



## ORIGINAL ARTICLE

# Psychoactive substance abuse and dependence and its association with anxiety disorders: a population-based study of young adults in Brazil

Mariana B. de Matos,<sup>1</sup> Christian L. de Mola,<sup>2</sup> Jéssica P. Trettim,<sup>1</sup> Karen Jansen,<sup>1</sup> Ricardo A. da Silva,<sup>1</sup> Luciano D. de Mattos Souza,<sup>1</sup> Liliane da Costa Ores,<sup>1</sup> Mariane L. Molina,<sup>1</sup> Fernanda T. Coelho,<sup>1</sup> Ricardo T. Pinheiro,<sup>1</sup> Luciana de A. Quevedo<sup>1</sup>

<sup>1</sup>Programa de Pós-Graduação em Saúde e Comportamento, Universidade Católica de Pelotas (UCPel), Pelotas, RS, Brazil. <sup>2</sup>Centro de Estudos Epidemiológicos, Universidade Federal de Pelotas (UFPeL), Pelotas, RS, Brazil.

**Objective:** To evaluate the association between abuse of and dependence on different psychoactive substances and the presence of anxiety disorders in a sample of young adults from a city in southern Brazil.

**Methods:** Between 2007 and 2009, we carried out a cross-sectional, population-based study of individuals aged 18-24 years who lived in Pelotas, a city in southern Brazil. We evaluated anxiety disorders using the Mini International Neuropsychiatric Interview 5.0 (MINI), and use of psychoactive substances with the Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST 2.0/OMS). We used Fisher's exact test for univariate analysis, and Poisson regression models with robust variance for multivariable analysis.

**Results:** The sample consisted of 1,560 young adults. The overall prevalence of abuse/dependence was 26.9% for alcohol, 24.9% for tobacco, and 7.3% for illicit substances. Individuals with agoraphobia had a 32% higher prevalence of tobacco abuse/dependence (prevalence ratio [PR] = 1.32 [95%CI 1.01-1.74]). Individuals with posttraumatic stress disorder (PTSD) or generalized anxiety disorder (GAD) had a 2.41-fold (95%CI 1.22-4.77) and 1.76-fold (95%CI 1.00-3.11) higher prevalence of illicit substance abuse/dependence, respectively.

**Conclusion:** In this population-based sample, we found associations between GAD, PTSD, and increased prevalence of illicit substance abuse/dependence. In addition, individuals with agoraphobia seem to have increased tobacco abuse/dependence.

**Keywords:** Epidemiology; adolescents; alcohol abuse; anxiety disorder, generalized; adult development

## Introduction

Young adulthood is a critical period for the transition from recreational to problematic use of psychoactive substances, including nicotine.<sup>1</sup> Studies show a prevalence of around 30% for tobacco use in this period, and 13% for alcohol abuse or dependence. According to the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC),<sup>2</sup> about 70% of young adults in the United States consumed alcohol in the year preceding the survey. Moreover, this prevalence may increase in the presence of anxiety disorders, as shown in a study by Mondin et al.<sup>3</sup>

Anxiety disorders include generalized anxiety disorder (GAD), obsessive-compulsive disorder (OCD), panic disorder (PD), social anxiety disorder (SAD), agoraphobia and posttraumatic stress disorder (PTSD).<sup>4</sup> All are characterized by anxiety-like symptoms, but each features particular psychopathological features.<sup>5</sup> The overall prevalence of

anxiety disorders is high; this group comprises the most frequent mental disorders in the general population. According to population-based surveys, up to 33.7% of individuals are affected by an anxiety disorder during their lifetime, usually following a chronic course, but there is a natural decrease in prevalence with advancing age.<sup>6,7</sup>

Studies are being conducted to assess whether a causal relationship exists between substance use and anxiety disorders. Different authors have proposed that the relationship between substance use or abuse and anxiety disorders occurs in individuals who experience negative feelings and, consequently, use these substances as a form of coping with them.<sup>8,9</sup> Some individuals may use substances non-abusively in an attempt to alleviate symptoms of anxiety. However, tobacco, alcohol, and drug use can be linked to reduced medication effectiveness and exacerbation of psychiatric symptoms.<sup>10</sup>

