LAURA TUUNANEN, HEIKKI LAURIKAINEN, TIINA FROM, ALEXANDER DENISSOFF, RAIMO K.R. SALOKANGAS, JARMO HIETALA, SOLJA NIEMELÄ

SUBSTANCE USE PROFILES IN FIRST-EPISODE PSYCHOSIS AND PSYCHOSIS-RISK PATIENTS - RESULTS OF THE TURKU EARLY PSYCHOSIS STUDY (TEPS)

ABSTRACT

***Background**: Substance use is known to be prevalent in first-episode psychosis (FEP). Substance use is also a known risk factor for psychosis in vulnerable individuals and forms one of the treatment targets in preventive early intervention protocols. **Aims**: The aim of this study was to evaluate prevalence and detailed characteristics of substance use profiles in patients with FEP and patients with a clinical psychosis risk compared to those in a general population sample. **Method**: The sample consisted of in- and outpatients recruited from the psychiatric services in South West Finland between years 2011 and 2017. The participants were divided into four groups based on standardized clinical evaluation: 1) patients with FEP (n=130); 2) patients with clinical high risk for psychosis (CHR-P) assessed with the Structured Interview for Psychosis-Risk Syndromes (SIPS) (n=61); 3) patients with clinical psychosis risk assessed by the clinical treatment team but not fulfilling the SIPS criteria (CHR-N) (n=44); and 4) general population controls (n=121). Past and current substance use data was collected using questionnaires. **Results**: Across all study groups, current regular cigarette smoking, hazardous alcohol use and illicit drug use during lifetime and during the past 12 months was most common in the FEP group. Lifetime and past 12 months cannabis use was significantly more common only in the FEP group compared to the control group. However, other illicit drug use during both lifetime and past 12 months was more common in all patient groups compared to the control group. While current regular smoking was more common in all patient groups compared to the control group, hazardous alcohol use defined as AUDIT score ≥8 points was not. **Conclusions**: Substance use is highly prevalent in first-episode psychosis and in patients with a clinically defined risk for psychosis. Thus, detailed screening of substance use in this vulnerable population is an important clinical priority in integrated early intervention strategies aimed at improving patient outcomes.*

KEYWORDS: FIRST-EPISODE PSYCHOSIS, CLINICAL HIGH RISK FOR PSYCHOSIS, SUBSTANCE USE, ALCOHOL USE, TOBACCO, CANNABIS

INTRODUCTION

Substance use is remarkably common among first-episode psychosis (FEP) patients; tobacco, alcohol and cannabis being the most frequently used substances (1–3). Substance use is an established adverse prognostic marker for FEP patients, as this comorbidity has been associated with various adverse outcomes including medication non-adherence (4), severity of symptoms (5) and frequent service use (5). However, research examining substance use of patients at clinical high-risk (CHR) for psychosis is limited and the literature is dominated by research on cannabis use. In the meta-analysis of Kraan et al., cannabis use disorder but not cannabis use was associated with transition to psychosis (6). As well, findings from population-based studies suggest the use of tobacco (7), cannabis (8) and inhalants (9), but not alcohol (10), to be associated with increased risk for subsequent psychotic disorders. Tobacco and cannabis have also been associated with earlier age of onset of FEP (1,11).

In previous studies, more than half of the FEP patients have been estimated to smoke cigarettes daily (12). Prevalence of current and lifetime use of cannabis has been estimated to be 30% and at least 50%, respectively (2,3). For other illicit drug use, estimates for current and lifetime prevalence have

been considerably higher among FEP patients compared to the general population (3,13,14). In addition, hazardous alcohol use and alcohol use disorder (AUD) are reported to be a common comorbidity among this group (13).

While substance use is known to be remarkably common among FEP patients, there is less literature about substance use frequency among CHR patients. Cigarette smoking has been reported to be more frequent among them compared to the controls, approximately one out of three CHR patients being a daily smoker (15). The prevalence of current and lifetime use of cannabis seems to be as common among CHR patients as among FEP patients (16). Research on other illicit drug use among CHR patients is limited, with the existing evidence base suggesting it to be rare (17). Studies also suggest that prevalence of comorbid AUD is high (reaching up to 38%) among CHR patients (15). On the other hand, previous studies have rarely compared alcohol use patterns of CHR patients with healthy controls (15,17).

There is a paucity of studies assessing the prevalence of substance use among Finnish FEP patients or those at clinically high-risk for psychosis, while substance use habits of patients with other psychotic disorders have been examined thoroughly. To our knowledge, there is only one clinical sample-based study addressing the issue of cannabis use and one of alcohol use among Finnish FEP patients. In the study of Karpov et al., prevalence of cannabis use among FEP patients (n=91) in the University Hospital District of Helsinki and Uusimaa was 26% during the past year and 19% during lifetime without recent use (16). Information on other substance use was not collected in that study. In a study of Talonen et al., self-reported alcohol abuse among Finnish adolescent FEP patients was relatively high: 52.8% (n=19) among male and 28.6% among female patients (n=20) (18). As far as we know, there is only one study examining the prevalence of substance use in Finnish patients at high risk for psychosis. In a study by Korkeila et al., self-reported alcohol abuse during lifetime was found to be more common among CHR patients (28%) compared to the controls (8%), as well as substance use disorder (SUD) with prevalence of 23% compared to 7%, respectively (19). In that study, most used illicit drugs were cannabis and amphetamine, but exact prevalence numbers were not provided.

The aim of our study was to assess the prevalence of cigarette smoking, alcohol, cannabis and other illicit drug use during lifetime and past 12 months among FEP and CHR patients from psychiatric services in South West Finland during 2011-2017.

PARTICIPANTS AND METHODS

PARTICIPANTS

The Turku Early Psychosis study (TEPS) (20) is a part of the larger VAMI project (Vakavien Mielenterveyshäiriöiden etiologia ja hoito – research programme; the Aetiology and Treatment of Severe Mental Health Disorders – research programme). The TEPS project includes in- or outpatients from the psychiatric clinics of the City of Turku and the Hospital district of South West Finland with their first psychiatric treatment contact due to psychotic symptoms. The recruitment phase was carried out between October 2011 and December 2017.

