



Cannabis use and violence in patients with severe mental illnesses: A meta-analytical investigation



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ABSTRACT

Background: The relationship between cannabis and violence remains unclear, especially amid those with severe mental illnesses (SMI). The objective of this meta-analysis was to investigate the cannabis-violence association in a population of individuals with a SMI.

Method: A systematic search of literature using PubMed, PsychINFO, Web of Science and Google scholar was performed (any time-August 2018). All peer-reviewed publications assessing both cannabis use and the perpetration of violence in an SMI sample were included. Data on several key study characteristics such as the proportion of SMI in the sample as well as the number of cannabis users and violent participants were extracted. Odds ratios (OR) were likewise extracted and aggregated with random-effects models.

Results: Of the potential 2449 articles that were screened for eligibility, 12 studies were analyzed using a random-effect meta-analysis. Results showed a moderate association between cannabis use and violence (OR = 3.02, CI = 2.01–4.54, $p = 0.0001$). The association was significantly higher when comparing cannabis misuse (OR = 5.8, CI = 3.27–10.28, $p = 0.0001$) to cannabis use (OR = 2.04, CI = 1.36–3.05, $p = 0.001$).

Conclusion: These findings are clinically relevant for violence prevention/management and highlight the necessity of further investigations with methodologically-sound studies. Thus, longitudinal studies adjusting for important confounding factors (i.e., psychopathic traits and stimulant use) are warranted.

1. Introduction

Cannabis is the most commonly consumed illicit drug in several countries around the world (United Nations Office on Drugs and Crime, 2016). In the public debate, cannabis use has been considered a more or less harmless drug compared to alcohol, central stimulants, and opioids (Berg et al., 2015). However, as a result of its high prevalence in adults with serious mental illnesses (SMI), the role of cannabis consumption is particularly essential in psychiatry regarding its substantial negative consequences found on the course and prognosis of these disorders (Johns, 2001; Patel et al., 2015; van Rossum et al., 2009). Several studies have found that cannabis use was associated with worsened symptomatology, higher risk of psychotic relapse as well as reduced treatment adherence (Gibbs et al., 2015; Schoeler et al., 2016a).

However, whereas individuals with SMI are at an increased risk of violence (Douglas et al., 2009; Swanson et al., 2006), less attention has

been paid to investigate the potential relationship between violence and cannabis use or cannabis misuse in this population. A wealth of research has shown that other substance use is amongst the most crucial risk factors of violence established in those with SMI (Fazel et al., 2009). A systematic review and meta-regression by Witt et al. (2013) found significant associations between violence and history of poly-substance misuse (OR = 10.3), recent alcohol misuse (OR = 2.2) and recent drug misuse (OR = 2.2). However, specifically for history of cannabis misuse, the association was positive but not significant (OR = 1.3); only 4 studies were considered in this review and the use of cannabis was not evaluated. Moreover, reporting adjusted Odds Ratios (OR) was not possible as no consistent adjustments for important confounding factors (i.e., psychopathy, substance use, impulsivity) were brought in the primary studies. Overall, to our knowledge, no clear consensus has emerged for the cannabis-violence relationship. We aimed to conduct a meta-analysis to further clarify the association between cannabis use/misuse and the perpetration of violence in

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Table 1
Electronic search strategy for the meta-analysis conducted in August 2018.

