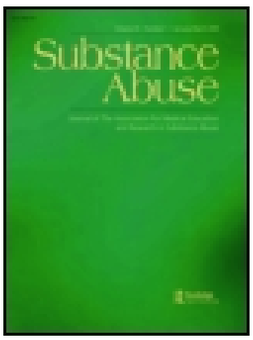

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BRIEF REPORT

Polysubstance use in a Brazilian national sample: Correlates of co-use of alcohol and prescription drugs

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ABSTRACT

Background: Responses to problem substance use have largely focused on illicit drugs, but reports on rising prescription drug misuse worldwide raise questions about their combined use with alcohol and potential consequences. The current study assessed prevalence of alcohol in conjunction with nonmedical opioid and benzodiazepine use across a nationally representative sample of adults in Brazil. *Methods:* Cross-sectional data on prevalence were estimated from the 2015 Brazilian Household Survey on Substance Use. We estimated past month nonmedical use of benzodiazepines and alcohol and past month nonmedical use of opioids and alcohol among adults who reported any past-year alcohol use. Zero-inflated Poisson models assessed independent correlates of alcohol and nonmedical opioid use, and alcohol and nonmedical benzodiazepine use. *Results:* Among adults who reported past year alcohol use, 0.4% ($N = 257{,}051$) reported past month alcohol and non-medical benzodiazepine use, and 0.5% ($N = 337{,}333$) reported past month alcohol and non-medical opioid use. Factors independently associated with co-use of alcohol and benzodiazepines included having depression (adjusted prevalence ratio (aPR):4.61 (95%CI 1.76–12.08)), anxiety (aPR:4.21 (95%CI 1.59–11.16)) and tobacco use (aPR: 5.48 (95%CI 2.26–13.27)). Factors associated with past-month alcohol and opioid use included having experienced physical or a threat of violence (aPR: 4.59 (95%CI 1.89–11.14)), and tobacco use (aPR:2.81(95%CI:1.29–6.12)). *Conclusions:* Co-use of prescription drugs with alcohol remains relatively rare among Brazilians, but findings point to a unique profile of persons at risk. Results of this study are important in light of changing dynamics and international markets of prescription drugs and the need for more research on use of these substances on a global scale.

KEYWORDS
Polysubstance; Latin America; prescription drugs; alcohol

1. Introduction

The ongoing US crisis of overdose deaths has shocked the global field of addiction and public health.[1] After decades of efforts to reduce access to illicit drugs, rising deaths and despair instigated by prescription drugs have shed light on the hidden realities of substance misuse.[2] Similarly, Latin American research and drug policy attention has historically focused on illicit drugs, particularly cocaine and marijuana. Brazil, specifically, has been largely consumed with crack-cocaine and legal battles over marijuana, with little attention to other illicit drugs. Alcohol remains one of the biggest drivers of substance-related problems in Brazil, albeit largely normalized by social customs.[3–5] Until recently, the nonmedical use of prescription opioids was thought to be largely nonexistent in Brazil. But findings on rising sales of prescription opioids throughout Brazil[6] and reported national rates of nonmedical prescription opioid use comparable to US rates in the early 2000s[7] have begun to change this picture. Nonmedical misuse of benzodiazepines, on the other hand, has been reported in Brazil since the 1980s,[8,9] but recent rising trends in benzodiazepine misuse[10] have further directed attention to prescription drug misuse in Brazil.

In view of potentially increasing prescription drug use in Brazil and elsewhere,[11] along with historically high rates of alcohol use, concerns arise about co-use of alcohol and prescription drugs. Simultaneous use of alcohol with prescription opioids or benzodiazepines has been reported in other settings[12–14] and the interaction of these central nervous system depressants is known to increase overdose risk.[15,16] While prior studies documented trends in prescription drug use, patterns of co-use of alcohol with prescription opioids or benzodiazepines has not been previously examined in Brazil. Thus, little is known about prevalence and demographic profiles or risk factors associated with such patterns of co-use. To address this gap, we assess the prevalence of

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co-use of alcohol with nonmedical benzodiazepine and nonmedical opioid use across a nationally representative sample of Brazilian adults and evaluate individual risk factors for co-use of these substances.

