Prevalence of Substance Use among Psychotic Patients and Determining Its Strongest Predictor

Seyyedeh Bentolhoda Mousavi1, Peter Higgs2, Negar Piri3, Ensieh Sadri4, Matina Pourghasem4, Sanaz Jafarzadeh Fakhari5, Mehdi Noroozi1, Mojtaba Miladinia6, Elaheh Ahounbar5, Asaad Sharhani7*

Abstract

Objective: Although comorbidity of psychotic disorders and substance use can lead to increase in mortality, less is known about the outbreak and predictors. Psychotic patients tend to be overlooked during assessment; hence, the possibility of an undertreated or missed condition such as increasing substance use. This investigation aimed to measure the prevalence of substance use in psychotic patients and to survey the powerful predictors.

Method: In a 1-year cross-sectional study, 311 psychotic patients were assessed using the Structured Interview Based on DSM-5 for diagnostic confirmation as well as questions surveying prevalence and possible predictors of substance use.

Results: Prevalence of substance use among psychotic patients was 37.9%. Several variables were identified as factors associated with drug abuse among the psychotic patients. These included male gender, younger age, being currently homeless, a history of imprisonment, and having family history of drug use. The strongest predictors of substance use, however, were family history of drug use, male gender, and being currently homelessness.

Conclusion: Policymakers should note the importance of substance use among psychotic patients. Developing active screening strategies and comprehensive preventive plans, especially in the high-risk population, is suggested.

Key words: Psychiatry; Substance-Related Disorders; Mental Disorders

1. Psychosis Research Center, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran.
2. Department of Public Health, La Trobe University, Bundoora, 3083 Australia.
3. School of Public Health and Safety, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
4. Department of Psychiatry, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran.
5. Student Research Committee, School of Nursing and Midwifery, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
6. Substance Abuse and Dependence Research Center, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran.
7. Department of Epidemiology and Biostatistics, School of Public Health, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

*Corresponding Author:
Address: International Affairs Office, Ahvaz Jundishapur University of Medical Sciences, Golestan Street, Ahvaz, Iran, Postal Code: 6135715794.
Tel: 98-61 3337789, Fax: 98-61 33738580, Email: sharhani-a@ajums.ac.ir - Second Email: Asaadsharhani3@gmail.com

Article Information:
Received Date: 2020/04/02, Revised Date: 2020/05/28, Accepted Date: 2020/06/13
Drug use is a prevalent comorbidity in mental health disorders with approximately 50% reported comorbidity and it can negatively affect the outcome with increased risk of suicide and self-destructive behaviors (1, 2). Drug use can both aggravate clinical presentations and obscure symptoms. It predisposes and perpetuates conditions, such as aggression, mood instability, cognitive deficits, psychosis, and even negative symptoms (3-5). In many cases it is impossible to distinguish whether the symptoms precede or are triggered by the substance use even after obtaining a comprehensive history (6).

Psychosis, as an experience of dissociation with the real world, shares the same etiology with addiction and both are related to dopamine dysregulation (7-9). Psychosis indicates the severity of many disorders and disrupt functionality. It also increases the burden of the disease, deteriorates the outcome, and increases morbidity and mortality (8, 10-12). Despite the prominence, prognostic role, and prevalence of substance use in psychotic disorders, the predictors remain poorly understood.

The main focus of the previous investigations has been on assessing the risk factors of substance use in distinct diagnostic categories, such as bipolar disorder and schizophrenia. For instance, according to a meta-analysis, prevalence of substance use was 42% in schizophrenia patients (1). In this study, using drugs was associated with early onset of the disorder and the prevalence increased over time. Meta-analysis on bipolar disorder have also shown a high comorbidity of more than 40%; however, specific risk factors has remained controversial (2, 13, 14). Such correlations and controversies around risk factors highlights the importance of addressing the factors associated with substance use in high-risk groups.

Diagnostic categories can be unstable over time and might substitute each other. Psychosis could be accurately considered as an etiological phenomenon; therefore, addressing it as an individual clinical syndrome, which has attracted significant interest among scholars (7). Numerous complications are associated with accurately estimating the prevalence of drug use, such as stigmatization, the religious and legal constraints that make respondents reluctant to reveal information about their status of substance use (19). This is aggravated in psychosis patients, as there are many barriers in communication. Patients with psychosis are often neglected, stigmatized, isolated, or misunderstood, as they might receive less attention from health care professionals and families (8, 11). Unique requirements of individuals who experience psychosis and comorbid substance use highlights the importance of identifying the outbreak and correlates to map the preventive strategies to reduce the likelihood of developing substance use disorder in at risk patients and to plan comprehensive treatment plans. To the best of our knowledge, this is the first attempt to determine the demographic characterization, prevalence, and correlates of substance use among psychotic patients, independent of their categorical diagnostic classification and comparison.