A study examined the relation between comorbid and pure (non-comorbid) anxiety disorders and both substance dependence and substance use problems in a community sample of 1,747 young adults aged 18-23 years, and found that, collectively, anxiety disorders – both pure and comorbid with other psychiatric diagnoses – were predictive of substance dependence.<sup>11</sup>

Correspondence: Mariana Bonati de Matos, Programa de Pós-Graduação em Saúde e Comportamento, Universidade Católica de Pelotas (UCPel), Rua Gonçalves Chaves, 373/411, CEP 96015-560, Pelotas, RS, Brazil. E-mail: marianabonatidematos@gmail.com

Submitted Feb 20 2017, accepted Oct 30 2017, Epub Feb 15 2018.

One explanation for this relationship is provided by the biological pathways linking anxiety disorders with the use and abuse of different legal and illegal substances. Research has shown that substance use in this setting is probably driven by the feeling of relief it provides, with a reduction in symptoms of anxiety, produced by interactions with the  $\Delta$ 9-THC, GABAergic, glutamatergic, serotonergic, and noradrenergic neurotransmitters.<sup>12</sup> However, there is still no consensus on the etiological mechanism of substance use in anxiety.

A meta-analysis published in 2017 by Groenman et al. stressed the importance of early detection and intervention in anxiety disorders to prevent substance-related disorders in adult life.<sup>5</sup> However, even though some studies have established an association between presence of any anxiety disorder and substance use or abuse, few have related specific disorders with specific substances; such data has come mostly in clinical settings, not from population-based studies.<sup>13-17</sup>

Within this context, this study aimed to evaluate the association between abuse of and dependence on different psychoactive substances and presence of different anxiety disorders in a sample of young adults from a city in southern Brazil.

## Methods

### *Sample and procedure*

This was a cross-sectional, population-based study of young adults (aged 18 to 24 years) living in the urban area of Pelotas, state of Rio Grande do Sul, Brazil. Sample selection was performed by clusters, considering a population of 39,667 in the age range of interest, according to the latest census of 448 sectors in the city.<sup>18</sup>

To ensure the necessary sample size, 89 census-based sectors were randomly selected. Household selection within the sectors was performed according to a systematic sampling process, the first house being the one on the corner designated by the Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatística – IBGE) as starting the sector; every third house thereafter was selected. Canvassing was performed by trained interviewers, who, after identifying the subjects, explained the aims of the study. Data collection was conducted from 2007 to 2009.

The study included seven interviewers, all of whom were undergraduate psychology or physical therapy students of Universidade Católica de Pelotas (UCPel). The interviewers were trained to administer the instrument by psychologists with extensive experience, and weekly meetings were conducted throughout the data collection period. All interviews were conducted at respondents' homes, and lasted about 40 minutes.

### *Instruments*

The sociodemographic characteristics of interest were gender, age, cohabitation, educational attainment (highest degree obtained), employment status (i.e., having a job at the time of the interview), and socioeconomic class

(based on ownership of durable and consumer goods, according to the Brazilian Association of Research Companies classification).<sup>19</sup>

Anxiety disorders (GAD, OCD, PD, SAD, agoraphobia, PTSD) and manic and hypomanic episodes were evaluated using the Mini International Neuropsychiatric Interview 5.0 (MINI).<sup>20</sup> We also evaluated the number of stressful events during the last year using the Social Readjustment Rating Scale of Holmes and Rahe<sup>21</sup> and depressive symptom intensity using the Beck Depression Inventory.<sup>22</sup>

In addition, we used the Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST 2.0/OMS), validated for Brazil,<sup>23,24</sup> to evaluate occasional use (0-3 points), substance abuse (4-15 points), and possible dependence (16-20 points) on tobacco, alcohol, marijuana, cocaine, amphetamines, inhalants, sedatives, hallucinogens, and opiates. We also included crack cocaine in the list of psychoactive substances explored. ASSIST items quantify the intensity, frequency, and problems associated with use of these substances.

