; 64(9):1–14. DOI: 10.15585/mmwr.ss6409a1

Posternak MA, Mueller TI. Assessing the risks and benefits of benzodiazepines for anxiety disorders in patients with a history of substance abuse or dependence. The American Journal on Addictions. 2001; 10(1):48–68. [PubMed: 11268828]

Rapoport MJ, Lanctot KL, Streiner DL, Bedard M, Vingilis E, Murray B, … Herrmann N. Benzodiazepine use and driving: a meta-analysis. J Clin Psychiatry. 2009; 70(5):663–673. DOI: 10.4088/JCP.08m04325 [PubMed: 19389334]

Rooney S, Kelly G, Bamford L, Sloan D, O'Connor JJ. Co-abuse of opiates and benzodiazepines. Ir J Med Sci. 1999; 168(1):36–41. [PubMed: 10098342]

Ross J, Darke S. The nature of benzodiazepine dependence among heroin users in Sydney, Australia. Addiction. 2000; 95(12):1785–1793. DOI: 10.1080/09652140020011090 [PubMed: 11177494]

Rowe C, Santos GM, Behar E, Coffin PO. Correlates of overdose risk perception among illicit opioid users. Drug and Alcohol Dependence. 2016; 159:234–239. DOI: 10.1016/j.drugalcdep.2015.12.018 [PubMed: 26754425]

SAMHSA. The TEDS Report: Substance Abuse Treatment Admissions for Abuse of Benzodiazepines. Rockville, MD: Center for Behavioral Health Statistics and Quality; 2011.

Schuman-Olivier Z, Hoeppner BB, Weiss RD, Borodovsky J, Shaffer HJ, Albanese MJ. Benzodiazepine use during buprenorphine treatment for opioid dependence: clinical and safety outcomes. Drug and Alcohol Dependence. 2013; 132(3):580–586. DOI: 10.1016/j.drugalcdep.2013.04.006 [PubMed: 23688843]

Stein MD, Anderson BJ, Thurmond P, Bailey GL. Comparing the life concerns of prescription opioid and heroin users. Journal of Substance Abuse Treatment. 2015; 48(1):43–48. DOI: 10.1016/j.jsat.2014.07.001 [PubMed: 25171955]

Stein MD, Kanabar M, Anderson BJ, Lembke A, Bailey GL. Reasons for Benzodiazepine Use Among Persons Seeking Opioid Detoxification. Journal of Substance Abuse Treatment. 2016; 68:57–61. DOI: 10.1016/j.jsat.2016.06.008 [PubMed: 27431047]

Substance Abuse and Mental Health Services Administration. The DASIS Report: Admissions for detoxification, 2001. Rockville, MD: Office of Applied Studies; 2004.

Vogel M, Knopfli B, Schmid O, Prica M, Strasser J, Prieto L, … Dursteler-Macfarland KM. Treatment or "high": benzodiazepine use in patients on injectable heroin or oral opioids. Addictive Behaviors. 2013; 38(10):2477–2484. DOI: 10.1016/j.addbeh.2013.05.008 [PubMed: 23770646]

Volkow ND, Frieden TR, Hyde PS, Cha SS. Medication-assisted therapies--tackling the opioid-overdose epidemic. New England Journal of Medicine. 2014; 370(22):2063–2066. DOI: 10.1056/NEJMp1402780 [PubMed: 24758595]

White JM, Irvine RJ. Mechanisms of fatal opioid overdose. Addiction. 1999; 94(7):961–972. [PubMed: 10707430]

Wilder CM, Miller SC, Tiffany E, Winhusen T, Winstanley EL, Stein MD. Risk factors for opioid overdose and awareness of overdose risk among veterans prescribed chronic opioids for addiction or pain. Journal of Addictive Diseases. 2016; 35(1):42–51. DOI: 10.1080/10550887.2016.1107264 [PubMed: 26566771]

Wu LT, Ling W, Burchett B, Blazer DG, Shostak J, Woody GE. Gender and racial/ethnic differences in addiction severity, HIV risk, and quality of life among adults in opioid detoxification: results from the National Drug Abuse Treatment Clinical Trials Network. Subst Abuse Rehabil. 2010; 2010(1):13–22. DOI: 10.2147/SAR.S15151 [PubMed: 21709734]

Highlights

- Over half of persons initiating inpatient opioid detoxification used a BZD in the prior month.
- BZD users (versus non-users) were more likely to be female and non-Hispanic White.
- BZD users (versus non-users) were more likely to report use of concurrent substances and past year overdose.
- Overall, BZD users accurately perceived the risks of BZD use.
- BZD users were less accurate than non-BZD users with respect to some BZD-related consequences.