Materials and Methods

Participants and Setting

A cross-sectional study was conducted in a random hospital sample of 311 psychotic patients admitting to the Razi Psychiatry Hospital in Tehran from October 2017 to November 2018, based on their medical record. The sample size was calculated assuming the prevalence of substance use to be 35% with a precision of 5%, a confidence level of 95%, and 80% power of the study. The calculated sample size was 320. Systematic random sampling method was used on the basis of the medical record numbers. Those who met the study inclusion criteria were assessed applying the Structured Clinical Interview for DSM-5 (SCID-5) to confirm their diagnosis. We also surveyed them by questions in terms of the prevalence rate and associated predicting factors of substance use. Other classifications were the duration of psychotic disorder and any existing comorbidities.

The study inclusion criteria were as follow: recovery from a psychotic episode and hospital discharge (based on the medical records), and participating in clinical interviews conducted by the psychiatry residents. The study exclusion criteria included the presence of severe cognitive or negative symptoms, reporting adverse effects of medications that could interfere with the interview procedure.

Measures

A researcher-made scale was designed in accordance with the opinions of a 10-member expert panel, consisting of epidemiologists and psychiatrists. Kappa coefficient and intraclass correlation coefficient (ICC) were applied to assess the reliability of the questionnaire. ICC was calculated between 0.84 to 1, and the kappa coefficient was measured as 0.9 to 1 for all study variables. The required data were collected through face-to-face interviews conducted by 3 trained psychiatry residents.

Ethics

This investigation was approved by the ethics committee affiliated with the University of Social Welfare and Rehabilitation Sciences, Iran (IR.USWR.REC.1396.70). Written informed consent was obtained, and participants' anonymity was ensured throughout the investigation.

Data Analysis

The mean (SD) and frequency and percentage were used to express the continuous variables, and the categorical variables. The relationship between substance abuse and its associated factors were estimated by logistic regression analysis, ie, presented as odds ratio (OR) and 95% confidence interval (CI). The variables with P < 0.2 were included in multiple regression analyses. The statistical analysis was performed in SPSS.
Results
In total, 311 patients were included to analysis. The study participants' mean (SD) age was 37.7 (12.3) years (age range, 18-77 y). Most study samples were unemployed (80.1%), and a small number were homeless (4.5%). In addition, 34.7% were married and 29.3% reported a history of imprisonment (Table 1). Furthermore, 37.9% of the participants reported recent substance use (right before admission into the hospital). Table 2 showing the demographic and behavioral characteristics of the participants in each group and the type and time of substances used, respectively.

The data achieved from the bivariate analysis identified several associated factors with substance use in the samples. These variables were male gender, younger age (26-49y), current homelessness, a history of imprisonment, and a family history of substance use (Table 3). According to the final model of the study, the most significant factor associated with substance use was found to be age (OR = 7.26; CI: 3.34-15.93). The adjusted OR for those with a family history of substance use was 6.15 times higher than that of those without such history (P = 0.000). The OR of substance use was 5.32 among homeless participants; however, this value was not significant in the final study model. The adjusted OR of substance use in those with a history of imprisonment was 1.64, compared to those without such history; however, it was not significant (P = 0.108). We also observed that younger age and male gender were statistically significant in the final model of study.

Thus, male gender, age, a family history of drug use, and current homelessness were the strongest predictors of substance use among the explored patients with psychosis (Table 3).

