Impact of cannabis use on outcomes of patients admitted to an involuntary psychiatric unit: A retrospective cohort study

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Introduction

Cannabis is the most widely-used illegal substance in the world. Consumption has increased in recent years globally, and about 188 million people used the drug in 2017 (World Drug Report 2019). In France, recent surveys showed that during their lifetime 44.8% of adults (18 to 64 years old) and nearly four in ten adolescents before 18 had tried cannabis at least once *(OFDT, 2017; OFDT, 2018)*. Although cannabis is not socially perceived to be a high-risk drug (Hughes et al., 2016), cannabis use is a risk factor for several mental disorders, including psychotic disorders and mood disorders (Gobbi et al., 2019; Wayne Hall & Degenhardt, 2008; Kiburi et al., 2021) and is associated with psychiatric hospitalizations (Lai & Sitharthan, 2012; Prince, 2012). The mechanisms connecting cannabis to these outcomes remain unclear (Hamilton & Sumnall, 2020).

For many years, the literature has highlighted the association between cannabis use and psychotic symptoms, such as a delusional states, hallucinations and emotional lability (W. Hall & Degenhardt, 2000; Cleghorn et al., 1991) or psychotic disorders (Lai & Sitharthan, 2012; Schimmelmann et al., 2012; Ksir & Hart, 2016; Singh &Balhara, 2017). The relative risk of developing psychosis among cannabis users is estimated to be 2:1 for occasional use and 6:1 for heavy users (Bagot et al., 2015; Di Forti et al., 2015). Several outcomes of cannabis use in terms of psychosis have been described: i) self-limited psychotic symptoms during acute intoxications; ii) brief psychotic episodes, immediately after the intoxication; and iii) the emergence of persistent psychotic symptoms later in life, an outcome that seems to be associated particularly with early, frequent and heavy use in adolescence (Kiburi et al., 2021; Rubino et al., 2012; Rylander et al., 2018). Importantly, in about half of the cases cannabis-induced psychosis converts to schizophrenia in the next few years (Starzer et al., 2018).

Another study estimated that people who abuse cannabis have three times more risk of being hospitalized for psychiatric disorders (Prince, 2012). This risk is also increased (odds ratio of 6) as a function of the dose consumed (Schubart et al., 2011). Consistently, cannabis use has been found to increase relapse rates, predispose to more hospitalizations, increase positive symptoms and increase suicidality in patients with schizophrenia (Østergaard et al., 2017; Prince, 2012; Rozin et al., 2019; Schoeler et al., 2017). Patients admitted in involuntary units seem to be more likely to have substance use disorders, including cannabis, compared with patients in other psychiatric units (Hustoft et al., 2013). According to the results of a Spanish study in a small sample, patients who used cannabis after an involuntary admission for a first psychotic episode had more problems of adherence to treatment (Barbeito et al., 2013). Once the psychotic episode is over, cannabis use may increase the risk of relapse (San et al., 2013; Bergé et al., 2016). However, the relationship between cannabis use and resistance to treatment has not been sufficiently studied (Legge et al., 2019).

The use of cannabis plays an important role in the development of psychotic disorders, relapse, and the number of psychiatric hospitalizations. In some cases, the severity of the symptoms can lead to forced hospitalizations. Our goal is to compare the clinical profile of cannabis users and non-users according to the urinary screening at admission in a secure unit for involuntary care. We hypothesize an impact of cannabis use on the number of hospitalizations, the length of hospital stays and the use of antipsychotics in this population.

Materials and methods

Population:

The study was conducted in a secured psychiatric intensive care unit with a capacity of 30 beds between January 1, 2016 and December 31, 2016. The total sample includes 370 involuntarily hospitalized patients (under request of a third party or a representative of the state) according to the terms of the law of 04 July 2011. Criteria for involuntary admission in France include the following: i) the person suffers a mental disorder, ii) the mental disorder renders the person incapable of giving consent, and iii) the person's mental state requires immediate care with constant monitoring (LOI N° 2011-803, 2011).

All patients who were hospitalized in the unit for the first time in 2016 were included. No exclusion criteria were applied since 1) we aim to reflect the reality of involuntary care, and 2) the retrospective nature of the study prevented a clinical assessment during which exclusion criteria could have been applied.

Only readmissions to the same unit were considered since it is the only involuntary unit in the catchment area. We did not take into account hospitalizations in other hospitals or non-involuntary units. In France, psychiatric care is organized in general psychiatry sectors providing care for about 70 000 adult patients each. Forced admissions are made only in public hospitals within those sectors. With the exception of homeless patients or a change of address, patients involved in our study would have been transferred to our unit in case of involuntary admission in another sector of care.

Tetrahydrocannabinol measurement:

All patients entering the unit were routinely screened for illegal drugs using a urinary test at the moment of admission that detected tetrahydrocannabinol (THC). The patients were accompanied during the urine collection to avoid potential distortions in the

results. The presence of 11-nor-Δ9 THC-9-carboxylic acid (Δ9 COOH-THC) was detected using the Cannabinoid II (THC2) assay (Roche) according to the manufacturer's instructions and analyzed on the Roche / Hitachi Cobas C system. The time from admission until urine drug testing was recorded for each patient.