Eligible participants were screened to determine if they were psychotic or at high risk for psychosis as determined by the treating clinical psychiatry team. First-episode psychosis was assessed with Structured Clinical Interview for Diagnostic and Statistical Manual for Mental Disorders 4th ed. text revision (Axis-I disorders, SCID-I) according to DSM-IV criteria, including schizophrenia, delusional and bipolar psychoses, acute transient psychoses and other psychoses. Patients with a previous psychotic disorder and IQ <70 were excluded (Wechsler Adult Intelligence Scale vocabulary test performance was used as a proxy for IQ in this study). Clinical high-risk psychosis was defined using the Structured Interview for Prodromal Syndromes version 5.0 (SIPS) category of prodromal syndromes criteria (COPS). Participants fulfilling these criteria form the CHR-P group (21). The other high-risk group was composed of participants who were originally assessed to have clinical features related to psychosis risk in an everyday standard clinical evaluation, but did not quite fulfil the formal SIPS/SOPS criteria. They form the CHR-N group. For the general population control group, through the Turku University Hospital, people were randomly identified from the population register who, based on their age, gender and place of residence, matched the patients included in the study. More detailed information about recruitment protocol and baseline examination is described in previous article (20).

In all, our study included 356 participants who were divided into four groups based on psychosis rate: patients with the first-episode psychosis (FEP, n=130), patients with clinical high risk for psychosis, defined with SIPS/SOPS (CHR-P, n=61), patients who didn't fulfil SIPS/SOPS criteria (CHR-N, n=44) and general population controls (GPC, n=121).

This study was performed in compliance with the 6th revision of the Declaration of Helsinki. The research plan was approved by the Ethics Committee of South West Finland (diary

numbers 64/180/2011 and 65/1801/2013) respectively. All participants gave written informed consent before participation. Capacity to consent was assessed by the patient's responsible clinician.

INFORMATION ON SUBSTANCE USE

Information concerning self-reported substance use was collected using questionnaires.

History of cigarette smoking was questioned as "*Have you ever smoked more than 5 packs of cigarettes during your lifetime?*" with answering options yes or no. Information about current regular smoking was investigated with a question "*Do you still smoke cigarettes regularly?*" with answering options yes or no. In addition, an average number of daily smoked cigarettes was asked with options *1-2, 3-5, 6-10, 11-15, 16-19, 20-25, 26-39* and *40 or more*. Answers were divided into two groups: 1) light daily smoking, i.e. smoking 1-19 cigarettes a day and 2) heavy daily smoking, i.e. smoking at least one pack (20 cigarettes) a day.

Alcohol use was assessed using the ten-item Alcohol Use Disorders Identification Test (AUDIT) since it has been examined to be valid among people with schizophrenia (22) and first-episode psychosis (23). As in previously cited studies, AUDIT score ≥8 points was used as a cut-off value to indicate hazardous alcohol use.

Besides the total AUDIT score value, answers for the first three questions were analysed in the results. The first question was "*How often do you have a drink containing alcohol?*" with answering options *never, monthly or less, 2-4 times a month, 2-3 times a week* and *4 times a week or more often*. The second question was "*How many drinks containing alcohol do you have on a typical day when you are drinking?*" with options *1 or 2, 3 or 4, 5 or 6, 7-9* and *10 or more*. For the statistical analysis, answers were grouped into three categories: 1-4, 5-9 and 10 or more. The third question – an indicator for binge drinking – was "*How often do you have six or more drinks on one occasion?*" with options *never, less than monthly, monthly, weekly*, and *daily or almost daily*. For the statistical analyses, two last answering options were grouped.

The questionnaire included also questions concerning self-reported illicit drug use, namely cannabis, MDMA, amphetamine or methamphetamine, cocaine or crack, heroine or morphine, buprenorphine, other central nervous system (CNS) drugs, LSD or other hallucinogens and inhalant use. In addition, the participants were allowed to report if they had used some other drug not mentioned above. The answering options in the questionnaire were *never, 1-5 times, 6-10 times, 11-50 times* and *50 or more times*. Substance use was examined for both during lifetime and past 12 months. Information on illicit drug use other than cannabis was pooled for the statistical analysis.

STATISTICAL ANALYSES

Statistical analyses were done using the IBM SPSS Statistics 25. Descriptive analyses were performed to establish background characteristics and substance use patterns of the participants. The reported background characteristics included gender (males, females), age (in years), occupation (employed/student, unemployed/incapacitated) and marital status (married/common-law, other).

Multinomial logistic regression analysis was used to compare tobacco, alcohol and illicit drug use of the FEP, CHR-P and CHR-N groups to the GPC group (General population comparison group). The results were reported with odds ratios (OR), corresponding 95% confidence intervals (CI) and p-values, setting the statistical significance at $p<0.05$.

RESULTS

BACKGROUND CHARACTERISTICS

The mean age (years) of all participants was 26.6 with a standard deviation (SD) of 6.2 and ranging from 18 to 49. Of all participants, 52.5% (n=187) were male and 47.5% (n=169) female. Proportion of unemployed or incapacitated ranged from 27.3% to 34.4% in the FEP, CHR-P and CHR-N groups, while 96.7% of the general population controls were employed or students. Less than 30% of the participants in the FEP, CHR-P and CHR-N groups were married or in common-law marriage, while the corresponding percentage in the GPC group was 70.2%. More detailed information about the background characteristics of the participants is reported in *Table 1*.