Table 1. The Demographic Characteristics of Substance Use among Psychiatric Patients

| Characteristics                                             | Number | Percent |
|-------------------------------------------------------------|--------|---------|
| Gender                                                      |        |         |
| Female                                                      | 106    | 34.1%   |
| Male                                                        | 205    | 65.9%   |
| Marital status                                              |        |         |
| Single                                                      | 203    | 65.3%   |
| Married                                                     | 108    | 34.7%   |
| Illiterate                                                  | 23     | 7.4%    |
| Literacy                                                    |        |         |
| Literate                                                   | 288    | 92.6%   |
| Employed                                                    | 62     | 19.9%   |
| unemployed                                                  | 249    | 80.1%   |
| Living with family                                          |        |         |
| Yes                                                        | 297    | 95.5%   |
| no                                                         | 14     | 4.5%    |
| Place of residence                                          |        |         |
| Urban                                                      | 275    | 88.4%   |
| Rural                                                      | 36     | 11.6%   |
| Substance use                                               |        |         |
| Yes                                                        | 193    | 63%     |
| no                                                         | 118    | 37%     |
| yes                                                       | 109    | 35.4%   |
| no                                                         | 202    | 64.6%   |
| yes                                                       | 75     | 24.1%   |
| no                                                         | 236    | 75.9%   |
| Bipolar Disorder                                            |        |         |
| Yes                                                        | 85     | 28%     |
| Substance induced psychotic disorder                        |        |         |
| Schizophrenia                                               |        |         |
| Yes                                                        | 69     | 22.7%   |
| Schizoaffective disorder                                    |        |         |
| Yes                                                        | 25     | 8.2%    |
| Unspecified psychotic disorder                              |        |         |
| Yes                                                        | 15     | 4.8%    |
| MDD                                                        |        |         |
| Yes                                                        | 12     | 3.9%    |
| Multi diagnosis                                             |        |         |
| Yes                                                        | 13     | 4.3%    |
| Dementia                                                    |        |         |
| Yes                                                        | 3      | 1%      |
| General Medical condition                                  |        |         |
| Yes                                                        | 3      | 1%      |
| Others                                                     |        |         |
| Yes                                                        | 4      | 1.3%    |
Table 2. Prevalence of Substance Use among Psychotic Patients and Determining Its Strongest Predictor

| Characteristics          | SUD (n=118) (37.9%) | No drug abuse (n=193) (62.1%) | P-value |
|--------------------------|---------------------|-------------------------------|---------|
| Gender                   | female              | 16 (13.7)                     | 90 (46.9) | 0.000 |
|                          | male                | 101 (86.3)                    | 102 (53.1) |       |
|                          | ≤25                 | 25 (21.2)                     | 30 (15.5) |       |
| Age, group (years)       | 26-49               | 75 (66.1)                     | 111 (57.5) | 0.2   |
|                          | ≥ 50                | 15 (12.7)                     | 52 (26.9) |       |
| Education                | ≤9                  | 77 (65.3)                     | 103 (53.4) | 0.03  |
|                          | >9                  | 41 (34.7)                     | 90 (46.6) |       |
| Marital status           | Single              | 78 (66.1)                     | 125 (64.8) | 0.9   |
|                          | Married             | 40 (33.9)                     | 68 (35.2) |       |
| Occupation               | Employed            | 30 (25.4)                     | 32 (16.6) |       |
|                          | Unemployed          | 88 (74.6)                     | 161 (83.4) | 0.07  |
| History of imprisonment  | Yes                 | 56 (47.5)                     | 35 (18.1) | 0.000 |
|                          | No                  | 62 (52.5)                     | 158 (81.9) |       |
| Currently Homelessness   | Yes                 | 10 (8.5)                      | 4 (2.1) | 0.011 |
|                          | No                  | 108 (91.5)                    | 189 (97.9) |       |

Chi-square test was used. Significant level (P value less than 0.05).

Table 3. Multiple Logistic Regression Analysis Results for Factors Associated with Substance Use in Psychotic Patients

| Characteristics          | Category | Unadjusted OR(95% CI) | P-value for Unadjusted OR | AOR**(95% CI) | P-value for adjusted OR |
|--------------------------|----------|------------------------|---------------------------|---------------|-------------------------|
| Age                      | Score    | 0.97(0.95-0.99)        | 0.004                     | 0.97(0.95-0.99) | 0.030                   |
|                          | Female   | 1                      |                           |               | 1                       |
|                          | Male     | 5.57(3.06-10.13)       | 0.000                     | 7.26(3.34-15.93) | 0.000                   |
| Occupation               | Employed | 1                      |                           |               | 1                       |
|                          | Unemployed | 1.71(0.97-3.0)       | 0.06                      | 1.14(0.58-2.24) | 0.703                   |
|                          | ≤9       | 1.64(1.02-2.63)        | 0.40                      |               |                         |
|                          | >9       | 1                      |                           |               | 1                       |
| Homelessness             | Yes      | 4.37(1.34-14.28)       | 0.015                     | 5.32(1.17-24.09) | 0.030                   |
|                          | No       | 1                      |                           |               | 1                       |
| Place of residency       | Urban    | 1                      |                           |               | 1                       |
|                          | rural    | 0.91(0.44-1.88)        | 0.81                      |               |                         |
| Family history of drug use| No       | 1                      |                           |               | 1                       |
|                          | Yes     | 6.33(3.57-11.24)       | 0.000                     | 6.15(3.08-12.25) | 0.000                   |
| HIV test result          | No       | 1                      |                           |               | 1                       |
|                          | Yes     | 10.28(1.22-86.53)      | 0.032                     | 3.26(0.30-34.64) | 0.326                   |
| History of imprisonment  | No       | 1                      |                           |               | 1                       |
|                          | Yes     | 4.07(2.43-6.82)        | 0.000                     | 1.64(0.89-3.03) | 0.108                   |