Collection of socio-demographic and diagnostic data:

All data used in this study was obtained retrospectively from patient clinical records with authorization of the CNIL (Commission Nationale de l'Informatique et des Libertés) and Institutional Review Board (N°19.10.06). Participants were not interviewed or assessed with regards to this study. Following advice from the Institutional Review Board, informed consent was waived because of the retrospective nature of the study and the low risk for participants. During the course of the study, a poster was displayed within the unit to inform patients that a study was underway and to invite them to contact a physician for further information or to oppose their inclusion. Age, sex, family and work status, were collected at the time of the patient interview for clinical purposes. The duration of hospitalization, the number of readmissions and the medical diagnoses were recorded.

Marital status was regrouped into single (single, divorced or separated) and in a relationship (including married and couples living together). Occupational situation was regrouped into inactive (people receiving benefits), non-active (people not working without resources) and active (people working and employed at the time of hospitalization). Schizoaffective disorder was regrouped with schizophrenia because of the small numbers of cases. Schizoaffective disorder is listed in international classifications within the categories of psychotic disorders rather than mood disorders.

Mental organic disorders were regrouped with MDD due to the small number of patients in both categories.

Data analysis:

Demographic and clinical characteristics of the patients were described with proportions for categorical variables and with means ± standard deviations (SD) for quantitative variables. The association between these characteristics and cannabis use was analyzed using univariate and multivariate logistic regression models to calculate raw and adjusted odds ratios and their 95% confidence intervals.

We then compared the average length of stay between the two groups (THC + and -) using univariate and multivariate linear regression model safter logarithmic transformation of the dependent variable (length of stay). Two multivariate models were constructed. The first model was adjusted for age, gender, lifestyle, and professional status. Psychiatric illnesses were added in the 2nd model. Adjusted least squares means were estimated from these two models and are presented after back-transformation [exp (ln (length of stay))].

Thirdly, we explored if readmission at 1 year or at 2 years could be explained by cannabis use, using univariate and multivariate logistic regression model. As previously, ORs were adjusted in a first model for age, sex, professional situation, lifestyle and, in a second model, also for psychiatric illnesses.

Finally, we examined if the class of psychotropic treatment at discharge was associated with cannabis use at admission. Univariate and multivariate logistic regression models were carried out for 4 treatment classes (antidepressants, benzodiazepines, antipsychotics and mood stabilizers).

Analyses were performed with a bilateral alpha level of 0.05 using the SAS Enterprise guide 7.15(SAS Institute, Cary, North Carolina).

Results

Description of the population:

Of the 370 patient records screened (69% men, p<0.0001), the toxicological tests identified 130 THC+ patients and 240 THC- patients. Urine was generally collected within 24 hours (mean=0.74 days, SD=1.20, IQR=0-1) following patient admission. THC+ patients are significatively younger (p<0.0001) and had an average age of 33 years (16-57 years old) compared to 48 years (14-90 years old) for THC- patients. Patient characteristics are shown in Table 1.

In multivariate analyses, after adjustment for all covariates, there were no differences between the two groups as regards to marital status or employment situation (Table 1). Male patients were more often THC+ (OR = 3.48, 95CI= 2.00-6.05, p <.0001). When age was compared in terciles, the decrease in risk was particularly evident from 49 years of age (OR=0.08, 95CI=0.04; 0.17, p<.0001).

Most THC+ patients were diagnosed with schizophrenia (24.6%) or bipolar disorder (45.4%). Patients with schizophrenia showed the highest rates of positive THC screens (46.6%, 34/73). Compared to patients with schizophrenia, patients diagnosed with major depression or mental organic disorders, regrouped as “other diagnoses”, were less likely to use THC at admission (OR=0.25; 95CI=0.07, 0.93; p=.04). Patients with personality disorders were also less likely to use THC at admission in crude analyses but this result was no longer significant after adjustment (OR=0.51; 95CI=0.23, 1.12; p=.09).

Among the 130 cannabis users, the concentration of THC at admission ranged from 4 to 1289 ng/mL with an average of 366.1±238.3ng/mL.

The presence of other drugs, (amphetamine, heroin, cocaine, MDMA) was sought with urinary tests at admission. Illicit drugs were detected only in a few patients (n=11). 36 patients showed positive alcohol levels in blood.

Cannabis use and length of hospitalization (Table 2):

After adjustment for sex, age in terciles, marital status and professional status, THC + patients showed a longer length of hospitalization than THC- patients (mean: 11.08 vs 8.26; p=.03). However, the association disappeared after adjustment for psychiatric disorders (mean: 9.44 vs 8.04; p=.22). Sensitivity analyses show that the association of cannabis use with a longer stay persisted when adjusting only by schizophrenia (p=0.05).

There was no significant correlation between THC concentration at admission and length of stay (Spearman ρ=-0.092; p=.30).