2. Methods

2.1. Data and setting

Data were gathered from the 2015 Brazilian Household Survey on Substance Use (BHSU-3), a representative national survey estimating epidemiologic parameters of substance use among Brazilians. Eligible participants included residents 12–65 living in private or collective households in an all Brazilian territories. Data were collected from 16,273 individuals who consented to the study between May and December, 2015. Estimates from participating individuals were weighted to represent a total population of 153,095,166 Brazilians (132,818,779 adults 18+), through a stratified multi-stage probability sample, the design of which was described at length elsewhere.[17,18] The Ethics Review Board of FIOCRUZ approved this study (CAAE #35283814.4.0000.5241). For the current analysis, only adults who reported any alcohol use in the 12 months before the interview were included (total analytic population estimate: 61,432,928).

2.2. Substance use measures

Alcohol use, nonmedical use of benzodiazepines and nonmedical use of opioids were assessed using three questions: Ever-used; used in the last 12 months; and used in the last 30 days. Nonmedical benzodiazepine use and nonmedical opioid use were defined as using such medications in a way not prescribed for own use or using in a way different than prescribed. Examples of benzodiazepines given included Diazepam, Rivotril®, Vallium®, Lexotan®, Olcadil®, Lorax®, Frontal®, which were the benzodiazepines most frequently mentioned by participants in a pilot study. Examples of opioids included Tylex®, Dolantina®, Codein® and Codex®. Measures and examples were field tested and revised based on pilot questionnaires in Rio de Janeiro. Interviewers additionally had access to a comprehensive list of all brand and generic benzodiazepine and opioid products listed in the Brazilian Thesaurus of Medicines ("DEF").[19]

Co-use outcomes of interest were defined as (1) indicating both past-month alcohol use and past-month benzodiazepine use; and (2) indicating both past-month alcohol use and past-month opioid use. Consistent with prior literature, we focused on past-month use of both substances[20] to capture current and potential concurrent use.

2.3. Risk factors for co-use

Primary covariates assessed as risk factors for co-use outcomes included sociodemographic characteristics (sex, age, race, education, monthly family income, employment, and residing in a capital city); as well as available health and substance use measures that have been associated with poly-substance use in prior research[14,21] (self-rated health, diagnosed depression, diagnosed anxiety, having a past-year experience of physical or a threat of violence, and past-year cocaine and tobacco use) (Appendix Table 1 provides a list of all covariates and their corresponding survey questions).

2.4. Analysis

For each substance, we estimated 12-month and 30-day weighted prevalence and 95% confidence intervals for adults using alcohol in the past 12 months. Prevalence and respective 95% confidence intervals were estimated considering the complex sampling design, including weights and calibration of the use of the respective substances.

Then we compared the distribution of sociodemographic, health, and substance use characteristics across those with and without past month co-use of alcohol and benzodiazepines and alcohol and opioids. Chi-square tests with Rao–Scott adjustment were used to test independence across the groups and significance level was set at 5%. Finally, we used zero-inflated Poisson models to assess independent factors associated with past-month alcohol and benzodiazepine use and past-month alcohol and opioid use.[22] Zero-inflated Poisson models were used given the outcomes of co-use were rare and this approach is effective for modeling rare outcomes with multiple zeros.[23,24] This approach has been previously used to effectively estimate prevalence ratios for rare binary outcomes in national survey data.[25] To achieve a parsimonious model, all variables with chi-squared p-values below 0.25 were included in a stepwise backward elimination zero-inflated Poisson model (with forced inclusion of sex and age group). Prevalence and chi-square tests with Rao–Scott adjustment analyses were conducted in R v.4.0.2 (survey and srvyr libraries) and zero-inflated Poisson models were conducted in Stata12.0. Our manuscript followed the STROBE checklist for reporting.[26]

3. Results

Overall, 61,432,928 adults were estimated to have used alcohol in the 12 months prior to the interview (46.2% of Brazilian adults). Of these, 0.4% reported past month use of both alcohol and benzodiazepines and 0.5% had past month use of both alcohol and opioids. Appendix Table 2 presents additional data on past year and past-month prevalence of nonmedical use of prescription opioids and benzodiazepines across the national population.