*Odds Ratio
**Adjusted Odds Ratio
Logistic regression was used. Significance level: P<0.2 for univariate and P<0.05 for multiple regression analysis.
Discussion
The present study explored the prevalence rate of substance use and associated factors in patients with psychosis, was done in an educational hospital of psychiatric. In this study, bipolar disorder, substance induced psychotic disorder, and schizophrenia were the most prevalent diagnostic groupings, respectively. We detected a high prevalence of substance use among all patients with psychotic, which is in line with the preceding studies in both clinical and community settings (2, 13, 14).

The most common type of used substance was opioids in all forms. This is consistent with existing epidemiologic research in Iran (15). This can be due to cultural influence that play an important part in start and continuing substance use. Opiates are more available in Iran; their consumption is even considered as a cultural norm in some areas (15, 16). Even though there is more recent research showing an increasing pattern of injecting heroin as well as stimulants use, traditional inhalation of opium remains the leading form of its consumption (15, 17-19).

The second most frequently abused drugs before the current admission in hospital was hypnotics and sedatives; however, most of the participants were prescribed with benzodiazepines in a hospital or as a medication by psychiatrists; thus, these were legally consumed. The next most prevalent abused drug was methamphetamine compounds (known as crystal or shisheh in Iran). Data on the prevalence rate of stimulant use among psychiatric patients in Iran are scarce. However, population-based investigations of recent decades discovered an increasing pattern for abusing this substance (16, 17). As a key substance to induce or trigger psychosis, amphetamine disrupt dopaminergic regulation in the brain (20). The current findings show the necessity of addressing amphetamine use in psychotic patients more rigorously.

The rate of alcohol drinking was well below the global epidemiological studies. Worldwide, 25% of patient with schizophrenia (1) and bipolar disorder (13) are prone to develop an alcohol use disorder at some life stage. Alcohol consumption is much less prevalent in Asia (21, 22), including Iran (15, 23). Cultural and religious restrictions and legal factors meaningfully influence availability of certain drugs. These data, however, should be interpreted cautiously. Though the anonymity of data was observed, these characteristics escalate stigma and is a barrier of revealing true levels of consumption. Some researches in specific clinical settings have found that after opiates, alcohol is the second most prevalent substance (24). Thus, further study in this topic is required. The use of Cannabis is massively shown to be associated with chronic psychotic syndromes (1, 25, 26). In the present study, however, only a few patients have reported consuming Cannabis. This is consistent with previous epidemiologic reports of substance use in Iran, which do not consider cannabis as a prevalent drug of use (15, 16, 24).

The strongest associated of substance abuse in the participants included male gender, younger age, a family history of drug use disorders, having a history of imprisonment, and current homelessness. Previous studies have shown that males are 2-3 times more vulnerable to drug use disorders (2, 14, 15). In a biopsychosocial formulation, men are more prone to perform risky behaviors, have more accessibility, and face less stigma than women. Literature supports the association of substance use in family and increased risk of current drug use (27, 28). In Iran, roughly half of the substance users have at least one close family member with substance abuse or dependence (16). Cross-sectional studies cannot reveal causative relationships; however, the biopsychosocial aspect could explain such relation. Genetic susceptibility has been supported by twins and adoption studies (9, 28). Families generate both the first role models of behaviors and structures for shaping it, which consist of distress exposure, conflicts, and nonadaptive coping styles (27, 28). Engaging families is a critical element of treating comorbid substance use and psychotic disorders. Psychotic patients may fail to provide a comprehensive family history during psychiatric assessments; therefore, engaging family members in inclusive evaluation is highly important. Such measures could help to screen and monitor high risk patients and implement essential preventive and treatment policies.