Factors influencing rehospitalisation (Table 3):

THC+ patients at admission were more likely to be re-hospitalized at 12 months independently from demographic and clinical variables (OR=2.29; 95CI=1.24, 4.24; p=.0082). Middle-aged patients (36-48) were less likely than younger patients to be re-hospitalized at 12 months (OR=0.46; 95CI=0.23, 0.89; p=.02). Concerning psychiatric disorders, patients with bipolar disorder (OR=0.46; 95CI=0.24, 0.93; p=.03), personality disorders (OR=0.27; 95CI=0.11, 0.63; p=.0025) and other diagnoses (OR=0.3; 95CI=0.09, 1.01; p=.05) were less likely to be re-hospitalized compared to patients diagnosed with schizophrenia. A similar trend was found for brief psychotic disorder.

Overall, we found similar results concerning the risk of re-hospitalization at 24 months but the association with THC+ was not significant (OR=1.62; 95CI=0.94, 2.81; p=.08) (Supplementary Table 1S).

Cannabis use and treatment prescription at discharge:

THC use at admission was associated with a more frequent prescription of benzodiazepines at discharge independently of demographic and clinical variables (OR=1.93; 95CI=1.13, 3.28; p=0.02). On the contrary, THC users were less likely to be prescribed an antidepressant at discharge (OR=0.22; 95CI=0.08, 0.66; p=.007). No association between THC use and the prescription of antipsychotics or mood stabilizers was found.

Discussion

Our purpose was to study if cannabis use influenced the evolution of patients who entered a secure psychiatric ward. To the best of our knowledge, very few studies have so far examined the effect of cannabis on patients involuntarily hospitalized, and none of them looked at the length of admission or the rates of rehospitalization.

Some studies in open hospitalization units found shorter stays among inpatients using cannabis compared to those who did not. In those studies, the selection criteria consisted on the presence of psychotic symptoms (Rylander et al., 2018), or discharge diagnoses of bipolar disorder, schizophrenia and other psychotic disorders (Johnson et al., 2016; Deng et al., 2019). Of note, one study found that cannabis users received less antipsychotics (Deng et al., 2019), while another reported more agitation and oral medication in the cannabis group (Johnson et al., 2016). On the other hand, a recent study in a community hospital concludes that cannabis use was associated with an increased length of stay in patients affected by schizophrenia spectrum disorders

(Olayinka et al., 2020). In our sample, the association of cannabis with longer hospitalizations disappeared after adjusting for mental disorders in the multivariate analysis. Since the association between cannabis use and longer hospital stays in involuntary units was moderated by mental disorders, we conducted a sensitivity analysis to investigate specifically the effect of each diagnostic category. The association with longer hospital stays disappeared after adjusting the analyses by any or all mental disorders, except in the case of schizophrenia. This finding suggests that the use of cannabis in patients with schizophrenia may lengthen the duration of hospitalization in these units, and that the association of THC positive screens with longer hospital stays may be best explained by a higher rate of schizophrenia in this group.

Cannabis use before hospitalization predicted, independently of other variables, involuntary readmissions within 12 months. Patients diagnosed with schizophrenia were also more likely to be re-hospitalized compared to any other disorder. These results are consistent with a recent record-linkage studying Danish treatment services indicating that cannabis use is a risk marker for the readmission of patients with schizophrenia (Rømer Thomsen et al., 2018). Collizi et al. also suggested that a history of cannabis use prior to hospitalization increased the risk of multiple hospitalizations and extended the length of stay. This risk would be higher in men and black ethnicity (Colizzi et al., 2018). However, in agreement with Rylander et al (2018), we found no effect of cannabis use on the risk of re-admission within one month of discharge (data not shown).

Few studies have reported THC concentrations among psychiatric inpatients. Duflot et al (Duflot et al., 2019) found two-times higher concentrations among patients that were specifically hospitalized to stop cannabis abuse (many of them with psychiatric

comorbidities). The average urinary concentration in their sample was 786 ± 1270 ng/mL.

Independently of the psychiatric diagnosis, THC + patients were discharged more often with a benzodiazepine prescription. Benzodiazepine prescription is likely to be linked to the treatment of cannabis abstinence during hospitalization, since cannabis users are subject to withdrawal symptoms such as irritability or nervousness, insomnia and craving (Dervaux, 2018; Sexton et al., 2019). The association of cannabis use and benzodiazepine prescription emerged when age and sex were controlled for. Female and older patients received more often benzodiazepines at discharge but the prescription of benzodiazepines associated with cannabis was particularly frequent among young men and heavy cannabis users.

Two results of the multivariate analyses were unexpected. First, patients affected by depressive disorders or mental organic disorders were less likely to use cannabis compared to the other diagnostic groups. According to Lucatch et al. (2018), patients suffering from depression, including bipolar depression, report higher rates of cannabis use than the general population. However, in their study cannabis use rates were substantially lower in depression compared to psychotic disorders, and no direct comparison with unaffected populations was made. Second, although few patients received antidepressants at discharge, these prescriptions were still less likely among cannabis users (only a handful of them). Given the small number of patients diagnosed with depression or receiving antidepressants, these results should be taken very cautiously.