Table 1 displays the distribution of sociodemographic, health and substance use risk factors for persons with past-year alcohol use, comparing those with and without co-use of benzodiazepines, and those with and without co-use of opioids. Those who used both alcohol and benzodiazepines differed statistically ($p \leq 0.05$) from those who used alcohol without benzodiazepines in that they were more likely to be female (73.1% vs. 41.8%, $p = 0.01$), more likely to self-rate their health as poor or very poor (35.3% vs. 2.7%, $p < 0.001$), to report a prior diagnosis of depression (51.7%

Table 1. Distribution (%) of demographic characteristics, depression, anxiety, violence and substance use among those with and without past-month co-use of alcohol and benzodiazepines and alcohol and opioids, among adults reporting past year alcohol use ($N = 61,432,928$).

Variables	Total	Alcohol without Benzo diazepines $N = 61,175,877$	Alcohol and Benzo diazepines $N = 257,051$	p value	Alcohol without Opioids $N = 61,095,595$	Alcohol and Opioids $N = 337,333$	p value
Sex							
Male	58.0	58.2	27.0	0.01	58.1	42.6	0.14
Female	42.0	41.8	73.1		41.9	57.4	
Age							
18–24	19.3	19.4	5.3		19.4	15.4	0.76
25–44	49.6	49.6	46.1	0.22	49.6	56.0	
45–65	31.0	31.0	48.6		31.0	28.6	
Race							
White	46.0	46.0	47.8	0.90	46.0	46.1	0.99
Nonwhite	54.0	54.0	52.2		54.0	53.9	
Education							
Less than high school	46.8	46.8	52.3		46.9	38.0	0.56
High school	39.4	39.5	28.1	0.61	39.4	48.5	
College or more	13.8	13.7	19.6		13.8	13.5	
Monthly family income							
R$0.0–R$1,500.00	43.2	43.2	50.5	0.61	43.3	28.3	0.11
R$1,501.00+	56.8	56.8	49.5		56.7	71.7	
Employed							
No	31.4	31.4	30.9	0.97	31.41	22.6	0.28
Yes	68.8	68.6	69.1		68.6	77.4	
Self-rated health							
Excellent/good	76.5	76.6	47.4	<0.001	76.6	77.0	0.82
Fair	20.5	20.6	17.3		20.6	21.3	
Poor/very poor	2.8	2.7	35.3		2.9	1.7	
Depression							
No	94.5	94.7	48.3	<0.001	94.6	87.3	0.05
Yes	5.4	5.2	51.7		5.4	12.6	
Anxiety							
No	85.1	85.3	33.3	<0.001	85.2	74,2	0.05
Yes	14.9	14.7	66.6		14.8	25.8	
Past-year physical or threat of violence							
No	91.9	92.0	91.8	0.96	92.1	70.3	<0.001
Yes	8.0	8.0	8.2		7.9	29.7	
Past-year cocaine use							
No	98.4	98.4	94.7	0.08	98.4	100.0	0.51
Yes	1.6	1.6	5.3		1.6	0.0	
Past-year tobacco use							
No	75.4	75.2	31.0	<0.001	75.3	51.1	<0.001
Yes	24.8	24.8	69.0		24.7	48.9	
Reside in capital cities							
No	74.2	74.2	70.6	0.75	74.1	87.6	0.08
Yes	25.8	25.8	29.4		25.9	12.4	

vs. 5.2%, $p < 0.001$) and anxiety (66.6% vs. 14.7%, $p < 0.001$) and to use tobacco in the past year (69.0% vs. 24.8%, $p < 0.001$). Those who used both alcohol and opioids differed statistically from those used alcohol without opioids in that they were more likely to report a prior diagnosis of depression (12.6% vs. 5.5%, $p = 0.05$) and anxiety (25.8% vs. 14.8%, $p = 0.05$), to have reported a past-year experience of physical or a threat of violence (48.9% vs. 24.7%%, $p < 0.001$) and to use tobacco in the past year (48.9% vs. 24.7%, $p < 0.001$).