### *Statistical analyses*

For bivariate analysis, we used Fisher's exact test to evaluate prevalence differences between groups. For this analysis, we divided illicit substances into five groups, according to Carlini<sup>25</sup>: stimulants (cocaine and amphetamines), central nervous system depressants (inhalants, sedatives, and opioids), disruptors (hallucinogens), cannabis, and crack. For each substance class, respondents were classified as occasional users or abusers/dependent. The abuse and dependence categories were merged due to the small sample size in the dependence category.

In addition, using Poisson regression with robust variance, we calculated prevalence ratios (PR) and evaluated three outcomes in crude and multivariable models: tobacco abuse/dependence, alcohol abuse/dependence, and abuse/dependence of at least one illicit substance. In this analysis, all illicit substances were pooled into a single variable, which was evaluated dichotomously (abuse of/dependence on at least one illicit substance vs. no abuse/dependence), in order to ensure greater power for analysis, given the small number of individuals who abused/were dependent on each of these substances individually.

The main exposure variables were the different anxiety disorders. All multivariable models were adjusted for socio-demographic characteristics, number of stressful events in the past year, depressive symptoms, and manic and/or hypomanic episode (at least one). In addition, models were adjusted for having any anxiety disorder other than that which constituted the main exposure variable in each model. Moreover, we also included as a possible confounder the presence of abuse/dependence of substances other than the outcome of interest. Statistical analysis was performed using STATA 9.0 software.

### *Ethical issues*

This project was approved by the UCPel ethics committee (protocol no. 2006/96). All participants provided written

informed consent. Subjects who were diagnosed as having any psychiatric disorders and/or drug abuse/dependence were referred for outpatient psychiatric care.

**Results**

The sampling strategy identified 1,762 young adults, of whom 202 (11.5%) refused to participate. Thus, the sample consisted of 1,560 young adults with a mean (SD) age of 20.5 (2.1) years. Of these, 56.4% were women, 48.1% were in the lower middle class, 46.0% were students, and 66.0% were employed. The overall prevalence of abuse/dependence was 24.9% for tobacco, 26.9% for alcohol, and 7.3% for illicit substances.

The prevalence of anxiety disorders is shown in Table 1. On univariate analysis, we observed that OCD was more prevalent among those who were abusing/dependent on alcohol (p = 0.012). The prevalence of GAD (p = 0.006), OCD (p < 0.001), agoraphobia (p = 0.014), and PTSD (p < 0.001) was significantly higher among those who abused/were dependent on stimulant substances. Cannabis abuse/dependence was more prevalent among all anxiety disorders, except panic disorder. Abuse/dependence of crack cocaine was higher only among those diagnosed with PTSD (p < 0.001). Disrupting substances were not associated with any anxiety disorder (Table 1).

Adjusted analysis showed that young individuals with agoraphobia had a 32% higher prevalence of tobacco abuse/dependence than individuals without this disorder (PR = 1.32 [95%CI 1.01-1.74]). Individuals who had PTSD or GAD had a higher prevalence of abuse/dependence of illicit substances compared to those without these disorders (PR = 2.41 [95%CI 1.22-4.77] and PR = 1.76 [95%CI 1.00-31.1], respectively) (Table 2).

In addition, when carrying this analysis using the variable use of illicit substances as continuous (number of illicit drugs for which abuse/dependence was detected), the risk of consuming illicit substances among those who had PTSD was 4.33 (95%CI 1.78-10.50) times higher than in those without PTSD.

**Discussion**

The aim of this study was to evaluate the association between abuse/dependence of different psychoactive substances with anxiety disorders in a sample of young adults from a city in southern Brazil. We found that young individuals with agoraphobia had a higher prevalence of tobacco abuse/dependence and that there is an increased risk of illicit substance abuse/dependence in individuals with GAD or PTSD.