Database; search	Search terms
1. PubMed; k = 9067	(substance[Title/Abstract] OR cannabidoids[MeSH Terms] OR cannabis[MeSH Terms] OR hashish[Title/Abstract] OR marijuana[Title/Abstract] OR marijuana abuse[MeSH Terms] OR marijuana use[MeSH Terms] OR tetrahydrocannabinol[Title/Abstract] OR THC[Title/Abstract]) AND (severe mental illness[Title/Abstract] OR severe mental disorder[Title/Abstract] OR MMD[Title/Abstract] OR SMI[Title/Abstract] OR major mental disorder[Title/Abstract] OR major mental illness[Title/Abstract] OR bipolar and related disorders[MeSH Terms] OR mental disorders[MeSH Terms] OR dissociative disorders[MeSH Terms] OR depressive disorder[MeSH Terms] OR schizophrenia spectrum and other psychotic disorders[MeSH Terms] OR psychosis[Title/Abstract]) AND (violence[Title/Abstract] OR crime[Title/Abstract] OR violent crime[Title/Abstract] OR patient violence[Title/Abstract] OR client violence[Title/Abstract] OR violent[Title/Abstract] OR aggression[Title/Abstract] OR aggressivity [Title/Abstract] OR aggressive[Title/Abstract])
2. PsychINFO; k = 1227	(title: substance OR abstract: substance OR title: cannabinoids OR abstract: cannabinoids OR title: cannabis OR abstract: cannabis OR title: hashish OR abstract: hashish OR title: marijuana OR abstract: marijuana OR title: tetrahydrocannabinol OR abstract: tetrahydrocannabinol OR title: THC OR abstract: THC OR MeSH: cannabis OR MeSH: marijuana abuse OR MeSH: marijuana use) AND (title: severe mental illness OR abstract: severe mental illness OR title: severe mental disorder OR abstract: severe mental disorder OR title: MMD OR abstract: MMD OR title: SMI OR abstract: SMI OR title: major mental disorder OR abstract: major mental disorder OR title: major mental illness OR abstract: major mental illness OR title: schizophrenia OR title: schizoaffective disorder OR title: psychosis OR title: delusions OR title: bipolar disorder OR title: major depression OR abstract: schizophrenia OR abstract: schizoaffective disorder OR abstract: psychosis OR abstract: delusions OR abstract: bipolar disorder OR abstract: major depression OR MeSH: mental disorders OR MeSH: psychotic disorders) AND (title: violence OR abstract: violence OR title: crime OR abstract: crime OR title: violent crime OR abstract: violent crime OR title: patient violence OR abstract: patient violence OR title: client violence OR abstract: client violence OR title: violent OR abstract: violent OR title: aggression OR abstract: aggression OR title: aggressivity OR abstract: aggressivity OR title: aggressive OR abstract: aggressive)
3. Web of Science; k = 1396	((TS = (substance OR cannabinoids OR cannabis OR hashish OR marijuana OR tetrahydrocannabinol OR THC) AND TS = ([severe mental illness] OR [severe mental disorder] OR MMD OR SMI OR [major mental disorder] OR [major mental illness] OR schizophrenia OR [schizoaffective disorder] OR psychosis OR delusions OR [bipolar disorder] OR [major depression])) AND TS = (violence OR crime OR [violent crime] OR [patient violence] OR [client violence] OR violent OR aggression OR aggressivity OR aggressive))) AND LANGUAGE: (English OR French)

Note: A search in **Google Scholar** enabled in the finding of additional $k = 2$ studies; $k = 10$ studies were further obtained from **hand searches** of bibliographies of retrieved sources.

individuals with SMI.

2. Methods

2.1. Selection procedures

2.1.1. Search strategies

A systematic search was performed in the electronic databases of PubMed, PsychINFO, Web Of Science and Google Scholar from their inception dates using text words and indexing (MeSH) terms with key words that were inclusive for SMI (e.g., [psychosis or schizophrenia or synonyms] or [affective disorders or depression or synonyms]), violence (e.g., [viol*, aggress*]) and cannabis use (e.g., [substance, cannabis or synonyms]). A full electronic search strategy is available in [Table 1](#). Reference lists were scanned by hand to identify additional studies. Corresponding authors were approached for clarification if there were any uncertainties regarding either participant recruitment and/or methodology. Searches were completed by August 2018. Abstracts were screened by M.B, M.L and B.D, and full articles by L.D, M.B and M.L. No setting, date or geographical restrictions were applied; searches were limited to English or French language sources.