Table 1. Background characteristics of the participants

	FEP n=130		CHR-P n=61		CHR-N n=44		GPC n=121	
Age, years	mean	SD	mean	SD	mean	SD	mean	SD
	26.6	5.9	25.0	6.2	27.1	8.1	27.4	5.6
Gender	*n*	*%*	*n*	*%*	*n*	*%*	*n*	*%*
Male	73	56.2	32	52.5	22	50.0	60	49.6
Female	57	43.8	29	47.5	22	50.0	61	50.4
Basic education								
Comprehensive school or less	52	40.0	26	42.6	21	47.7	21	17.6
General upper secondary education	78	60.0	35	57.4	23	52.3	98	82.4
Professional education								
None	57	43.8	30	49.2	19	43.2	31	26.1
Vocational school	54	41.5	26	42.6	19	43.2	34	28.6
University	19	14.6	5	8.2	6	13.6	54	45.4
Occupation								
Employed or student	72	55.4	29	47.5	23	52.3	117	96.7
Unemployed or incapacitated	37	28.5	21	34.4	12	27.3	1	0.8
Other	21	16.2	11	18	9	20.5	3	2.5
Marital status								
Married or common-law or common-law	31	23.8	17	27.9	13	29.5	85	70.2
Other	99	76.2	44	72.1	31	70.5	36	29.8

SUBSTANCE USE

Cigarette smoking

Information about cigarette smoking is described in Table 2. Current regular tobacco smokers represented 61.7% in the FEP group, 37.5% in the CHR-P group, 47.1% in the CHR-N group and 14.9% in the GPC group. Current regular smoking was significantly more likely in the FEP group (OR: 9.2, 95% CI: 3.4-24.9, p<0.001), in the CHR-P group (OR: 3.4, 95% CI: 1.1-10.9, p=0.036) and in the CHR-N group (OR: 5.1, 95% CI: 1.5-17.7, p=0.011) compared to the general population controls. History of smoking (>5 packs of cigarettes) didn't differ in any group compared to the control group. Heavy daily smoking, i.e. smoking at least 20 cigarettes per day, was more prevalent among the FEP patients (21.9%) compared to other groups (CHR-P 9 %, CHR-N 15.4 %, and 0% in the GPC).

Alcohol

Alcohol use variables, assessed with the ten-question AUDIT questionnaire, among participants are described in *Table 2*. Prevalence of hazardous alcohol use, defined as AUDIT score ≥8 points ranged from 32.7% to 40.0%. The proportion of those who exceeded that score did not differ in any group compared to the control group. When asked the alcohol use frequency,

the highest proportion of the FEP group (n=53, 50.5%) and the CHR-P group (n=20, 40.8%) reported drinking once a month or more rarely, while in the control group, the highest proportion (n=52, 47.3%) were used to drinking 2-3 times per week. However, participants in the FEP group (OR: 4.9, 95% CI: 1.6-15.4, p=0.006) as well as CHR-N group (OR: 5.1, 95% CI: 1.3-19, p=0.017), but not CHR-P group, were more likely to consume 10 units or more during one drinking session, even though when questioning frequency of binge drinking results do not suggest higher frequencies among them.

Illicit drug use

In all groups, the most used illicit drug both during lifetime and past 12 months was cannabis, followed by CNS drugs. MDMA was the third most used illicit drug during lifetime, while amphetamine was the third most frequently used illicit drug during the past 12 months (See *Figures 1-2* and *Table 3*).

Cannabis use

In all, prevalence of cannabis use during lifetime ranged from 40.0% (CHR-N group) to 61.5% (FEP group), and cannabis use during past 12 months from 12.5% (CHR-N group) to 37.1% (FEP group). Prevalence of heavy use (>50 times) ranged from 4.5% (GPC group) to 23.1% (FEP group).

Compared to the GPC group, both lifetime cannabis use (OR: 2, 95% CI: 1.2-3.4, p=0.013) and cannabis use during the past 12 months (OR: 2.3, 95% CI: 1.3-4.3, p=0.007) was more prevalent only in the FEP group.

Other types of illicit drug use

In all, prevalence of other illicit drug use than cannabis ranged from 12.7% (GPC group) to 42.9% (FEP group) during lifetime, and from 4.6% (GPC group) to 27.9% (FEP group) during past 12 months.

The use of other illicit drugs during lifetime was more likely in the FEP group (OR: 5.1, 95% CI: 2.6-10.2, p<0.001), in the CHR-P group (OR: 4, 95% CI: 1.8-9.0, p=0.001) and in the CHR-N group (OR: 4.1, 95% CI: 1.8-9.6, p<0.001) when compared to the GPC group. The use of other illicit drugs during the past 12 months was more likely in all patient groups when compared to the GPC group: the FEP group (OR: 8, 95% CI: 3-21.7, p<0.001), the CHR-P group (OR: 4.8, 95% CI: 1.5-15.2, p=0.008) and the CHR-N group (OR: 4.4, 95% CI: 1.3-14.8, p=0.016).

Table 2. Alcohol and tobacco use among VAMI participants compared to general population controls