Studies on patient compliance, in patients with both a drug use disorder and a psychotic disorder, are rare. It appears, however, that in two-thirds of cases, readmissions could be due to poor compliance (Ameller & Gorwood, 2015). Cannabis use is one of the three

most important explanatory factors for poor compliance in subjects after a first psychotic episode and more particularly for schizophrenia (Miller et al., 2009). In schizophrenia, as much as 18% of the risk of poor compliance and approximately 30% of relapses with hospitalization could be attributable to drug use disorders (Ameller & Gorwood, 2015).

Our results highlight the importance of developing strategies to improve the management of cannabis use among patients with severe mental disorders. The continuity of cannabis use in this population has been clearly associated with bad adherence to treatment and care (Barbeito et al, 2013). A variety of interventions, such as motivational interviews and cognitive-behavioral therapies, can be used with the aim of encouraging abstinence or reducing cannabis use (Lee et al., 2019).

This study is based on an unselected and relatively large sample. All patients that did not express opposition to the study were included, thus reducing selection biases. However, it is important to note three limitations. First, the immunoassays used for the urinary cannabis screen may be subject to cross-reactivity with other compounds potentially yielding false-positive results (Saitman et al., 2014). False negative results by adulteration of the samples are also possible (Matriciani et al., 2018), although improbable in our sample because of the conditions in which the screening was made. Second, due to the retrospective nature of the study, we were unable to adjust the results by other factors such as symptom severity, other substance use or the frequency/level of cannabis use. Finally, a detailed assessment retracing the patient's consumption patterns and history would have been more reliable than a single point measure.

Conclusions:

While a lot of research has been performed on the psychiatric outcomes of cannabis use, the consequences for involuntarily treated patients have received less attention. Our

data suggests the involvement of cannabis use in the unfavorable evolution of involuntary psychiatric care, increasing the risk of readmission and modifying the pattern of prescription at discharge. Nevertheless, further studies on the effect of cannabis in this population are warranted. The management strategies of cannabis use may need to be reinforced in psychiatric secure units given the specific profile of cannabis users, in terms of diagnosis, treatment and re-hospitalization.

Key points:

- Cannabis use is independently associated with benzodiazepine prescriptions at discharge and 12-month readmissions among patients involuntarily admitted to a psychiatric ward.

- Young male patients with psychotic disorders are particularly at risk of using cannabis in secure psychiatric wards.

- The systematic screening of cannabis use at admission could help to organize clinical care in these units.

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Declaration of interest:

Nothing to declare

References

Ameller, A., & Gorwood, P. (2015). [Attributable risk of co-morbid substance use disorder in poor observance to pharmacological treatment and the occurrence of relapse in schizophrenia]. *L'Encephale*, *41*(2), 174–183. https://doi.org/10.1016/j.encep.2015.02.002

Bagot, K. S., Milin, R., & Kaminer, Y. (2015). Adolescent Initiation of Cannabis Use and Early-Onset Psychosis. *Substance Abuse*, *36*(4), 524–533. https://doi.org/10.1080/08897077.2014.995332

Barbeito, S., Vega, P., Ruiz de Azúa, S., Saenz, M., Martinez-Cengotitabengoa, M., González-Ortega, I., Bermudez, C., Hernanz, M., Corres, B. F. de, & González-Pinto, A. (2013). Cannabis use and involuntary admission may mediate long-term adherence in first-episode psychosis patients: A prospective longitudinal study. *BMC Psychiatry*, *13*, 326. https://doi.org/10.1186/1471-244X-13-326

Bergé, D., Mané, A., Salgado, P., Cortizo, R., Garnier, C., Gomez, L., Diez-Aja, C., Bulbena, A., & Pérez, V. (2016). Predictors of Relapse and Functioning in First-Episode Psychosis: A Two-Year Follow-Up Study. *Psychiatric Services (Washington, D.C.)*, *67*(2), 227–233. https://doi.org/10.1176/appi.ps.201400316

Cleghorn, J. M., Kaplan, R. D., Szechtman, B., Szechtman, H., Brown, G. M., & Franco, S. (1991). Substance abuse and schizophrenia: Effect on symptoms but not on neurocognitive function. *The Journal of Clinical Psychiatry*, *52*(1), 26–30.

Colizzi, M., Burnett, N., Costa, R., De Agostini, M., Griffin, J., & Bhattacharyya, S. (2018). Longitudinal assessment of the effect of cannabis use on hospital readmission rates in early psychosis: A 6-year follow-up in an inpatient cohort. *Psychiatry Research*, *268*, 381–387. https://doi.org/10.1016/j.psychres.2018.08.005

Deng, H., Desai, P. V., Mohite, S., Okusaga, O. O., Zhang, X. Y., Nielsen, D. A., & Kosten, T. R. (2019). Hospital Stay in Synthetic Cannabinoid Users With Bipolar Disorder, Schizophrenia, or Other Psychotic Disorders Compared With Cannabis Users. *Journal of Studies on Alcohol and Drugs*, *80*(2), 230–235.

Dervaux, A. (2018). [Cannabis use disorders and psychiatric comorbidities]. *La Revue Du Praticien*, *68*(6), 670–674.