Younger age has been identified as correlated with substance use in this study, although previous studies have found controversial data around it (1, 2, 15). Adolescences are the most at-risk group for consuming substances and they might try to show their independence by carrying out risky behaviors. Socioeconomic status is highly related to enlarged risk of using substance (15). Homelessness indicates lack of social support and consequently is an important risk factor in psychotic disorders patients. In this study, however, only a few reported current homelessness: therefore, the obtained results should be interpreted cautiously. The history of imprisonment, on the other hand, can be related to both risk taking and antisocial behaviors. The mediator remains to be studied more.

Limitation
Due to the cross-sectional nature of this study, the predicting factors failed to be interpreted as causal characteristics. Consequently, the results should be interpreted as association and correlates, which are important in screening and treatment measures.

Conclusion
The prevalence of substance use was high among all psychosis patients. Of these participants, those with younger age, males, and homeless individuals with a
family history of drug use disorders should be specifically addressed by health care professionals.

Acknowledgment
This work was supported by the Research and Technology Deputy, Psychosis Research Center, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran.

Conflict of Interest
None.

Authors' Contributions
ASH, NP, PH, and SBM: study concept and design. ES, MP, MM, and SJF: gathering data and drafting the manuscript. MN, NP, EA, and ASH: statistical analysis, AS, SBM, PH: analysis and interpretation of data. ASH, SBM, PH, NP, MM, and MN: critical revision of the manuscript for valuable intellectual content.

References
1. Hunt GE, Large MM, Cleary M, Lai HMX, Saunders JB. Prevalence of comorbid substance use in schizophrenia spectrum disorders in community and clinical settings, 1990-2017: Systematic review and meta-analysis. Drug Alcohol Depend. 2018;191:234-58.
2. Hunt GE, Malhi GS, Cleary M, Lai HM, Sitharthan T. Prevalence of comorbid bipolar and substance use disorders in clinical settings, 1990-2015: Systematic review and meta-analysis. J Affect Disord. 2016;206:331-49.
3. Glasner-Edwards S, Mooney LJ. Methamphetamine psychosis: epidemiology and management. CNS Drugs. 2014;28(12):1115-26.
4. Arciniegas DB. Psychosis. Continuum (Minneap Minn). Behav Neurol 2015 Jun;21(3):715-36.
5. McKetin R, Baker AL, Dawe S, Voce A, Lubman DJ. Differences in the symptom profile of methamphetamine-related psychosis and primary psychotic disorders. Psychiatry Res. 2017;251:349-54.
6. Voce A, Calabria B, Burns R, Castle D, McKetin R. A Systematic Review of the Symptom Profile and Course of Methamphetamine-Associated Psychosis(Substance Use and Misuse). Subst Use Misuse. 2019;54(4):549-59.
7. Gaebel W, Zielasek J. Focus on psychosis. Dialogues Clin Neurosci. 2015;17(1):9-18.
8. Silver, J. M. (2006). Behavioral neurology and neuropsychiatry is a subspecialty. Am Neuropsych Assoc.Reginsson GW, Ingason A, Euesden J, Bjornsrott G, Olafsson S, Sigurdsson E, et al. Polygenic risk scores for schizophrenia and bipolar disorder associate with addiction. Addict Biol. 2018;23(1):485-92.
9. Rabinowitz J, Berardo CG, Bugarski-Kirola D, Marder S. Association of prominent positive and prominent negative symptoms and functional health, well-being, healthcare-related quality of life and family burden: a CATIE analysis. Schizophr Res. 2013;150(2-3):339-42.
10. Suetani S, Rosenbaum S, Scott JG, Curtis J, Ward PB. Bridging the gap: What have we done and what more can we do to reduce the burden of avoidable death in people with psychotic illness? Epidemiol Psychiatr Sci. 2016;25(3):205-10.
11. Lally J, Ajnakina O, Stubbs B, Cullinan M, Murphy KC, Gaughran F, et al. Remission and recovery from first-episode psychosis in adults: systematic review and meta-analysis of long-term outcome studies. Br J Psychiatry. 2017;211(6):350-8.
12. Hunt GE, Malhi GS, Cleary M, Lai HM, Sitharthan T. Comorbidity of bipolar and substance use disorders in national surveys of general populations, 1990-2015: Systematic review and meta-analysis. J Affect Disord. 2016;206:321-30.
13. Messer T, Lammers G, Müller-Siecheneder F, Schmidt RF, Latifi S. Substance abuse in patients with bipolar disorder: A systematic review and meta-analysis. Psychiatry Res. 2017;253:338-50.
14. Amin-Esmaili M, Rahimi-Movaghar A, Sharifi V, Hajebi A, Radgooodarzi R, Mojtabai R, et al. Epidemiology of illicit drug use disorders in Iran: prevalence, correlates, comorbidity and service utilization results from the Iranian Mental Health Survey. Addiction. 2016;111(10):1836-47.
15. Mokri A. Brief overview of the status of drug abuse in Iran. Arch Iranian Med 2002; 5 (3): 184–90.
16. Noori R, Daneshmand R, Farhoodian A, Ghaderi S, Aryanfard S, Moradi A. Amphetamine-type stimulants in a group of adults in Tehran, Iran: a rapid situation assessment in twenty-two districts. Iranian Journal of Psychiatry and Behavioral Sciences. 2016;10(4):e7734.
17. Razzaghi E, Rahimi A, Hosseini M, Chatterjee A. Rapid Situation Assessment (RSA) of drug abuse in Iran. Prevention Department, State Welfare Organization, Ministry of Health, IR of Iran and United Nations International Drug Control Program. 1999.
18. Shadloo B, Amin-Esmaili M, Haft-Baradaran M, Noroozi A, Ghorban-Jahromi R, Rahimi-Movaghar A. Use of amphetamine-type stimulants in the Islamic Republic of Iran, 2004-2015: a review. East Mediterr Health J. 2017;23(3):245-56.
19. Glasner-Edwards S, Mooney LJ. Methamphetamine psychosis: epidemiology and management. CNS Drugs. 2014;28(12):1115-26.