2.1.2. Study eligibility

Studies were included if they met the following criteria: (1) more than 65% of study participants were diagnosed with a SMI (schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, bipolar disorder and major depression); (2) the total sample of participants had a mean age of 18 years or older; (3) any violent/aggressive outcome was investigated; (4) cannabis use or cannabis use disorder independently of other substances was assessed (if many substances were measured, substances were not to be collapsed together); (5) both cannabis use and violence were binary variables; (6) a cross-sectional, retrospective or longitudinal design was used. Patients could be either inpatients or outpatients. Since the definition of violence as well as the way to assess it was diverse between studies, studies were not restricted so long as they evaluated any type of violence/aggression (i.e., clinical observation, self-report). This allowed in the inclusion of the most studies on the subject. Additionally, studies were subdivided into those assessing cannabis users, those assessing only individuals with a cannabis use disorder and those assessing cannabis users as well as individuals with a cannabis use disorder (referred to as

mixed use). Further studies were excluded from final evaluation if they comprised of methodological issues (i.e., inadequate statistical analyses, missing data, inadequate data to compute any effect size) even after contacting the authors of the study. Disagreements on the inclusion of studies were resolved by group discussions to obtain a final consensus.

2.1.3. Data extraction

Data were extracted with a standardized form and double checked for consistency by the authors. Reported effect sizes with 95% confidence intervals (CI) were recorded with other key information (e.g., sample size (proportion of SMI sample), number of violent participants, number of cannabis users, adjustment for confounding factors). Quality assessment was independently undertaken by L.D and S.P against a set of criteria based on the GRADE Checklist for observational studies (Guyatt et al., 2011). Studies were assigned to categories of High, Moderate, Low and Very Low quality. Extracted data were independently cross-checked and any queries were resolved by discussion with A.D and S.P. To achieve a high standard of reporting, we followed the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) guidelines (Moher et al., 2009).

2.2. Statistical analysis

Data were entered into an electronic database and analyzed with a quantitative meta-analytical approach using *Comprehensive Meta-Analysis* (CMA) software, version 2 (Borenstein, 2005). CMA software employs the same computational algorithms used by the Cochrane collaborators to weigh studies by the inverse variance method. As the reporting of statistical results varied between studies, they were converted to comparable measures into ORs. The following qualitative descriptions of the strength of reported ORs were used (Rosenthal and DiMatteo, 2001): weak (OR = 1.0–1.5), moderate (OR = 1.6–2.5), strong (OR = 2.6–9.9) and very strong (OR = 10.0 and above). Heterogeneity among study point estimates was assessed with the Q statistics (Paulson and Bazemore, 2010) with magnitude of heterogeneity being evaluated with the I^2 index (Lipsey and Wilson, 2001). As studies were characterized by high heterogeneity (see results below), we employed random-effects models that are more conservative than fixed-effects models, and seem to better address heterogeneity between studies and study populations (Cooper et al., 2009). The possibility of

publication bias in the present meta-analysis was examined using Egger's test (Egger et al., 1997). To determine whether categorical factors modified the effect size, subgroup analyses were performed (Paulson and Bazemore, 2010). Sensitivity analyses were conducted for: (1) prevalence of SMI; (2) type of substance use; and (3) adjustment for confounding factors. Outlier studies were defined as studies having an effect size of 2 standard deviations above or below the composite effect estimate.

3. Results

3.1. Description of studies

This literature search identified 2449 potential articles that were screened for eligibility after removing duplicates. Ten additional studies were identified by cross-referencing. Among these articles, 162 full texts were assessed and 150 were then excluded. After assessment, 12 final articles were included in this meta-analysis amounting to a total of 3873 subjects. Most studies (75%) comprised of only individuals diagnosed with SMI. Moreover, concerning study design, 8 studies were cross-sectional, 2 were prospective and 2 were retrospective. The PRISMA flowchart for the inclusion of studies in the meta-analysis is found in Fig. 1. The details of the retrieved studies are described in Table 2. The study by Arseneault et al. (2000) was found to be an outlier since the OR was more than 2 standard deviations over the composite effect estimate.

3.2. Heterogeneity and publication bias

The overall database was characterized by a high level of

heterogeneity (Qvalue = 37.5, $p = 0.0001$, $I^2 = 70.7\%$). Egger's test indicated no publication bias ($t = 0.8$; $p = 0.43$) (see Fig. 2).