Di Forti, M., Marconi, A., Carra, E., Fraietta, S., Trotta, A., Bonomo, M., Bianconi, F., Gardner-Sood, P., O'Connor, J., Russo, M., Stilo, S. A., Marques, T. R., Mondelli, V., Dazzan, P., Pariante, C., David, A. S., Gaughran, F., Atakan, Z., Iyegbe, C., … Murray, R. M. (2015). Proportion of patients in south London with first-episode psychosis attributable to use of high potency cannabis: A case-control study. *The Lancet. Psychiatry*, *2*(3), 233–238. https://doi.org/10.1016/S2215-0366(14)00117-5

Duflot, T., Vasse, M., Guillerme, J., Schrapp, A., Mory, C., Imbert, L., Djerada, Z., Protais, Y., Guillin, O., Goetz, H., & Lamoureux, F. (2019). Interest of adjusting urine cannabinoids to creatinine level to monitor cannabis cessation therapy in heavy smokers with psychiatric disorders. *Drug Testing and Analysis*, *11*(9), 1453–1459. https://doi.org/10.1002/dta.2672

Gobbi, G., Atkin, T., Zytynski, T., Wang, S., Askari, S., Boruff, J., Ware, M., Marmorstein, N., Cipriani, A., Dendukuri, N., & Mayo, N. (2019). Association of Cannabis Use in Adolescence and Risk of Depression, Anxiety, and Suicidality in Young Adulthood: A Systematic Review and Meta-analysis. *JAMA Psychiatry*, *76*(4), 426–434. https://doi.org/10.1001/jamapsychiatry.2018.4500

Hall, W., & Degenhardt, L. (2000). Cannabis use and psychosis: A review of clinical and epidemiological evidence. *The Australian and New Zealand Journal of Psychiatry*, *34*(1), 26–34. https://doi.org/10.1046/j.1440-1614.2000.00685.x
Hall, Wayne, & Degenhardt, L. (2008). Cannabis use and the risk of developing a psychotic disorder. *World Psychiatry: Official Journal of the World Psychiatric Association (WPA)*, *7*(2), 68–71. https://doi.org/10.1002/j.2051-5545.2008.tb00158.x
Hamilton, I., & Sumnall, H. (2020). Are we any closer to identifying a causal relationship between cannabis and psychosis? *Current Opinion in Psychology*, *38*, 56–60. https://doi.org/10.1016/j.copsyc.2020.07.027
Hughes, Lipari, and Williams (2016). Marijuana use and perceived risk of harm from marijuana use varies within and across states. The CBHSQ Report: July 26, 2016. Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Rockville, MD.
Hustoft, K., Larsen, T. K., Auestad, B., Joa, I., Johannessen, J. O., & Ruud, T. (2013). Predictors of involuntary hospitalizations to acute psychiatry. *International Journal of Law and Psychiatry*, *36*(2), 136–143. https://doi.org/10.1016/j.ijlp.2013.01.006
Johnson, J. M., Wu, C. Y., Winder, G. S., Casher, M. I., Marshall, V. D., & Bostwick, J. R. (2016). The Effects of Cannabis on Inpatient Agitation, Aggression, and Length of Stay. *Journal of Dual Diagnosis*, *12*(3–4), 244–251. https://doi.org/10.1080/15504263.2016.1245457
Kiburi, S. K., Molebatsi, K., Ntlantsana, V., & Lynskey, M. T. (2021). Cannabis use in adolescence and risk of psychosis: Are there factors that moderate this relationship? A systematic review and meta-analysis. *Substance Abuse*, 1–25. https://doi.org/10.1080/08897077.2021.1876200
Ksir, C., & Hart, C. L. (2016). Cannabis and Psychosis: A Critical Overview of the Relationship. *Current Psychiatry Reports*, *18*(2), 12. https://doi.org/10.1007/s11920-015-0657-y
Lai, H. M. X., & Sitharthan, T. (2012). Exploration of the comorbidity of cannabis use disorders and mental health disorders among inpatients presenting to all hospitals in New South Wales, Australia. *The American Journal of Drug and Alcohol Abuse*, *38*(6), 567–574. https://doi.org/10.3109/00952990.2012.694523
Lee, D. C., Schlienz, N. J., Peters, E. N., Dworkin, R. H., Turk, D. C., Strain, E. C., & Vandrey, R. (2019). Systematic review of outcome domains and measures used in psychosocial and pharmacological treatment trials for cannabis use disorder. *Drug and Alcohol Dependence*, *194*, 500–517. https://doi.org/10.1016/j.drugalcdep.2018.10.020
Legge, S. E., Dennison, C. A., Pardiñas, A. F., Rees, E., Lynham, A. J., Hopkins, L., Bates, L., Kirov, G., Owen, M. J., O'Donovan, M. C., & Walters, J. T. R. (2019). Clinical indicators of treatment-resistant psychosis. *The British Journal of Psychiatry: The Journal of Mental Science*, 1–8. https://doi.org/10.1192/bjp.2019.120
LOI n° 2011-803 du 5 juillet 2011 relative aux droits et à la protection des personnes faisant l'objet de soins psychiatriques et aux modalités de leur prise en charge (1), 2011-803 (2011). Accessed from https://www.legifrance.gouv.fr/jorf/id/JORFTEXT000024312722/ on Mars the 1st, 2021.
Lucatch, A. M., Coles, A. S., Hill, K. P., & George, T. P. (2018). Cannabis and Mood Disorders. *Current Addiction Reports*, *5*(3), 336–345. https://doi.org/10.1007/s40429-018-0214-y