Table 1

Background Characteristics by Recent Benzodiazepine Use. Significant Differences in **Bold**.

		Recent Benzodiazepine Use		
	Sample (n = 476)	**No (n = 231)**	**Yes (n = 245)**	**χ2 or t (p =)**
Years Age	32.2 (± 8.64)	32.0 (± 8.72)	32.3 (± 8.59)	−0.34 (.732)
Gender (Male)	339 (71.2%)	**178 (77.1%)**	**161 (65.7%)**	**7.62 (.006)**
Hispanic Ethnicity	42 (8.8%)	**30 (13.0%)**	**12 (4.9%)**	**9.67 (.002)**
Race				
White	412 (86.6%)	197 (84.9%)	222 (88.5%)	
Black	26 (5.5%)	13 (5.6%)	13 (5.2%)	1.69 (.429)
Other	38 (8.0%)	22 (9.5%)	16 (6.4%)	
Years Education	11.8 (± 1.87)	11.6 (± 1.98)	12.0 (± 1.75)	−1.81 (.071)
Detox From Heroin (Yes)	412 (86.6%)	202 (87.5%)	210 (85.7%)	0.31 (.580)
Recent IDU (Yes)[a]	327 (68.7%)	149 (64.5%)	178 (72.7%)	3.67 (.055)
Recent Cocaine Use (Yes)[a]	197 (41.4%)	**84 (36.4%)**	**113 (46.2%)**	**4.67 (.031)**
Recent Stimulant Use (Yes [a b]	37 (7.8%)	**12 (5.2%)**	**25 (10.2%)**	**4.16 (.041)**
Hazardous Drinking (Yes)	115 (24.2%)	**44 (19.1%)**	**71 (29.0%)**	**6.40 (.011)**
Recent Overdose (Yes)[c]	119 (25.1%)	**40 (17.3%)**	**79 (32.4%)**	**14.33 (<.001)**
PHQ-2 Depression	3.73 (± 2.01)	**3.39 (± 2.08)**	**4.06 (± 1.88)**	**−3.65 (<.001)**
PHQ-2 Depression ≥ 3	310 (66.7%)	**137 (59.8%)**	**173 (73.3%)**	**9.50 (.002)**
PHQ-2 Anxiety	3.71 (± 2.15)	**3.28 (± 2.29)**	**4.14 (± 1.91)**	**−4.40 (<.001)**
PHQ-2 Anxiety ≥ 3	298 (64.4%)	**125 (54.6%)**	**173 (73.9%)**	**18.89 (<.001)**

[a]Recent IDU, cocaine use, and stimulant use were defined as any reported use during the past 30-days.

[b]Stimulant use included any reported use of methamphetamines.

[c]Recent overdose was defined as overdose within the past 12-months.

Table 2

Beliefs About Benzodiazepines by Recent Benzodiazepine Use (n and % reporting they believe the statement is true). Statistically Significant Differences are in **Bold.**

	Full Sample	**Recent BZD Use**		
	(n = 476)	**No (n=231)**	**Yes (n=245)**	**χ^2 (p =)**
Benzos can make depression worse.	344 (72.3%)	**186 (80.5%)**	**158 (64.5%)**	**15.24 (<.001)**
Benzos can Increase the risk of overdosing from opiates.	439 (92.2%)	212 (91.8%)	227 (92.7%)	0.13 (.721)
Benzos can fog a person's thinking.	445 (93.5%)	218 (94.4%)	227 (92.7%)	0.58 (.447)
Benzos can be addictive.	457 (96.1%)	218 (94.4%)	239 (97.6%)	3.13 (.077)
Benzos can make you feel overtired during the day.	442 (92.9%)	214 (92.6%)	228 (93.1%)	0.03 (.859)
Benzos can increase the risk of a driving accident.	448 (94.1%)	216 (93.5%)	232 (94.7%)	0.30 (.582)
Benzos can cause withdrawal if you stop suddenly.	449 (94.3%)	216 (93.5%)	233 (95.1%)	0.57 (.452)
Benzos can cause problems staying in methadone or buprenorphine treatment.	394 (82.8%)	**200 (86.6%)**	**194 (79.2%)**	**4.56 (.033)**