3.3. Cannabis-violence relationship

The OR from the pooled 12 studies was 3.02 (CI = 2.01–4.54, $p = 0.0001$) (Fig. 3). When removing the study by Arseneault et al. (2000) as an outlier, the OR diminished slightly to 2.6 (CI = 1.88–3.58, $p = 0.0001$). For details on the sub-analyses, please see Table 3. First, there was no difference between studies comprising of entirely SMI (OR = 3.01, CI = 1.8–5.04, $p = 0.0001$) in comparison to more mixed study samples (OR = 3.05, CI = 1.35–6.91, $p = 0.007$). Second, the risk of violence was significantly higher for cannabis use disorder (OR = 5.08, CI = 3.27–10.28, $p = 0.0001$) in comparison to cannabis use (OR = 2.04, CI = 1.36–3.05, $p = 0.001$). Mixed use (both use and misuse together) had an OR of 4.7 (CI = 1.56–14.18, $p = 0.006$). Third, when considering the 4 studies having adjusted for confounding factors, the OR was 2.82 (CI = 1.89–4.23, $p = 0.0001$).

4. Discussion

Our meta-analytical investigation aimed to elucidate the association between cannabis and violence in patients with SMI. The findings of this meta-analysis show a moderate association in the reviewed studies. Particularly of clinical interest and also as may be expected, the risk is substantially stronger for cannabis misuse. These findings are relevant as we exposed that cannabis use and violence are associated.

However, it is noteworthy that there is no single theory that purports to explain this specific relationship. The adverse acute psychopharmacological effects of cannabis use might have an effect on

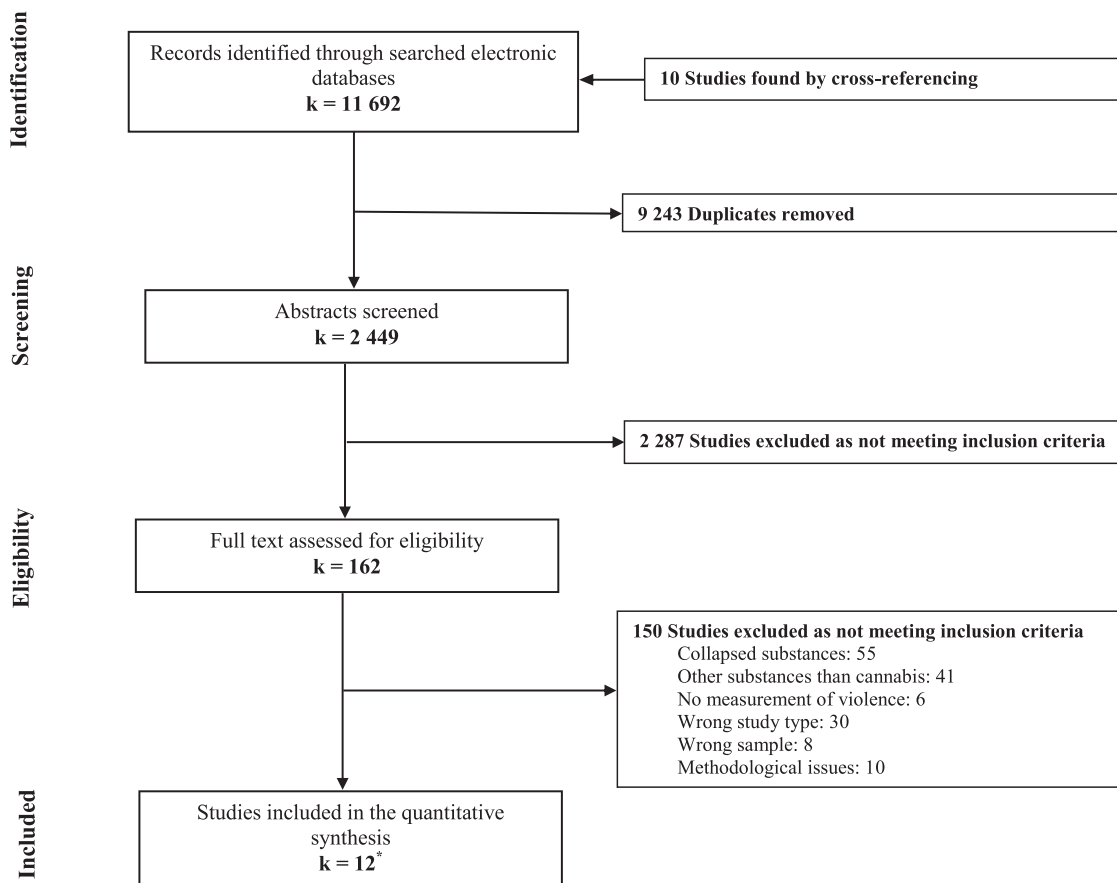


Fig. 1. Flowchart depicting the search strategy employed to find the 12 studies included in the meta-analysis.