	GPC		FEP					CHR-P					CHR-N				
	n	*%*	*n*	*%*	*OR*	*95% CI*	*p-value*	*n*	*%*	*OR*	*95% CI*	*p-value*	*n*	*%*	*OR*	*95% CI*	*p-value*
Alcohol use frequency																	
Never	5	4.5	12	11.4	2.7	0.9-8.0	0.070	11	22.4	6.1	2.0-19	**0.002**	5	12.8	3.1	0.8-11.3	0.09
Once a month or more rarely	36	32.7	53	50.5	2.1	1.2-3.6	**0.009**	20	40.8	1.4	0.7-2.8	0.33	17	43.6	1.6	0.8-3.4	0.23
2-4 times a month	52	47.3	34	32.4	0.5	0.3-0.9	**0.03**	17	34.7	0.6	0.3-1.2	0.14	14	35.9	0.6	0.3-1.3	0.22
2-3 times a week	15	13.6	3	2.9	0.2	0.05-0.6	**0.01**	0	0				3	7.7	0.5	0.1-1.9	0.33
4 times a week or more	2	1.8	3	2.9	1.6	0.3-9.7	0.62	1	2	1.1	0.1-12.7	0.92	0	0			
Usual number of units consumed per drinking session																	
1-4 units	66	62.9	52	56.5	0.8	0.4-1.4	0.37	21	53.8	0.7	0.3-1.5	0.327	19	52.8	0.66	0.3-1.4	0.29
5-9 units	35	33.3	25	27.1	0.7	0.4-1.4	0.35	13	33.3	1.0	0.5-2.2	1.000	11	30.6	0.88	0.4-2.0	0.76
10 units or more	4	3.8	15	16.3	4.9	1.6-15.4	**0.006**	5	12.8	3.7	0.9-14.6	0.061	6	16.7	5.1	1.3-19	**0.017**
Frequency of binge drinking																	
Never	19	17.8	26	26.8	1.7	0.9-3.3	0.12	13	31	2.1	0.9-4.7	0.081	10	25	1.5	0.6-3.7	0.33
Less than monthly	40	37.4	42	43.3	1.3	0.7-2.2	0.39	17	40.5	1.1	0.5-2.4	0.72	16	40	1.1	0.5-2.4	0.77
Monthly	40	37.4	22	22.7	0.49	0.3-0.9	**0.024**	9	21.4	0.46	0.2-1.1	0.066	9	22.5	0.49	0.2-1.1	0.092
Weekly	8	7.5	7	7.2	0.96	0.3-2.8	0.94	3	7.1	0.95	0.2-3.8	0.94	5	12.5	1.8	0.5-5.8	0.34
AUDIT score 8 or more	36	32.7	40	38.1	1.3	0.7-2.2	0.41	17	34.7	1.1	0.5-2.2	0.81	16	40	1.4	0.6-2.9	0.41
Cigarette smoking																	
Ever smoking (>5 packs of cigarettes)	50	45.5	60	57.1	1.6	0.9-2.7	0.087	25	51	1.3	0.6-2.5	0.52	22	55	1.5	0.7-3.0	0.30
Current regular smoking	7	14.9	29	61.7	9.2	3.4-24.9	**<0.001**	9	37.5	3.4	1.1-10.9	**0.036**	8	47.1	5.1	1.5-17.7	**0.01**

Table 3. Drug use during lifetime and past 12 months among VAMI participants compared to general population controls

	GPC		FEP					CHR-P					CHR-N				
	n	*%*	*n*	*%*	*OR*	*95% CI*	*p-value*	*n*	*%*	*OR*	*95% CI*	*p-value*	*n*	*%*	*OR*	*95% CI*	*p-value*
Cannabis use during lifetime	49	44.5	64	61.5	2	**1.2-3.4**	**0.013**	24	49	1.2	0.6-2.3	0.605	16	40	0.8	0.4-1.7	0.620
Other drug use during lifetime	14	12.7	45	42.9	5.1	**2.6-10.2**	**<0.001**	18	36.7	4	**1.8-9**	**0.001**	15	37.5	4.1	**1.8-9.6**	**0.000**
Cannabis use during past 12 months	22	20.2	39	37.1	2.3	**1.3-4.3**	**0.007**	12	25	1.3	0.6-2.9	0.500	5	12.5	0.6	0.2-1.6	0.285
Other drug use during past 12 months	5	4.6	29	27.9	8	**3-21.7**	**<0.001**	9	18.8	4.8	**1.5-15.2**	**0.008**	7	17.5	4.4	**1.3-14.8**	**0.016**