The relationship between each type of anxiety disorder and substance abuse/dependence is still not well established, especially in young adults. A recent meta-analysis found that childhood anxiety disorders are risk factors for substance abuse in adult life. These findings emphasize the need for early detection and intervention to prevent debilitating substance-related disorders in later life.<sup>5</sup>

Other research has found a reduction in anxiety and depressive symptoms among adolescents who received

**Table 1** Prevalence of anxiety disorders and its association with abuse of/dependence on legal and illicit substances in young adults from the city of Pelotas, Rio Grande do Sul, Brazil

	Legal substances		Illicit substances									
	Tobacco		Alcohol		CNS depressants		Stimulants		Cannabis		Crack cocaine	
	n (%)	p-value	n (%)	p-value	n (%)	p-value	n (%)	p-value	n (%)	p-value	n (%)	p-value
GAD	152 (9.7)	0.001	49 (32.2)	0.139	14 (9.2)	< 0.001	10 (6.6)	0.006	13 (8.6)	0.001	3 (2.0)	0.425
OCD	51 (3.3)	0.004	22 (43.1)	0.012	4 (7.8)	0.032	7 (13.7)	< 0.001	8 (15.7)	0.001	2 (3.9)	0.167
PD	39 (2.5)	0.03	12 (30.8)	0.708	8 (20.5)	< 0.001	2 (5.1)	0.674	1 (2.6)	0.803	1 (2.6)	0.872
SAD	63 (4.0)	0.044	22 (34.9)	0.184	7 (11.1)	< 0.001	4 (6.3)	0.166	7 (11.1)	0.031	2 (3.2)	0.276
Agoraphobia	192 (12.3)	< 0.001	62 (32.3)	0.084	11 (5.7)	0.003	11 (5.7)	0.014	17 (8.9)	0.006	4 (2.1)	0.242
PTSD	32 (2.1)	0.002	11 (34.4)	0.443	5 (15.6)	< 0.001	5 (15.6)	< 0.001	5 (15.6)	0.011	4 (12.5)	< 0.001
Overall	1,560 (100.00)	-	419 (26.9)	-	37 (2.2)	-	43 (2.8)	-	73 (4.7)	-	16 (1.0)	-

CNS = central nervous system; GAD = generalized anxiety disorder; OCD = obsessive-compulsive disorder; PD = panic disorder; PTSD = posttraumatic stress disorder; SAD = social anxiety disorder.  
 All p-values obtained using Fisher's exact test for the association between each anxiety disorder and abuse/dependence of each substance.  
 Disruptors (hallucinogens) were not included in the table because only four participants reported intake of these substances.

**Table 2** Crude and multivariable analysis of tobacco, alcohol, and illicit substance abuse/dependence and their association with anxiety disorders

	Tobacco		Alcohol		Illicit substances	
	Crude PR (95%CI)	Adjusted PR (95%CI)	Crude PR (95%CI)	Adjusted PR (95%CI)	Crude PR (95%CI)	Adjusted PR (95%CI)
GAD	1.53 (1.21-1.92)	0.96 (0.72-1.28)	1.23 (0.96-1.57)	1.03 (0.75-1.44)	2.87 (1.93-4.28)	1.76 (1.00-3.11)
OCD	1.77 (1.28-2.46)	0.91 (0.54-1.53)	1.64 (1.18-2.27)	1.13 (0.69-1.86)	4.14 (2.55-6.73)	0.49 (0.21-1.16)
PD	1.67 (1.14-2.46)	0.91 (0.57-1.45)	1.15 (0.71-1.85)	1.08 (0.67-1.74)	3.34 (1.83-6.10)	0.69 (0.25-1.88)
SAD	1.49 (1.07-2.09)	0.9 (0.55-1.47)	1.32 (0.93-1.86)	0.95 (0.60-1.54)	3.6 (2.23-5.83)	0.93 (0.41-2.12)
Agoraphobia	1.6 (1.30-1.96)	1.32 (1.01-1.74)	1.24 (0.99-1.55)	0.92 (0.67-1.27)	2.54 (1.73-3.75)	0.98 (0.50-1.94)
PTSD	2.05 (1.43-2.93)	0.86 (0.53-1.40)	1.29 (0.79-2.09)	0.71 (0.36-1.36)	4.59 (2.66-7.93)	2.41 (1.22-4.77)