*Note: Arseneault et al. (2000) was considered as an outlier since the OR was more than 2 standard deviations over the composite effect estimate. A sub-analysis was further conducted excluding this study.

Table 2
Details of the retrieved studies included in the meta-analysis.

Author, year	Geographic setting	Study design	Setting	Population with severe mental illness Sample analyzed	% Severe mental illness	Measure: cannabis	Measure: violence	Quality of observational study (GRADE system)
Arseneault et al. (2000)	New Zealand	Cross-sectional	General population	39	100	Dependence; DSM-III-R	-Court convictions for violence (i.e., inciting or threatening violence, using an attack dog on a person, presenting an offensive weapon, threatening a police officer, rape, assault, aggravated robbery & homicide) -Self-reports of violence using a private standardized interview developed for the National Youth Survey and National Institute of Justice multisite surveys (i.e., simple assault, aggravated assault, robbery, rape and gang-fighting)	LOW
Carabellese et al. (2013)	Italy	Retrospective	Outpatient	1582	69	Cannabis use/abuse; Medical records	-All violent hetero-lesions behavioral episode measured with a standardized questionnaire (i.e., verbal violence & threats, maltreatment, assault and battery, injuries by assault with an object/weapon, attempted murder & murder)	LOW
Dharmawardene and Menkes (2017)	New Zealand	Cross-sectional	Inpatient	141	100	Cannabis use disorder; Cannabis Use Disorders Identification Test, Revised (CUDIT-R)	-History of violence measured by interview and clinical record review (i.e., violent acts against individuals or property, threats excluded)	MODERATE
Dugré et al. (2017)	United States	Prospective	Recently discharged	592	74	Persistent cannabis use; DSM-III-R Checklist & self-reported	-Aggressive behaviors measured with the MacArthur Community Violence Instrument (MCVI) (i.e., assaults, acts of battery, threats made with a weapon, use of a weapon against others & rape)	HIGH
Harris et al. (2010)	Australia	Cross-sectional	Inpatient/outpatient	85	100	THC use frequency; Purpose-designed instruments	-Aggression was assessed in an interview (subject and relative/carer report) with the Aggressive Behaviour Questionnaire (ABQ) (i.e., verbal threats, physical aggression to a person, use of a weapon, inappropriate sexual behavior, sexual assault, damage to property, fire setting, harm to animals & self-harm)	LOW
Hodgins et al. (2011)	England	Cross-sectional	Inpatient/outpatient	138	100	Cannabis use; Sporadic or regular use	-Official criminal records obtained from Home Office Offenders Index (OI) and the Police National Computer (i.e., violence against a person, sexual offenses, robbery)	LOW
Johnson et al. (2016)	United States	Retrospective	Inpatient/outpatient	95	100	Cannabis use; Medical records/self-reported	-Self-reported or documented history of violence	MODERATE
Koen et al. (2004)	Africa	Cross-sectional	Inpatient	70	100	Cannabis use; Urine drug screening test	-Physical violence against self, others or objects, or violent verbal threats as reported by family, or by staff or observed during interviews	LOW
Krakowski et al. (2016)	United States	Cross-sectional	Inpatient/outpatient	59	100	Cannabis abuse; DSM-IV	-Overt Aggression Scale -Life History of Aggression (LHA) completed on the basis of self-report, chart review and official records of arrests, convictions, parole, and probation obtained from the Division of Criminal Justice Services	VERY LOW
Moulin et al. (2018)	Switzerland	Prospective	Inpatient/outpatient	240	100	Cannabis use disorder; DSM-IV/Case Manager Rating Scale (CMRS)	-Information regarding the occurrence of violent offenses (Swiss Criminal Code) and violent behavior (i.e., assault & battery) with a self-reported baseline questionnaire -Additional information through contact with a significant other and the forensic psychiatric services (hetero reporting of aggression) -Staff Observation Aggression Scale (SOAS-R Scale) during hospitalization	MODERATE