Figure 1. Drug use (%) during lifetime

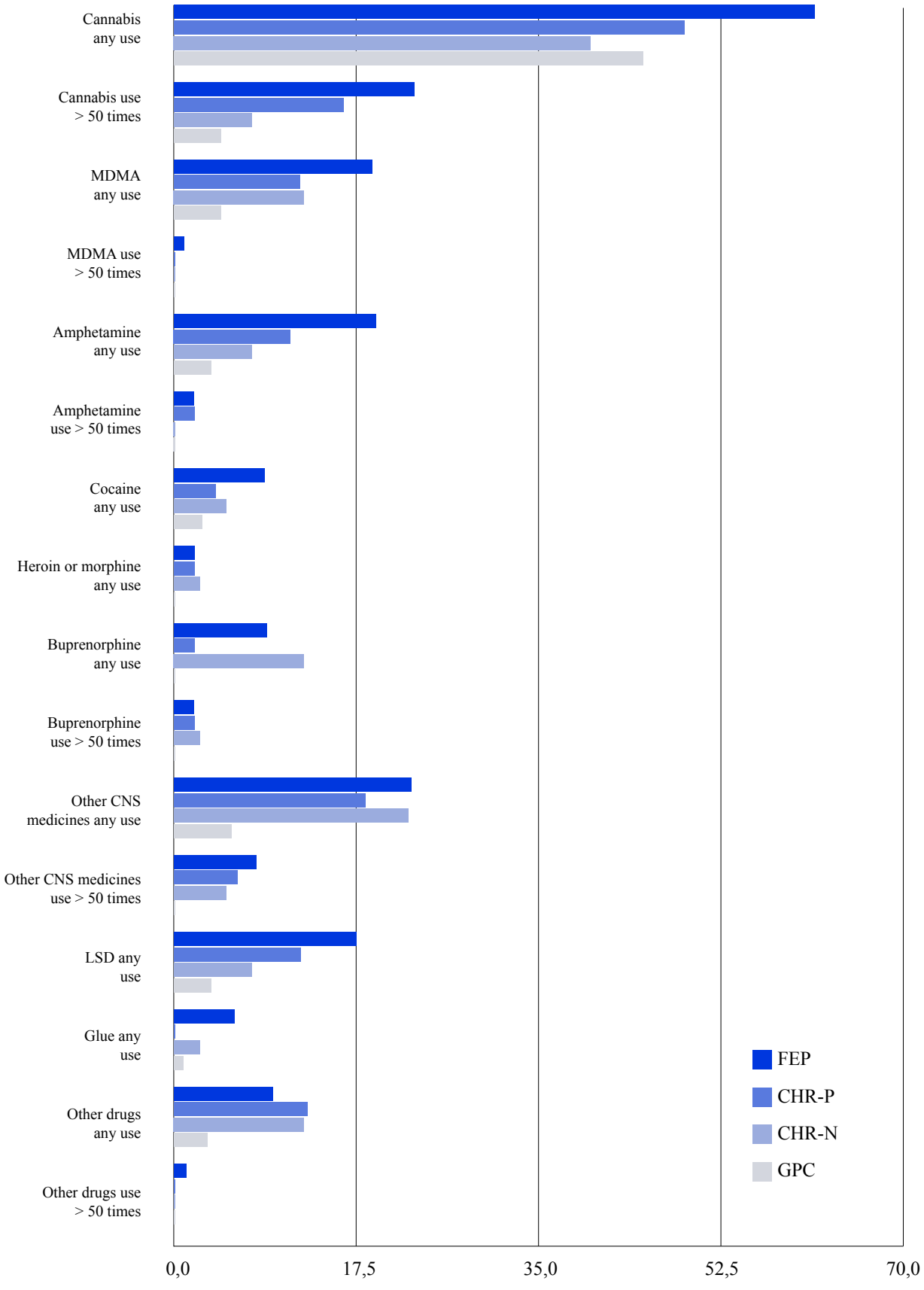
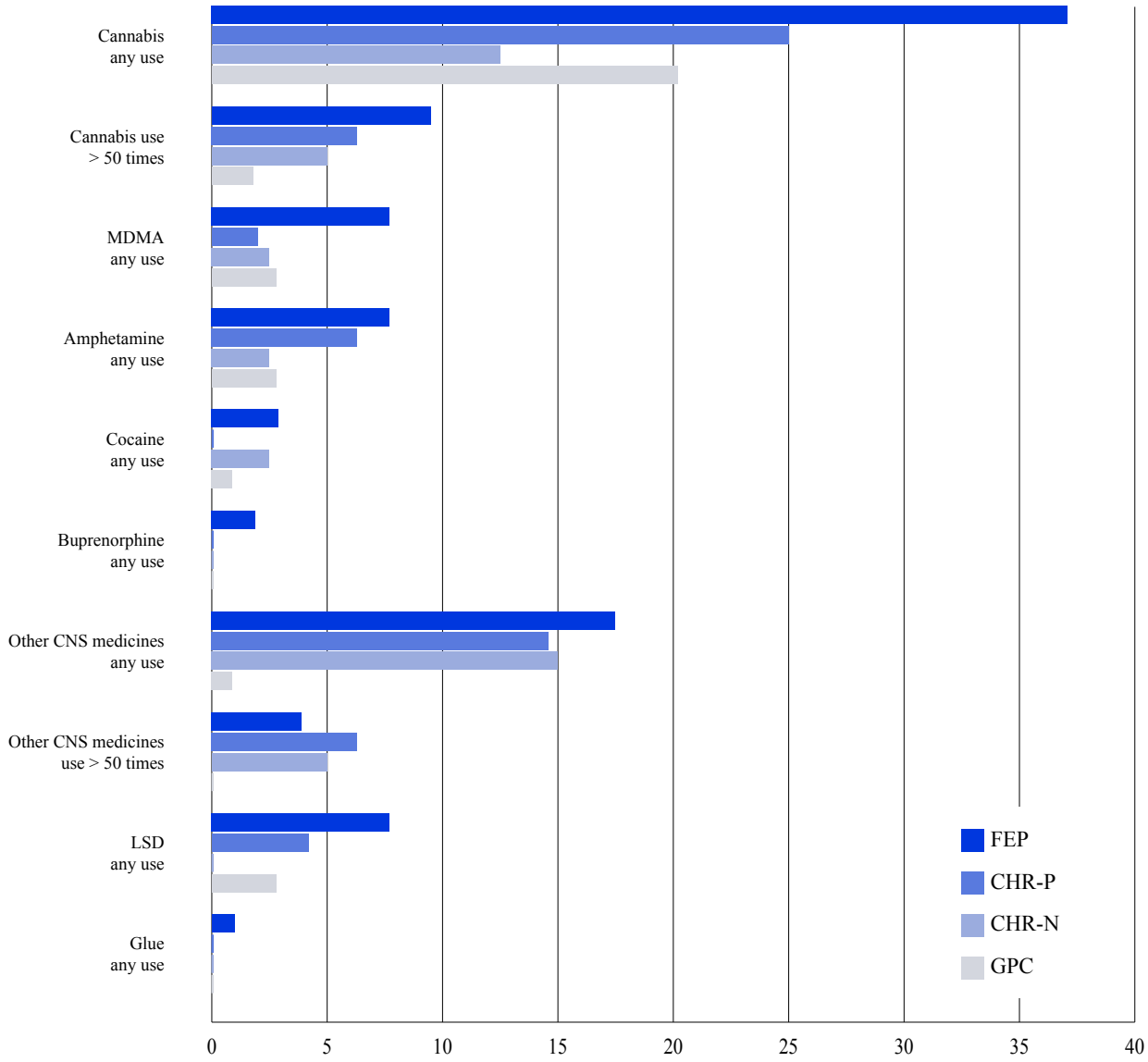


Figure 2. Drug use (%) during past 12 months



DISCUSSION

This study examined prevalence of substance use in a Finnish sample of first-episode psychosis (FEP) and psychosis risk patients (CHR-P and CHR-N), compared to general population (GPC). The key finding was the consistently higher burden of substance use among persons with FEP and in terms of current regular smoking, hazardous alcohol use and illicit drug use (both lifetime and past 12 months). Notably, cannabis use was more common in persons with FEP than in the general population, whereas this difference was not observed in the other patient groups. Although current regular smoking was more common in all patient groups than in general population controls, hazardous alcohol use was not.

Even though prevalence of substance use in psychosis risk patients was not as high as in FEP patients, it was still notably common. When compared to general population, cigarette smoking and illicit drug use except cannabis were more common among them; also, the pattern was the same regardless of whether psychosis risk assessment was made with structured interview or not.