Figure 1 presents results of the adjusted zero-Poisson inflated regression models. Factors independently associated with co-use of alcohol and benzodiazepines (Figure 1a) included having a diagnosis of depression (adjusted prevalence ratio (aPR: 4.61 (95% CI 1.76–12.08)), anxiety (aPR:4.21 (95% CI 1.59–11.16)) and tobacco use (aPR:5.48 (95% CI 2.26–13.27)). Factors associated with past-month alcohol and opioid use (Figure 1b) included having experienced physical or a threat of violence (aPR: 4.59 (95% CI 1.89–11.14)), and tobacco use (aPR:2.81(95% CI:1.29–6.12)).

4. Discussion

The current study assessed patterns of polysubstance use of alcohol and prescription drugs in a nationally representative sample of Brazilian adults. Past-year prevalence of alcohol use (46.2%) was found to be similar to estimates from prior Brazilian household surveys,[27] although comparisons are challenged by distinct sampling, weighting and analysis methodologies across surveys.[18] Still, this prevalence is significantly lower than that of past-year alcohol use among US adults in the same year (70.1%),[28] which is consistent with World Health Organization estimates in which the US has one of the highest rates of alcohol use in the Americas.[29] Overall, prevalence of any lifetime nonmedical use of opioids was found to be slightly lower than that of nonmedical use of benzodiazepines (3.0% vs. 4.3%) but past-month prevalence was higher for opioids (0.6% vs. 0.4%). As a comparison, in the US, past-month nonmedical use of opioids is markedly higher than in Brazil but use of benzodiazepines is lower (respectively 2.4% and 0.2%).[30] As benzodiazepine misuse has historically been