95%CI = 95% confidence interval; GAD = generalized anxiety disorder; OCD = obsessive-compulsive disorder; PD = panic disorder; PTSD = posttraumatic stress disease; SAD = social anxiety disorder.

Multivariable models adjusted for gender, age, socioeconomic status, educational attainment, working in the last year, studying in the last year, cohabitation, number of stressful events in the last year, another anxiety disorder, depressive symptoms, manic and/or hypomanic episode, and abuse/dependence of other substances.

treatment for substance abuse.<sup>26</sup> These findings have important clinical implications, indicating that the focus of intervention may be broader than substance use and abuse, and may be useful in reducing anxiety symptoms as well as having an impact on the likelihood of late diagnosis.

In a cross-sectional study of 155 individuals, McCabe et al. evaluated smoking behaviors across three anxiety disorders: PD with or without agoraphobia, SAD, and OCD. They found that smokers were more prevalent in the PD group (40.4%) compared to the SP (20%) and OCD (22.4%) groups.<sup>27</sup> On the other hand, in a 10-year longitudinal study with adolescents and adults, Swendsen et al. found that five of seven anxiety disorders (PD, specific phobia, SAD, PTSD, and separation anxiety) were predictors of at least one form of substance dependence; however, agoraphobia was not associated.<sup>28</sup>

A previous study with hospitalized patients found that those diagnosed with GAD were more likely to have a history of illicit drug abuse compared to those without this disease.<sup>29</sup> However, studies showing a clear relationship between GAD and illicit drug use are scarce.

Regarding PTSD, a review study that aimed to understand the relationship between PTSD and dependence on illicit substances showed a strong association between both, but the origin of symptoms remained unclear.<sup>30</sup> One hypothesis for this association is that the problems associated with substance abuse increase the risk for PTSD secondary to exposure of the subject to traumas. Substance use could also intensify the effects of trauma, leading to the onset of PTSD.<sup>31</sup> In our study, we also found an association between PTSD and use/abuse of illegal drugs, but did not assess a potential relationship with exposure to traumatic situations.

Some limitations of this study should be pointed out. First, although we have found associations between some anxiety disorders and substance abuse or dependence, we cannot establish the causality of these relationships. Even when the logical direction of events is that anxiety disorders could lead to greater abusive use of psychoactive substances, we cannot rule out that use of some of these substances could actually lead to or trigger onset of some anxiety symptoms or other mental disorders. A prospective design could be a better approach for elucidating

these causal pathways. However, even though causality could not be established, we have identified groups at risk for substance abuse.

The prevalence of illicit substance use and abuse may have been underestimated. Due to the young age of the population, illegal nature of these substances, and potential for social stigmatization, we may have misclassified some individuals. However, there is no reason to suspect that anxiety disorders would have been misclassified on the basis of substance use. Consequently, our results probably were not biased in this sense. Nevertheless, there may have been some degree of non-differential misclassification, which could have underestimated some of the analyzed associations with illicit substances. The use of a social desirability scale could have avoided this limitation. As for the generalizability of our findings, although the study was conducted in a single city, the present results can be generalized for the same age group to other communities with a similar culture.

As for positive aspects, this was one of the first studies to evaluate the risk of substance abuse and anxiety disorders with a population-based design, in a middle-income country, using a validated diagnostic tool to evaluate mental disorders. Another strength was the sample selection, which meant that data were derived from a representative sample of young adults.

