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## The relative prevalence of schizophrenia among cannabis and cocaine users attending addiction services

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### ABSTRACT

**Background:** Cannabis and cocaine are the most common illicit drugs for which people are treated in addiction services in Latin America. Much research has suggested that the use of cannabis increases the risk of schizophrenia; there is less evidence concerning cocaine. The aim of the present study was to establish the relative prevalence of schizophrenia in people treated for cannabis use and cocaine use disorders in Chile.

**Methods:** A sample of 22,615 people treated for illicit drug use disorders was obtained from a national registry of addiction service users in Chile. Clinical diagnoses were established at admission to substance use treatment programs or at any point during the period of treatment. Prevalence rates of schizophrenia and related disorders, and affective disorders were calculated for the groups of people with cocaine use disorders, and cannabis use disorders. Odds ratios (OR) for schizophrenia and for affective disorders were calculated for cannabis users using the group of people treated for cocaine use disorders as reference category.

**Results:** The prevalence of schizophrenia and related disorders was 1.1% in those with cocaine use disorders, but 5.2% in those with cannabis use disorders (OR 4.9;  $p < 0.01$ ). The prevalence of affective disorders was 9.3% in cocaine use disorders, and 13.2% in cannabis use disorders (OR 1.5;  $p < 0.01$ ).

**Conclusions:** The prevalence of schizophrenia and to a lesser extent affective disorders is higher among people with cannabis use disorder than cocaine use disorder among those attending addiction services.

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### 1. Introduction

Cannabis is the most commonly used illicit drug worldwide (Hall and Degenhardt, 2007; United Nations Office on Drugs and Crime, 2016). Its use has been consistently associated with an increased risk of psychosis (Radhakrishnan et al., 2014; Murray and Di Forti, 2016). Frequent users of cannabis have a two-fold increased risk of psychosis compared to non-users (Moore et al., 2007), and the risk appears to increase with the dose and frequency of use (Henquet et al., 2005; Moore et al., 2007; Zammit et al., 2002; Marconi et al., 2016), as well as in those who use more potent cannabis (Di Forti et al., 2009; Di Forti et al., 2014; Murray et al., 2016). One report suggests that people with a lifetime diagnosis of cannabis dependence have a 3.5 fold increased risk to have a

lifetime diagnosis of non-affective psychosis, and are twice as likely to have mood disorders (Agosti et al., 2002).

Cocaine is the second most commonly used illicit drug after cannabis in Latin America (Inter-American Drug Abuse Control Commission, 2015). Although other stimulants and especially amphetamines increase the risk for acute and temporary psychoses (Hermens et al., 2009; Niemi-Pynttari et al., 2013; Paparelli et al., 2011), evidence concerning a possible association between cocaine use and schizophrenia is still inconclusive.

Among those attending addiction services in Latin America, cocaine use is by far the most common problem followed by use of cannabis (United Nations Office on Drugs and Crime, 2016). Given the robust association of cannabis and schizophrenia in the general population and in clinical samples, whereas cocaine use mostly associates with acute temporary psychoses, we hypothesized that people using services for cannabis use problems had higher rates of schizophrenia than people using services for cocaine use disorders. The aim of the present study was to establish the relative prevalence of schizophrenia and affective disorders in people treated for cannabis and/or cocaine use disorders in public addiction services in Chile.

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## 2. Methods

### 2.1. Study population

A nationwide registry from the National Prevention and Rehabilitation Service for Drug and Alcohol Use in Chile (Servicio Nacional para la Prevención y Rehabilitación del Consumo de Drogas y Alcohol, SENDA) was studied. SENDA provides public health services for the assessment and treatment of people with substance use disorders, and covers about 80% of the population in Chile. The remaining 20% are treated in private addiction services. SENDA collects data on people at admission to outpatient and residential care treatment programs throughout the country.

The database comprised 30,502 people, who entered substance use treatments from January 2007 to October 2013. We studied those 22,615 people who had substance use disorders according to the International Classification of Diseases tenth edition (ICD-10) and their principal drug of addiction was cannabis and/or cocaine products (inhaled cocaine and smoked cocaine as base paste). We excluded patients who were primarily addicted to alcohol; however, people with primary addiction to cocaine and/or cannabis and comorbid alcohol use disorders were included.