Consistent with a meta-analysis by Myles et al., more than half of the FEP patients in our sample reported current regular cigarette smoking. Among the participants in the CHR-P and CHR-N groups, prevalence was not as high (37.5% and 47.1%), although significantly higher than in the control group (14.9%) and substantially similar as that reported in previous studies (15). Previous literature provides limited information about smoking among Finnish FEP or high-risk patients, yet three Finnish studies with schizophrenia patients proposed approximately 44% for self-reported daily smoking (24–26). Interestingly, in two of these studies the prevalence of daily smoking was lower, below 30% among people with affective or other non-affective psychosis (24,25). Examining tobacco smoking habits of patients with psychotic disorders is important since it is a major preventable risk factor for cardiometabolic disease – an important cause of premature death among people with schizophrenia (15). For adolescents, tobacco smoking might be an independent risk factor for developing psychotic disorders (7). However, it is still unclear to what extent tobacco smoking among high-risk patients is associated with increased risk for first psychotic episode, or could ceasing tobacco smoking prevent the onset of psychotic disorder among them, since to this date causality has not been proven (27).

In our sample, the percentage of the risk-level alcohol use, defined as AUDIT score ≥8 points, varied between 32.7% in the GPC group and 40% in the CHR-N group. There was no statistically significant difference between any clinical group compared to the GPC group. Participants from the FEP and CHR-N groups were more likely to consume 10 or more units of alcohol during one session, even though the frequency of binge drinking was not higher among them compared to the GPC group. Nevertheless, the percentage of the AUDIT-positive participants in our FEP group (38.1%) was equivalent to a previous study with Finnish schizophrenia patients (38.9%)(26). In this study, 22.1% of schizophrenia patients had a diagnosis for an alcohol use disorder; however, in this sample the percentage was higher among bipolar patients. These findings highlight that hazardous alcohol use is a common comorbidity among psychiatric patients in general, not exclusively among patients with psychotic disorders.

Among the participants presenting with FEP in this study, prevalence of cannabis use during lifetime (61.5%) and past 12 months (37.1%) was consistent with findings from previous studies (2,3) and significantly higher than in the GPC group (44.5% and 20.2%, respectively). Of note, among FEP patients, as many as one out of ten reported cannabis use 50 times or more during the past 12 months. In previous studies, especially heavy cannabis use has been associated with increased risk for developing schizophrenia (28). In another Finnish study, lifetime prevalence of cannabis use among FEP patients was found to be slightly lower (26%) (16). In that study cannabis use was evaluated with the combination of self-report questionnaire, clinical assessment and medical records. In a study with Finnish schizophrenia patients, prevalence of harmful use or dependence of cannabis was even lower (10.9%). However, in that study information of cannabis use was collected retrospectively from medical files suggesting that under-reporting might be an issue with the data (29). Moreover, cannabis use might be more prevalent among FEP patients compared to those with chronic schizophrenia, as cannabis use has been found to be more common among young patients (30). In our study, prevalence of cannabis use among other patient groups was similar to the GPC group. This finding might reflect the fact that cannabis use is widespread among the general population (31). However, a meta-analysis focusing on the association of cannabis abuse or dependence and onset of psychosis specifically in CHR populations reported a significant positive finding (6). Notably, a corresponding association between lifetime cannabis use and subsequent psychosis was not seen, which suggests a dose-response relationship. Also, a large birth cohort study has suggested rising substance use, especially cannabis, to be associated with higher prevalence of psychotic disorders (32). These findings highlight that even though cannabis use was not more common among CHR patients when compared to the

GPC group, and causality is still in debate, it is important to consider the frequency of use when treating this patient group.

In our study, prevalence of other illicit drug use was significantly more common in all patient groups compared to the general population controls. However, the prevalence of other illicit drug use was small, and power issues thus precluded from analysing different illicit drugs separately in the logistic regression models. In line with our result, a study with Finnish schizophrenia patients revealed relatively high lifetime prevalence of amphetamine (8.9%) and opioid (4.1%) abuse, both based on medical files (29).

The reason why substance use among people with psychotic disorders is markedly prevalent is not fully understood. FEP patients with comorbid substance use are typically described being male (33,34) and less educated than non-using patients (5). Male sex and low education have been associated with substance use in general population as well (35). Self-reported reasons for substance use among FEP patients include self-medication and facilitation of social interaction (36,37). Moreover, evidence from Mendelian randomization studies indicates shared genetic vulnerability for substance use and psychotic illnesses (38)

STRENGTHS AND LIMITATIONS

Strengths of this study include investigating use of several different substances, i.e. cigarette smoking, alcohol and wide variety of illicit drugs, within both first-episode and clinical high-risk patients. In addition, alcohol use was evaluated comprehensively with several variables. Importantly, psychosis status of the participants was assessed comprehensively using validated instruments, including the SCID-I and SIPS/SOPS interviews.

Some limitations need to be considered. In our study substance use was assessed by self-reports, and thus under-reporting might be a concern with our data (39). Also, the total number of participants wasn't significantly large, so power issues precluded from studying other illicit drugs than cannabis separately in the regression models. Our study did not consider polysubstance use either, which is known to be a common phenomenon (40). In addition, it needs to be considered that our data was collected from 2011 to 2017, and in the Finnish population there have been changes in the realm of substance use. The use of illicit drugs, especially cannabis, has become more common whereas the use of alcohol and smoking tobacco has decreased (41). Also, the study is cross-sectional in design and does not allow studying causality. Lastly, as this study was accomplished in the hospital district of South West Finland, results might not be generalizable to some other geographical or cultural contexts.

CONCLUSIONS

Our study provides new data on substance use among patients at clinical high risk for psychosis, an area with limited prior research. Our findings also align with earlier reports of high substance use in first-episode psychosis (FEP) in particular.

Our results highlight the importance of awareness and routine evaluation of substance use, not only among FEP but also psychosis-risk patients as a part of early interventions. Education of personnel is important for raising awareness on this topic. In clinical work, substance use can be evaluated with systematic interview, questionnaires and, if necessary, laboratory samples. Also, the opportunity to offer integrated substance use interventions for these patients would most likely have a favourable impact on their treatment outcomes.