Matriciani, B., Huppertz, B., Keller, R., & Weiskirchen, R. (2018). False-negative results in the immunoassay analysis of drugs of abuse: Can adulterants be detected by sample check test? *Annals of Clinical Biochemistry*, *55*(3), 348–354. https://doi.org/10.1177/0004563217725089
Miller, R., Ream, G., McCormack, J., Gunduz-Bruce, H., Sevy, S., & Robinson, D. (2009). A prospective study of cannabis use as a risk factor for non-adherence and treatment dropout in first-episode schizophrenia. *Schizophrenia Research*, *113*(2–3), 138–144. https://doi.org/10.1016/j.schres.2009.04.018
OFDT. (2017). *Drug use in 17-year-olds: Analysis of the 2017 ESCAPAD survey—Tendances 123—February 2018—OFDT*. https://en.ofdt.fr/publications/tendances/drug-use-17-year-olds-analysis-2017-escapad-survey-tendances-123-february-2018/
OFDT. (2018). *Levels of illicit drug use in France in 2017—Tendances 128—November 2018—OFDT*. https://en.ofdt.fr/publications/tendances/levels-illicit-drug-use-france-2017-tendances-128-november-2018/
Olayinka, O., Ojimba, C., Alemu, B., Olaolu, O., Edomias, D., Popoola, O., Kallikkadan, J., Tumenta, T., Gayam, V., Valbrun, L., Olupona, T., & Hershberger, J. (2020). Cannabis Use in Inpatients With Schizophrenia Spectrum Disorders at a Community Hospital. *Journal of Clinical Medicine Research*, *12*(4), 243–250. https://doi.org/10.14740/jocmr4110
Østergaard, M. L. D., Nordentoft, M., & Hjorthøj, C. (2017). Associations between substance use disorders and suicide or suicide attempts in people with mental illness: A Danish nation-wide, prospective, register-based study of patients diagnosed with schizophrenia, bipolar disorder, unipolar depression or personality disorder. *Addiction (Abingdon, England)*, *112*(7), 1250–1259. https://doi.org/10.1111/add.13788
Prince, J. D. (2012). Risk of inpatient stay for mental illness among individuals with substance use disorders. *Psychiatric Services (Washington, D.C.)*, *63*(9), 938–941. https://doi.org/10.1176/appi.ps.201100455
Rømer Thomsen, K., Thylstrup, B., Pedersen, M. M., Pedersen, M. U., Simonsen, E., & Hesse, M. (2018). Drug-related predictors of readmission for schizophrenia among patients admitted to treatment for drug use disorders. *Schizophrenia Research*, *195*, 495–500. https://doi.org/10.1016/j.schres.2017.09.026
Rozin, E., Vanaharam, V., D'Mello, D., Palazzolo, S., & Adams, C. (2019). A retrospective study of the role of long-acting injectable antipsychotics in preventing rehospitalization in early psychosis with cannabis use. *Addictive Behaviors Reports*, *10*, 100221. https://doi.org/10.1016/j.abrep.2019.100221
Rubino, T., Zamberletti, E., & Parolaro, D. (2012). Adolescent exposure to cannabis as a risk factor for psychiatric disorders. *Journal of Psychopharmacology (Oxford, England)*, *26*(1), 177–188. https://doi.org/10.1177/0269881111405362
Rylander, M., Winston, H. R., Medlin, H., Hull, M., & Nussbaum, A. (2018). The association of cannabis use on inpatient psychiatric hospital outcomes. *The American Journal of Drug and Alcohol Abuse*, *44*(1), 73–84. https://doi.org/10.1080/00952990.2017.1329313
Saitman, A., Park, H.-D., & Fitzgerald, R. L. (2014). False-Positive Interferences of Common Urine Drug Screen Immunoassays: A Review. *Journal of Analytical Toxicology*, *38*(7), 387–396. https://doi.org/10.1093/jat/bku075
San, L., Bernardo, M., Gómez, A., & Peña, M. (2013). Factors associated with relapse in patients with schizophrenia. *International Journal of Psychiatry in Clinical Practice*, *17*(1), 2–9. https://doi.org/10.3109/13651501.2012.687452

Schimmelmann, B. G., Conus, P., Cotton, S., Kupferschmid, S., McGorry, P. D., & Lambert, M. (2012). Prevalence and impact of cannabis use disorders in adolescents with early onset first episode psychosis. *European Psychiatry: The Journal of the Association of European Psychiatrists*, *27*(6), 463–469. https://doi.org/10.1016/j.eurpsy.2011.03.001