### 2.2. Variables

Socio-demographic data were collected. The following variables were extracted from the database: 1) Gender, 2) Age at admission to treatment, 3) Primary drug of abuse indicated by the patients as causing the addiction problem and motivating their request for treatment, 4) Secondary drugs used (other substances of harmful use or dependency), 5) Age of initial use of primary drug, 6) Educational level, and 7) Comorbid mental disorder (if present). The following variables were calculated based on the available data: 9) number of years of use of the primary drug, 10) starting use of the primary drug before the age of 18.

### 2.3. Assessments

All addiction service users were clinically assessed for substance use disorders and comorbid mental disorders at their enrollment in the treatment programs. In addition, comorbid mental disorders may have been diagnosed at any point of time during the treatment. General physicians and psychiatrists in the treatment facilities assessed mental disorders using ICD-10 criteria in clinical interviews. When a psychotic disorder is present, diagnoses are usually confirmed by psychiatrists.

### 2.4. Study design

The study was cross-sectional, based on a nationwide database of public addiction service users. The sample was divided into three groups according to the drugs of use: 1) Users of cocaine based products without use of other illicit drugs; 2) Cannabis users without other illicit drug use; and 3) Users of both cannabis and cocaine.

Comorbid mental disorders were the outcome variables. The disorders studied were: 1) Schizophrenia and related psychoses (SCZRP) (ICD-10: F20–29); and 2) Affective Disorders including major depression and bipolar disorders (ICD-10 Code: F30–39) were studied as a comparison.

### 2.5. Statistical analysis

Descriptive statistics were used to describe socio-demographic variables for the three different groups of substance use disorders. The variables were gender, age at admission to substance use treatment, age at first use of the primary substance, first use before the age of 18 years, years of use of the primary drug, duration of treatment, comorbid alcohol use disorder, educational level and comorbid mental disorders.

Logistic regression analyses were conducted with the groups of drug use disorders as independent variables and the groups of psychiatric disorders as dependent variables. To compare the risk of psychiatric disorders in those with cocaine use disorder versus those with cannabis use disorders, the group with cocaine use disorders without other illicit drug use was the reference category. Odds ratios (OR) and 95% confidence intervals of the odds ratios were calculated. Multivariate analyses were conducted for each group of psychiatric disorders adjusting for gender, age at admission to substance use treatment, age at first use of the primary substance, comorbid alcohol use disorder and educational level.

To explore a possible effect of severity of cannabis use, we subdivided the group of users of both cannabis and cocaine into two subgroups: 1) using cannabis as primary drug and cocaine as secondary 2) using cocaine as primary and cannabis as secondary drug. We propose that people using cannabis as the primary drug had a more severe use of cannabis than those using it as secondary drug. In the subgroup that used cannabis as primary drug, cannabis was the primary problem causing people to use addiction services.

We calculated the ORs and 95% CI of the ORs for SCZRP for both subgroups compared to the reference category.

Statistical analyses were conducted using the software package R 3.01.

### 2.6. Ethical considerations

This work was carried out with the ethical authorization of SENDA. Data used in this study were part of the routine clinical data collection in public treatment facilities for substance use disorders. Researchers accessed processed and analyzed anonymized data. Identity and confidentiality of the patients were protected. Patient identifiers were encoded with an alphanumeric code untraceable to the individual.

## 3. Results

### 3.1. Socio-demographic characteristics and groups of drug use disorders

The sample comprised 74.1% of the total population entering public substance use services. Regarding the primary drug of use, 20.9% had harmful use, and 79.1% dependence. The majority were male (72.3%), and their ages ranged from 18 to 77 years, with a mean age of 31.7 (standard deviation 8.3); 75% were younger than 37 years. 35.8% of the sample were in basic outpatient treatment (one contact per week), while 42.6% received intensive outpatient treatment (two to five contacts per week) and 21.6% underwent residential treatment. The mean duration of treatment was 217 days with a standard deviation of 163 days, and the median duration was 172 days.

Cocaine was used by 94.4% of the sample, alcohol by 71.6%, and cannabis by 57.9%. Among the cocaine users, 79.5% inhaled cocaine, and 48.8% smoked it as base paste. 88.5% of the sample reported cocaine as their primary drug of use while 11.5% reported cannabis as their primary drug of use.

Table 1 shows characteristics of the patients grouped according to their use of cannabis and/or cocaine: 1) cocaine without other illicit drug use 2) cannabis without other illicit drug use and 3) use of both cocaine and cannabis.

A majority in all groups was male, had low educational levels and comorbid alcohol use. The mean age of enrollment in treatment was in the early thirties and did not differ between groups. The group of cannabis users without other illicit drug had an especially young age of onset with a majority initiating use before the age of 18 years and particularly long duration of the disorder.

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