It is essential to identify individuals with a tendency to develop anxiety disorders with increasing consumption of alcohol, tobacco, and other drugs, while also searching for determinants or factors associated with behavior change, especially in young adults. This may help guide actions for the prevention and treatment of problems resulting from use of psychoactive substances.<sup>32</sup>

## Disclosure

The authors report no conflicts of interest.

## References

- 1 Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005;62:593-602.

- 2 Substance Abuse and Mental Health Services Administration (SAMHSA). Results from the 2013 national survey on drug use and health: summary of national findings. Rockville: Substance Abuse and Mental Health Services Administration; 2014. HHS Publication N° (SMA) 14-4887.
- 3 Mondin TC, Konradt CE, Cardoso Tde A, Quevedo Lde A, Jansen K, Mattos LD, et al. Anxiety disorders in young people: a population-based study. *Rev Bras Psiquiatr.* 2013;35:347-52.
- 4 Pires AJ, Casanova CC, Quevedo Lde A, Jansen K, Silva RA. Panic disorder and psychoactive substance use in primary care. *Trends Psychiatry Psychother.* 2014;36:113-8.
- 5 Groenman AP, Janssen TW, Oosterlaan J. Childhood psychiatric disorders as risk factor for subsequent substance abuse: a meta-analysis. *J Am Acad Child Adolesc Psychiatry.* 2017;56:556-69.
- 6 Martin P. The epidemiology of anxiety disorders: a review. *Dialogues Clin Neurosci.* 2003;5:281-98.
- 7 Bandelow B, Michaelis S. Epidemiology of anxiety disorders in the 21st century. *Dialogues Clin Neurosci.* 2015;17:327-35.
- 8 Johnson JG, Cohen P, Pine DS, Klein DF, Kasen S, Brook JS. Association between cigarette smoking and anxiety disorders during adolescence and early adulthood. *JAMA.* 2000;284:2348-51.
- 9 Roberts MC, Emsley RA, Pienaar WP, Stein DJ. Anxiety disorders among abstinent alcohol-dependent patients. *Psychiatr Serv.* 1999; 50:1359-61.
- 10 Ziedonis D, Nickou C. Substance abuse in patients with schizophrenia. In: Hwang MY, Bermanzohn PC, editors. *Schizophrenia and comorbid conditions: diagnosis and treatment.* Washington: American Psychiatric Association; 2001. p. 187-222.
- 11 Lopez B, Turner RJ, Saavedra LM. Anxiety and risk for substance dependence among late adolescents/young adults. *J Anxiety Disord.* 2005;19:275-84.
- 12 Crippa JA, Zuardi AW, Martín-Santos R, Bhattacharyya S, Atakan Z, McGuire P, et al. Cannabis and anxiety: a critical review of the evidence. *Hum Psychopharmacol.* 2009;24:515-23.
- 13 Encrenaz G, Kovess-Masféty V, Jutand MA, Carmona E, Sapinho D, Messiah A. Use of psychoactive substances and health care in response to anxiety and depressive disorders. *Psychiatr Serv.* 2009; 60:351-7.
- 14 Clark DB, Pollock N, Bukstein OG, Mezzich AC, Bromberger JT, Donovan JE. Gender and comorbid psychopathology in adolescents with alcohol dependence. *J Am Acad Child Adolesc Psychiatry.* 1997;36:1195-203.
- 15 Marmorstein NR, White HR, Loeber R, Stouthamer-Loeber M. Anxiety as a predictor of age at first use of substances and progression to substance use problems among boys. *J Abnorm Child Psychol.* 2010;38:211-24.
- 16 Swendsen JD, Merikangas KR, Canino GJ, Kessler RC, Rubio-Stipec M, Angst J. The comorbidity of alcoholism with anxiety and depressive disorders in four geographic communities. *Compr Psychiatry.* 1998;39:176-84.