Schoeler, T., Petros, N., Di Forti, M., Klamerus, E., Foglia, E., Murray, R., & Bhattacharyya, S. (2017). Poor medication adherence and risk of relapse associated with continued cannabis use in patients with first-episode psychosis: A prospective analysis. *The Lancet. Psychiatry*, *4*(8), 627–633. https://doi.org/10.1016/S2215-0366(17)30233-X

Schubart, C. D., Boks, M. P. M., Breetvelt, E. J., van Gastel, W. A., Groenwold, R. H. H., Ophoff, R. A., Sommer, I. E. C., & Kahn, R. S. (2011). Association between cannabis and psychiatric hospitalization. *Acta Psychiatrica Scandinavica*, *123*(5), 368–375. https://doi.org/10.1111/j.1600-0447.2010.01640.x

Sexton, M., Cuttler, C., & Mischley, L. K. (2019). A Survey of Cannabis Acute Effects and Withdrawal Symptoms: Differential Responses Across User Types and Age. *Journal of Alternative and Complementary Medicine (New York, N.Y.)*, *25*(3), 326–335. https://doi.org/10.1089/acm.2018.0319

Singh, S., & Balhara, Y. P. S. (2017). A review of Indian research on co-occurring cannabis use disorders& psychiatric disorders. *The Indian Journal of Medical Research*, *146*(2), 186–195. https://doi.org/10.4103/ijmr.IJMR_791_15

Starzer, M. S. K., Nordentoft, M., & Hjorthøj, C. (2018). Rates and Predictors of Conversion to Schizophrenia or Bipolar Disorder Following Substance-Induced Psychosis. *The American Journal of Psychiatry*, *175*(4), 343–350. https://doi.org/10.1176/appi.ajp.2017.17020223

Table 1. Comparison of demographic and clinical characteristics between patients who used cannabis at the time of entry into secure care (THC+) and those who did not (THC-).

	THC- N=240	*THC+ N=130*	*Total[d] N=370*	*OR* [95% CI]*	*P-value*	*Adjusted OR ** [95% CI]*	*P-value*
Gender							
Male	121 (53.8%)	104 (46.2%)	225 (61%)	3.93 [2.39;6.48]	**<.0001**	3.48 [2.00;6.05]	**<.0001**
Female	119 (82.1%)	26 (17.9%)	145 (39%)				
Age[a]	48.4±15.5	32.8±10.7		0.42[a] [0.34;0.52]	**<.0001**		
Age in terciles							
35 and less	49 (38.9%)	77 (61.1%)	126 (34%)	1		1	
36-48	82 (66.1%)	42 (33.9%)	124 (34%)	0.33 [0.19;0.55]	**<.0001**	0.33 [0.19;0.59]	**.0002**
49 and older	109 (90.8%)	11 (9.2%)	120 (32%)	0.06 [0.03;0.13]	**<.0001**	0.08 [0.04;0.17]	**<.0001**
Marital status							
Single	157 (60.6%)	102 (39.4%)	259 (70%)	0.52 [0.32;0.85]	**.0095**	0.76 [0.41;1.39]	0.37
In a relationship	83 (74.8%)	28 (25.2%)	111 (30%)				
Professional status							
Active	46 (63%)	27 (37%)	73 (20%)	1		1	
Non-active	41 (54.7%)	34 (45.3%)	75 (20%)	1.41 [0.73;2.73]	0.30	1.10 [0.51;2.39]	0.80
Inactive	153 (68.9%)	69 (31.1%)	222 (60%)	0.77 [0.44;1.34]	0.35	0.96 [0.47;1.96]	0.91
Psychiatric Disorders							
Schizophrenia[b]	39 (53.4%)	34 (46.6%)	73 (20%)	1		1	
Bipolar disorder	93 (61.2%)	59 (38.8%)	152 (41%)	0.73 [0.41;1.28]	0.27	1.00 [0.50;2.02]	0.997
Brief psychotic episode	24 (70.6%)	10 (29.4%)	34 (9%)	0.48 [0.20;1.14]	0.10	0.52[0.18;1.48]	0.22
Personality disorder	60 (72.3%)	23 (27.7%)	83 (22%)	0.44 [0.23;0.86]	**0.02**	0.51 [0.23;1.12]	0.09
Other[c]	24 (85.7%)	4 (14.3%)	28 (8%)	0.19 [0.06;0.61]	**0.05**	0.25 [0.07;0.93]	**0.04**

*Unadjusted model

**Adjusted model on Sex, Age in tertiles, Marital Status, Professional status, Psychiatric disorders

[a] OR for 10 years increase

[b] Includes schizoaffective disorder

[c] Includes major depression and mental organic disorders

[d] Total percentages correspond to the sum within the column, group percentages correspond to the sum within the row.

Table 2. Effect of cannabis use at admission on length of stay (days hospitalized).