Substance Use among Psychosis Patients
20. Cheng HG, Phillips MR, Li X, Zhang J, Shi Q, Xu G, et al. Co-occurrence of DSM-IV mental disorders and alcohol use disorder among adult Chinese males. Psychol Med. 2017;47(16):2811-22.
21. Chou SP, Lee HK, Cho MJ, Park JI, Dawson DA, Grant BF. Alcohol use disorders, nicotine dependence, and co-occurring mood and anxiety disorders in the United States and South Korea-a cross-national comparison. Alcohol Clin Exp Res. 2012;36(4):654-62.
22. Amirabadizadeh A, Nezami H, Vaughn MG, Nakhaee S, Mehrpour O. Identifying Risk Factors for Drug Use in an Iranian Treatment Sample: A Prediction Approach Using Decision Trees. Subst Use Misuse. 2018;53(6):1030-40.
23. Alavi SS, Mehrdad R, Makarem J. Prevalence of substance abuse/alcohol consumption and their predictors among patients admitted in operating rooms of a General Educational Hospital, Tehran, Iran. AJPRHC. 2016;8(1):63.
24. Koskinen J, Löhönen J, Koponen H, Isohanni M, Miettunen J. Rate of cannabis use disorders in clinical samples of patients with schizophrenia: a meta-analysis. Schizophr Bull. 2010;36(6):1115-30.
25. Kuepper R, van Os J, Lieb R, Wittchen HU, Höfler M, Henquet C. Continued cannabis use and risk of incidence and persistence of psychotic symptoms:10-year follow-up cohort study. Bmj. 2011;342:d738.
26. McCutcheon VV, Agrawal A, Kuo SI, Su J, Dick DM, Meyers JL, et al. Associations of parental alcohol use disorders and parental separation with offspring initiation of alcohol, cigarette and cannabis use and sexual debut in high-risk families. Addiction. 2018;113(2):336-45.
27. Bierut LJ, Dinwiddie SH, Begleiter H, Crowe RR, Hesselbrock V, Nurnberger JL, Jr., et al. Familial transmission of substance dependence: alcohol, marijuana, cocaine, and habitual smoking: a report from the Collaborative Study on the Genetics of Alcoholism. Arch Gen Psychiatry. 1998;55(11):982-8.
28. ASHERY, R.; ROBERTSON, E.; and KUMPFER, K., eds. Drug Abuse Prevention Through Family Interventions. NIDA Research Monograph Number 177, Pub. No. 99-4135. Rockville, MD: National Institute on Drug Abuse, 1998.