- 17 Schuckit MA, Irwin M, Brown SA. The history of anxiety symptoms among 171 primary alcoholics. *J Stud Alcohol.* 1990;51:34-41.
- 18 Instituto Brasileiro de Geografia e Estatística (IBGE). Geociências [Internet]. 2008 May 15 [cited 2017 Nov 13]. [https://downloads.ibge.gov.br/downloads\\_geociencias.htm](https://downloads.ibge.gov.br/downloads_geociencias.htm).
- 19 Associação Brasileira de Empresas de Pesquisa (ABEP). Dados com base no Levantamento Sócio Econômico 2003 [Internet]. [cited 2008 May]. [www.abep.org/criterio-brasil](http://www.abep.org/criterio-brasil).
- 20 Amorim P. Mini International Neuropsychiatric Interview (MINI): validação de entrevista breve para diagnóstico de transtornos mentais. *Rev Bras Psiquiatr.* 2000;22:106-15.
- 21 Savoia MG. Escalas de eventos vitais e de estratégias de enfrentamento (coping). *Rev Psiquiatr Clin.* 1999;26:57-67.
- 22 Cunha JA. Manual da versão em português das Escalas Beck. São Paulo: Casa do Psicólogo; 2001.
- 23 Henrique IF, De Micheli D, Lacerda RB, Lacerda LA, Formigoni ML. [Validation of the Brazilian version of Alcohol, Smoking and Substance Involvement Screening Test (ASSIST)]. *Rev Assoc Med Bras (1992).* 2004;50:199-206.
- 24 Humeniuk R, Ali RL, World Health Organization (WHO). Validation of the alcohol, smoking and substance involvement screening test (ASSIST) and pilot brief intervention: a technical report of phase II findings of the WHO ASSIST project [Internet]. 2006 [cited 2017 Nov 13]. [http://www.who.int/substance\\_abuse/activities/assist\\_technical\\_report\\_phase2\\_final.pdf](http://www.who.int/substance_abuse/activities/assist_technical_report_phase2_final.pdf).
- 25 Carlini EA. Drogas psicotrópicas. In: Noto AR, Nappo S, Galduróz JCF, Mattei R, Carlini EA. III Levantamento sobre o Uso de Drogas entre Meninos e Meninas em Situação de Rua de Cinco Capitais Brasileiras – 1993. São Paulo: Centro Brasileiro de Informações sobre Drogas Psicotrópicas, Departamento de Psicobiologia da Escola Paulista de Medicina; 1994. p. 93-7.
- 26 Horigian VE, Weems CF, Robbins MS, Feaster DJ, Ucha J, Miller M, et al. Reductions in anxiety and depression symptoms in youth receiving substance use treatment. *Am J Addict.* 2013;22:329-37.
- 27 McCabe RE, Chudzik SM, Antony MM, Young L, Swinson RP, Zolvensky MJ. Smoking behaviors across anxiety disorders. *J Anxiety Disord.* 2004;18:7-18.
- 28 Swendsen J, Conway KP, Degenhardt L, Glantz M, Jin R, Merikangas KR, et al. Mental disorders as risk factors for substance use, abuse and dependence: results from the 10-year follow-up of the National Comorbidity Survey. *Addiction.* 2010;105:1117-28.
- 29 Compton WM 3rd, Cottler LB, Jacobs JL, Ben-Abdallah A, Spitznagel EL. The role of psychiatric disorders in predicting drug dependence treatment outcomes. *Am J Psychiatry.* 2003;160:890-5.
- 30 Dantas HS, Andrade AG. Comorbidade entre transtorno de estresse pós-traumático e abuso e dependência de álcool e drogas: uma revisão da literatura. *Rev Psiquiatr Clin.* 2008;35:55-60.
- 31 Jacobsen LK, Southwick SM, Kosten TR. Substance use disorders in patients with posttraumatic stress disorder: a review of the literature. *Am J Psychiatry.* 2001;158:1184-90.
- 32 Horta RL, Horta BL, Pinheiro RT, Moraes B, Strey MN. [Tobacco, alcohol, and drug use by teenagers in Pelotas, Rio Grande do Sul State, Brazil: a gender approach]. *Cad Saude Publica.* 2007;23: 775-83.