Acknowledgements

The authors would like to thank the TEPS Research group: Mirka Kolkka, Anu Ellilä, Akseli Mäkelä, Otto Turtonen, Maarit Lehtinen, Henri Pesonen, Maria Tikka and Antti Luutonen for their valuable work in the TEPS study.

Funding

TEPS has been funded by the EVO Funding of Turku City Health Care and Turku University Hospital (grant nos. TEPS600083, P13196, P3860, and P3848) and by the Academy of Finland (grant nos. 278155 and 278171).

Contributions

Conceptualization: All authors
Methodology: All authors
Formal analysis: LT, SN, JH
Investigation: JH, HL, TF, RKRS
Resources: JH, HL, TF, RKRS
Data management: LT, TF
Writing (original draft): LT, SN, JH
Writing (review & editing): All authors

Declaration of interests

SN reports receiving personal fees from Camurus, dne Pharma, Lundbeck, Navamedic, Otsuka, Recordati and Takeda, all outside of this work.

Authors

Laura Tuunanen[1]
Heikki Laurikainen[1,b2]
Tiina From[1]
Alexander Denissoff [1,3]
Raimo K.R. Salokangas[1]
Jarmo Hietala[1,2]
Solja Niemelä[1,3]

[1]Department of Psychiatry, University of Turku, Turku Finland
[2]Department of Psychiatry, Turku University Hospital, Wellbeing Services County of South West Finland (VarHa), Turku, Finland
[3]Psychiatry Unit, Wellbeing Services County of Päijät-Häme, Lahti, Finland
[4]Wellbeing Services County of South West Finland (VarHa), Turku, Finland

ORCID
Solja Niemelä 0000-0003-1130-9161

Correspondence

Solja Niemelä
E-mail: solnie@utu.fi

References

1. Gurillo P, Jauhar S, Murray RM, MacCabe JH. Does tobacco use cause psychosis? Systematic review and meta-analysis. Lancet Psychiatry. 2015;2(8):718-725. doi:10.1016/S2215-0366(15)00152-2

2. Myles H, Myles N, Large M. Cannabis use in first episode psychosis: Meta-analysis of prevalence, and the time course of initiation and continued use. Aust N Z J Psychiatry. 2016;50(3):208-219. doi:10.1177/0004867415599846

3. Wisdom JP, Manuel JI. Prevalence of Substance Use in People With First-Episode Psychosis. J Dual Diagn. 2011;7(1-2):39-49. doi :10.1080/15504263.2011.569876

4. Colizzi M, Carra E, Fraietta S, et al. Substance use, medication adherence and outcome one year following a first episode of psychosis. Schizophr Res. 2016;170(2-3):311-317. doi:10.1016/j.schres.2015.11.016

5. Abdel-Baki A, Ouellet-Plamondon C, Salvat É, Grar K, Potvin S. Symptomatic and functional outcomes of substance use disorder persistence 2 years after admission to a first-episode psychosis program. Psychiatry Res. 2017;247:113-119. doi:10.1016/j.psychres.2016.11.007

6. Kraan T, Velthorst E, Koenders L, et al. Cannabis use and transition to psychosis in individuals at ultra-high risk: review and meta-analysis. Psychol Med. 2016;46(4):673-681. doi:10.1017/S0033291715002329

7. Mustonen A, Ahokas T, Nordström T, et al. Smokin' hot: adolescent smoking and the risk of psychosis. Acta Psychiatr Scand. 2018;138(1):5-14. doi:10.1111/acps.12863

8. Mustonen A, Niemelä S, Nordström T, et al. Adolescent cannabis use, baseline prodromal symptoms and the risk of psychosis. Br J Psychiatry. 2018;212(4):227-233. doi:10.1192/bjp.2017.52

9. Mustonen A, Niemelä S, McGrath JJ, et al. Adolescent inhalant use and psychosis risk - a prospective longitudinal study. Schizophr Res. 2018;201:360-366. doi:10.1016/j.schres.2018.05.013

10. Sarala M, Miettunen J, Koskela J, et al. Frequent intoxication and alcohol tolerance in adolescence: associations with psychiatric disorders in young adulthood. Addiction. 2020;115(5):888-900. doi:10.1111/add.14889

11. Large M, Sharma S, Compton MT, Slade T, Nielssen O. Cannabis use and earlier onset of psychosis: a systematic meta-analysis. Arch Gen Psychiatry. 2011;68(6):555-561. doi:10.1001/archgenpsychiatry.2011.5

12. Myles N, Newall HD, Curtis J, Nielssen O, Shiers D, Large M. Tobacco use before, at, and after first-episode psychosis: a systematic meta-analysis. J Clin Psychiatry. 2012;73(4):468-475. doi:10.4088/JCP.11r07222

13. 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;191:234-258. doi:10.1016/j.drugalcdep.2018.07.011

14. Sara G, Burgess P, Malhi GS, Whiteford H, Hall W. Differences in associations between cannabis and stimulant disorders in first admission psychosis. Schizophr Res. 2013;147(2-3):216-222. doi:10.1016/j.schres.2013.04.017

15. Carney R, Cotter J, Bradshaw T, Firth J, Yung AR. Cardiometabolic risk factors in young people at ultra-high risk for psychosis: A systematic review and meta-analysis. Schizophr Res. 2016;170(2-3):290-300. doi:10.1016/j.schres.2016.01.010

16. Karpov B, Lindgren M, Kieseppä T, Wegelius A, Suvisaari J. Cognitive functioning and cannabis use in first-episode psychosis. Nord J Psychiatry. 2022;76(7):551-558. doi:10.1080/08039488.2021.2018038

17. Addington J, Case N, Saleem MM, Auther AM, Cornblatt BA, Cadenhead KS. Substance use in clinical high risk for psychosis: a review of the literature. Early Interv Psychiatry. 2014;8(2):104-112. doi:10.1111/eip.12100

18. Talonen S, Väänänen J, Kaltiala-Heino R. Gender differences in first onset Schizophrenia spectrum psychoses. Nord J Psychiatry. 2017;71(2):131-138. doi:10.1080/08039488.2016.1245783

19. Korkeila JA, Svirskis T, Heinimaa M, et al. Substance abuse and related diagnoses in early psychosis. Compr Psychiatry. 2005;46(6):447-452. doi:10.1016/j.comppsych.2005.03.008

20. Salokangas RKR, From T, Ilonen T, et al. Short-term functional outcome in psychotic patients: results of the Turku early psychosis study (TEPS). BMC Psychiatry. 2021;21(1):602. Published 2021 Dec 2. doi:10.1186/s12888-021-03516-4

21. MCGLASHAN, T. H., et al. Structured interview for prodromal syndromes. New Haven, CT: PRIME Research Clinic, Yale School of Medicine, 2001.