	Length of stay (days)								
	Unadjusted Model			Model 1*			Model 2**		
Thc	**Mean$_a$**	**[ic 95%]$_a$**	**Pvalue**	**AdjustedMean$_a$**	**[95%CI]$_a$**	**Pvalue**	**AdjustedMean$_a$**	**95%CI]$_a$**	**Pvalue**
Yes	13,67	11.33 ;16.50	.**0002**	11.08	8.81 ; 13.77	**0.03**	9.44	7.48 ; 11.93	0.22
No	8.78	7.65 ; 10.08		8.26	7.07; 9.66		8.04	6.81 ; 9.49	

$_a$After back-transformation: exp(ln(length of stay))
*Adjusted model for Sex, Age in terciles, Marital Status, Professional status
**Adjusted model for Sex, Age in terciles, Marital Status, Professional status, Psychiatric disorders.

Table 3. Effect of THC status at admission, sociodemographic and clinical features of participants based on re-hospitalization in the 12 months.

	Re-hospitalizationafter 1 year							
	Non N=285	*Oui N=85*	*OR* [IC 95%]*	*P-value*	*OR1** [IC 95%]*	*P-value*	*OR2*** [IC 95%]*	*P-value*
Cannabis use								
THC-	201 (83.8%)	39 (16.3%)	1		1		1	
THC+	84 (64.6%)	46 (35.4%)	2.82 [1.72;4.64]	**<.0001**	2.51 [1.38;4.57]	**.0026**	2.29 [1.24;4.24]	**.0082**
Gender								
Female	116 (80%)	29 (20%)	1		1		1	
Male	169 (75.1%)	56 (24.9%)	1.33 [0.80;2.20]	0.28	0.91[0.52,1.61]	0.75	0.88 [0.49;1.58]	0.67
Age in terciles								
35 and less	85 (67.5%)	41 (32.5%)	1		1		1	
36-48	101 (81.5%)	23 (18.5%)	0.47 [0.26;0.85]	**0.01**	0.47 [0.24;0.90	**0.02**	0.46 [0.23;0.89]	**0.02**
49 and older	99 (82.5%)	21 (17.5%)	0.44 [0.24;0.80]	**.0073**	0.54 [0.26;1.13]	0.10	0.58 [0.28;1.24]	0.16
Marital status								
Single	188 (72.6%)	71 (27.4%)	1		1		1	
In a relationship	97 (87.4%)	14 (12.6%)	0.38 [0.20;0.71]	**.0025**	0.54 [0.28;1.05]	0.07	0.62 [0.32,1.22]	0.17
Professional status								
Active	61 (83.6%)	12 (16.4%)	1		1		1	
Non-active	64 (85.3%)	11 (14.7%)	0.87 [0.36;2.13]	0.77	0.66 [0.26;1.68]	0.38	0.66 [0.26;1.69]	.0.39
Inactive	160 (72.1%)	62 (27.9%)	1.97 [0.99;3.91]	0.05	2.25 [1.07;4.72]	**0.03**	1.78 [0.82;3.87]	0.14
PsychiatricDisorders								
Schizophrenia[a]	41 (56.2%)	32 (43.8%)	1				1	
Bipolar disorder	119 (78.3%)	33 (21.7%)	0.36[0.20;0.65]	**.0008**			0.46 [0.24;0.93]	**0.03**
Briefpsychotic episode	28 (82.4%)	6 (17.6%)	0.28 [0.10;0.74]	**0.01**			0.40 [0.14;1.14]	0.09
Personality disorder	73 (88%)	10 (12%)	0.18 [0.08;0.39]	**<.0001**			0.27 [0.11;0.63]	**.0025**
Other[b]	24 (85.7%)	4 (14.3%)	0.21 [0.07;0.68]	**.0088**			0.30 [0.09;1.01]	**0.05**

*Unadjusted OR

**OR adjusted forsex, age, marital status, professional status

***OR adjusted forsex, age, marital status, professional status, psychiatric disorders

[a] Includes schizoaffective disorder

[b] Includes major depression and mental organic disorders

Table 4. Psychiatric treatment at discharge depending on cannabis use at admission.

THC Status	***Psychiatric treatment at discharge***					
	No N(%)	*Yes N(%)*	*OR*[IC95%]*	*P-value*	*ORa**[CI95%]*	*P-value*
	Antidepressants					
	N=330	*N=40*				
THC-	205 (85.4%)	35 (14.6%)	1		1	
THC+	125 (96.2)	5 (3.8)	0.23 [0.09;0.61]	**.0031**	0.22 [0.08;0.66]	**.0070**
	Benzodiazepines					
	N=152	*N=218*				
THC-	105 (43.8%)	135 (56.3%)	1		1	
THC+	47 (36.2)	83 (63.8)	1.37 [0.89;2.13]	0.16	1.93 [1.13;3.28]	**0.015**
	Antipsychotics					
	N=77	*N=293*				
THC-	55 (22.7)	185 (77.1%)	1		1	
THC+	22 (16.9)	108 (83.1)	1.46 [0.84;2.53]	0.18	1.22 [0.62;2.41]	0.57
	Mood stabilizers					
	N=330	*N=40*				
THC-	192 (80%)	48 (20%)	1		1	
THC+	113 (86.9)	17 (13.1)	0.60 [0.33;1.10]	0.10	0.61 [0.29;1.24]	0.17

*Unadjusted model

** OR adjusted for sex, age, marital status, professional status, psychiatric disorders