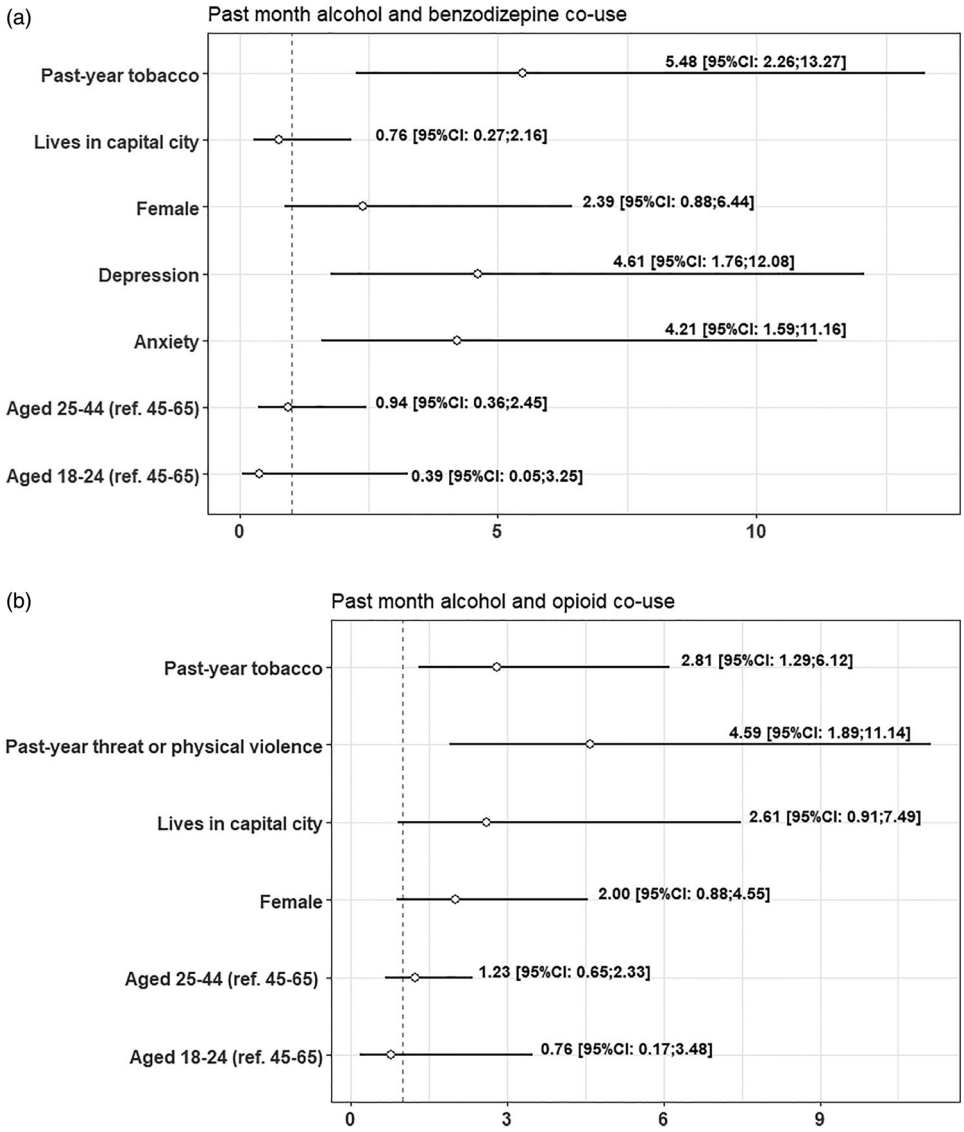

Figure 1. Adjusted prevalence ratios for past month alcohol and benzodiazepine co-use and alcohol and opioid co-use calculated with Zero-Poisson inflated regression models, Brazil 2015.

subject to greater research in Brazil,[31] findings on higher rates of past-month nonmedical use of opioids may imply a need for greater attention to these types of prescription medications.

We were particularly interested in examining co-use of alcohol and prescription drugs given people who use multiple substances tend to have more severe substance use and health problems and are at greater risks of overdose, especially when using multiple depressants.[32,33] When we examined risk factors for both past-month use of alcohol and benzodiazepines and past-month use of alcohol and opioids, we found important similarities and differences between these groups: Both types of polysubstance users were more likely to be female, over age 25, and employed. Using tobacco was associated with both co-use of alcohol and benzodiazepines and alcohol and opioids, but was much more prevalent among alcohol and benzodiazepine users. People who used alcohol and benzodiazepines were much more likely to report depression and anxiety and to have worse self-rated health, indicating this population may experience higher morbidity overall. However, having experienced physical or a threat of violence was only associated with use of alcohol and opioids.

Prior studies on polysubstance use have similarly found that comorbid mental health and substance use conditions are associated with greater polysubstance use,[14,21,34–36] and have also emphasized that demographic risk profiles for polysubstance use vary substantially depending on the substances involved.[32] For example, a study focused on illicit substances in multiple Latin American countries found greater polysubstance use among younger men.[20] In contrast, prior research among college students in Brazil found women to be at greater risk of alcohol and prescription sedative and stimulant use.[37] This variation in profiles points to the need to develop targeted research and interventions to address co-use of specific substances and underlying health needs across multiple risk groups.

This study is subject to several limitations. First, data are cross sectional and do not allow for assessment of causality. Data were derived from surveys of adults residing in

Brazilian households, and are therefore subject to self-report bias and exclude populations who are hospitalized or incarcerated or who are not stably housed. Given co-use of substances of interest are relatively rare events, many estimates have wide confidence intervals. Last, we could not determine whether substances were used simultaneously or separately during the defined past-month period.