22. Dawe S, Seinen A, Kavanagh D. An examination of the utility of the AUDIT in people with schizophrenia. J Stud Alcohol. 2000;61(5):744-750. doi:10.15288/jsa.2000.61.744

23. Nesvåg R, Lange EH, Faerden A, et al. The use of screening instruments for detecting alcohol and other drug use disorders in first-episode psychosis. Psychiatry Res. 2010;177(1-2):228-234. doi:10.1016/j.psychres.2010.01.007

24. Suvisaari J, Partti K, Perälä J, et al. Mortality and its determinants in people with psychotic disorder. Psychosom Med. 2013;75(1):60-67. doi:10.1097/PSY.0b013e31827ad512

25. Partti K, Vasankari T, Kanervisto M, et al. Lung function and respiratory diseases in people with psychosis: population-based study. Br J Psychiatry. 2015;207(1):37-45. doi:10.1192/bjp.bp.113.141937

26. Karpov B, Joffe G, Aaltonen K, et al. Psychoactive substance use in specialized psychiatric care patients. Int J Psychiatry Med. 2017;52(4-6):399-415. doi:10.1177/0091217417738937

27. Buchy L, Perkins D, Woods SW, Liu L, Addington J. Impact of substance use on conversion to psychosis in youth at clinical high risk of psychosis. Schizophr Res. 2014;156(2-3):277-280. doi:10.1016/j.schres.2014.04.021

28. Zammit S, Allebeck P, Andreasson S, Lundberg I, Lewis G. Self reported cannabis use as a risk factor for schizophrenia in Swedish conscripts of 1969: historical cohort study. BMJ. 2002;325(7374):1199. doi:10.1136/bmj.325.7374.1199

29. Kivimies K, Repo-Tiihonen E, Kautiainen H, et al. Opioid abuse and hospitalization rates in patients with schizophrenia. Nord J Psychiatry. 2016;70(2):128-132. doi:10.3109/08039488.2015.1059884

30. Cookey J, McGavin J, Crocker CE, Matheson K, Stewart SH, Tibbo PG. A Retrospective Study of the Clinical Characteristics Associated with Alcohol and Cannabis use in Early Phase Psychosis. Can J Psychiatry. 2020;65(6):426-435. doi:10.1177/0706743720905201

31. Knaappila N, Marttunen M, Fröjd S, Lindberg N, Kaltiala R. Changes in cannabis use according to socioeconomic status among Finnish adolescents from 2000 to 2015. J Cannabis Res. 2020;2(1):44. Published 2020 Dec 24. doi:10.1186/s42238-020-00052-y

32. Myran DT, Gibb M, Pugliese M, et al. First-episode psychosis and substance use involvement across birth cohorts in Canada: a retrospective longitudinal population-based study. Lancet Psychiatry. 2026;13(3):223-232. doi:10.1016/S2215-0366(25)00395-5

33. Carr JA, Norman RG, Manchanda R. Sociodemographic and clinical characteristics of patients presenting with first-episode psychosis and concurrent substance misuse. Early Interv Psychiatry. 2009;3(1):75-79. doi:10.1111/j.1751-7893.2008.00100.x

34. Brunette MF, Mueser KT, Babbin S, et al. Demographic and clinical correlates of substance use disorders in first episode psychosis. Schizophr Res. 2018;194:4-12. doi:10.1016/j.schres.2017.06.039

35. Onyeka IN, Uosukainen H, Korhonen MJ, et al. Sociodemographic characteristics and drug abuse patterns of treatment-seeking illicit drug abusers in Finland, 1997-2008: the Huuti study. J Addict Dis. 2012;31(4):350-362. doi:10.1080/10550887.2012.735563

36. Lobbana F, Barrowclough C, Jeffery S, et al. Understanding factors influencing substance use in people with recent onset psychosis: A qualitative study. Soc Sci Med. 2010;70(8):1141-1147. doi:10.1016/j.socscimed.2009.12.026

37. Archie S, Boydell KM, Stasiulis E, Volpe T, Gladstone BM. Reflections of young people who have had a first episode of psychosis: what attracted them to use alcohol and illicit drugs?. Early Interv Psychiatry. 2013;7(2):193-199. doi:10.1111/j.1751-7893.2012.00355.x

38. Pasman JA, Verweij KJH, Gerring Z, et al. Author Correction: GWAS of lifetime cannabis use reveals new risk loci, genetic overlap with psychiatric traits, and a causal effect of schizophrenia liability. Nat Neurosci. 2019;22(7):1196. doi:10.1038/s41593-019-0402-7

39. Møller T, Linaker OM. Using brief self-reports and clinician scales to screen for substance use disorders in psychotic patients. Nord J Psychiatry. 2010;64(2):130-135. doi:10.3109/08039480903274423

40. Lähteenvuo M, Batalla A, Luykx JJ, et al. Morbidity and mortality in schizophrenia with comorbid substance use disorders. Acta Psychiatr Scand. 2021;144(1):42-49. doi:10.1111/acps.13291

41. Karoliina Karjalainen. Suomalaisten huumeiden käyttö ja huumeasenteet – Huumeaiheiset väestökyselyt Suomessa 1992–2022. Terveyden ja hyvinvoinnin laitos (THL). Raportti 12/2023. 139 sivua. Helsinki 2023.