Results of the present study are important in light of changing dynamics and international markets of prescription drugs and the need for more research on use of these substances beyond North America.[11,38] Public health responses to misuse of legal alcohol and prescription drugs may require unique and distinct strategies from those targeting illicit drug use. Future work should focus on understanding underlying causes for non-medical use of these substances, including undertreated physical and emotional distress or increased marketing on behalf of drug companies. In addition, more research is needed to understand sources for acquiring these substances through both legal (e.g., physician prescribing) and illegal (e.g., black market) means. Future research and public health responses that work to better measure and address polysubstance use rather than focus on one substance at a time are needed to improve more effective responses to substance-related harms in Latin America and across the globe.

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Author contributions

NK drafted the manuscript; JM conducted the primary analyses; PLNS, MV, and NB carried out sampling design and planning of the survey; CC oversaw the execution of the survey, data collection and analysis; MC contributed to conceptualization of the manuscript and analysis; FIB was the principal investigator for the survey, oversaw data collection and analysis and contributed to the manuscript. All authors significantly revised and reviewed the manuscript and approved of the final version.

Disclaimer

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any agency of the Brazilian government.

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Appendix Table 1. Covariate measures and corresponding survey questions and response options (English translation)

Study variable	Survey question	Response options
Sex	What is your sex?	Male; Female
Age	What is your age?	(integer)
Race	What is your color or race?	White; Black; Yellow; Mixed race; Indigenous[a]
Education	What is your level of education?	No formal education and incomplete primary school; full primary school and incomplete high school; full high school and incomplete college; full college
Monthly family income	What is your family income?	Without income; up to R$ 750.00; between R$ 750.00 and R$ 1,500.00; between R$ 1,501.00 and R$ 3,000.00; between R$ 3,001.00 and R$ 6,000.00; between R$ 6,001 and R$9,000.00; more than R$9,000.00; don't know; refuse to respond
Employed	What is your current employment situation?	Regular employment with fixed schedule; irregular employment without fixed schedule (freelancing); unemployed and actively looking for work; out of the labor market not working and not actively looking for work
Self-rated health	In general, how do you consider your health?	Excellent; good; fair; poor; very poor
Depression	Has a doctor or another health professional told you you have depression?	Yes; no; don't know; refuse to respond
Anxiety	Has a doctor or another health professional told you you have anxiety?	Yes; no; don't know; refuse to respond
Physical or threat of violence	In the last 12 months, have you been a victim of any of the following situations: A. A threat of being hit, pushed, or kicked B. Being hit, pushed, or kicked C. A beating or attempted strangulation (hanging) D. Stabbing or shooting E. Being threatened with a knife or fire weapon	No; yes
Past-year cocaine use	In the last 12 months, have you used cocaine?	Yes; no; don't know; refuse to respond
Past-year tobacco use	In the last 12 months, have you used marijuana?	Yes; no; don't know; refuse to respond

Note. All survey questions were originally in Portuguese and translated to English by members the research team that include both native Portuguese and English speakers.
[a]Race categories reflect typical census categorization of race/skin color in Brazil.

Appendix Table 2. Point prevalence and respective 95% confidence intervals of alcohol, nonmedical opioid use, and nonmedical benzodiazepine among adults 18+, Brazil, 2015

Substance	Users	Prevalence (%)	95% CI
Prevalence among all Brazilian adults 18+ ($N = 132,818,779$)[a]			
Alcohol use			
Past year	61,432,928	46.2	44.7–47.8
Past month	44,251,673	33.3	31.9–34.7
Nonmedical benzodiazepines use			
Past year	1,980,106	1.5	1.2–1.8
Past month use	566,507	0.4	0.3–0.6
Nonmedical prescription opioid use			
Past year	2,025,494	1.5	1.2–1.9
Past month use	863,775	0.6	0.5–0.9
Prevalence among analytic sample of adults reporting past-year alcohol use ($N = 61,432,928$)			
Past month alcohol and benzodiazepine co-use	257,051	0.4	0.2–0.7
Past month alcohol and opioid co-use	337,333	0.5	0.4–0.8

[a]Population estimates derived from complex sample design and application of sampling weights to the study sample (16,273). See Silva et al. (2018), for details on survey design and analysis.[17]