(continued on next page)

Table 2 (continued)

Author, year	Geographic setting	Study design	Setting	Population with severe mental illness Sample analyzed	% Severe mental illness	Measure: cannabis	Measure: violence	Quality of observational study (GRADE system)
Rao et al. (2007)	England	Cross-sectional	Inpatient/ outpatient	459	72	Cannabis use; Semi-structured interview	-History of violence (i.e., any conscious action against a person that produced injury including bruising); Verbal aggression and damage to inanimate objects & property were examined separately -Violence ideation or behavior based on self-reports, collaterals and medical records	MODERATE
Rolin et al. (2018)	United States	Cross-sectional	Inpatient/ outpatient	373	100	Cannabis use; Self report, collaterals, medical record and urine toxicology screening		MODERATE

emotions and cognition by producing panic, loss of control, paranoia and the feeling of depersonalization; such effects may lead to aggressive behaviors. Particularly in those with SMI, cannabis use intoxication has been shown to produce an exacerbation in symptomatology (i.e., psychotic symptoms) that may further heighten the risk of violence (Gibbs et al., 2015; Moore and Stuart, 2005; Norström and Rossow, 2014; Schoeler et al., 2016a; van Rossum et al., 2009). Furthermore, the cannabis-violence association may be strong even during withdrawal (Smith et al., 2013). Hence, in dependent users, abstinence and withdrawal from cannabis may result in unpleasant effects leading to the likelihood of emotional outbursts (Moore and Stuart, 2005). Heightened aggression may further be an indication of a developmental predisposition for aggressive behavior (i.e., type of temperament, antisocial traits) (Moore and Stuart, 2005).

Nevertheless these theories rarely account for other factors that are not related to the pharmacological effects of cannabis such as interpersonal factors (i.e., peer influences) as well as contextual factors that may explain the positive association (Moore and Stuart, 2005). More precisely, the lifestyle of cannabis users may include a subgroup of individuals that present a higher tolerance for delinquency, greater desire to engage in risk-taking, rebellious and antisocial behaviors as well as more inclination to use other substances that are associated with violence such as alcohol (Goode, 2008; Hall and Degenhardt, 2007; Moore and Stuart, 2005).

Additionally, concerning the direction of the association, it is possible that a reverse relationship exists, that is that externalizing problems such as violence may result in the use of cannabis; the association may likewise be reciprocal (Duarte et al., 2003; Schoeler et al., 2016b). Though few longitudinal investigations have been brought on the matter to clarify the direction, which is even more limited among studies on SMI. One of the studies included in the meta-analysis nevertheless concluded that persistent cannabis use predicted violence, whereas the reverse direction (i.e., persistent violence predicting cannabis use) was not statistically significant (Dugré et al., 2017).

This meta-analysis is not without its limitations. The available studies show numerous methodological weaknesses that should not be overlooked when interpreting our results. First, due to the paucity of definitions for violence and methods of assessment, we did not restrict studies to specific acts of violence, rather we were inclusive of all types of violent/aggressive behaviors to gain better insight on the matter. Second, beyond frequency of use, current studies did not conduct a detailed assessment of cannabis exposure/usage patterns (i.e., type of cannabis, number of joints, dosage, cannabis potency) (Temple et al., 2011), which may differentially be associated with violence. Studies that target dose-response analyses are needed. Moreover, studies should better differentiate between acute and chronic use of cannabis or intoxication and withdrawal and focus on disentangling the possible role of each one in their relationship with violence. Third, very limited studies have reported controlling for important static (i.e., psychopathic traits) and dynamic (i.e., alcohol and stimulant use) confounding factors, which are correlated with cannabis use and may have better explained the relationship (Macleod et al., 2004). Studies not having adjusted for the effects of these variables may have therefore overestimated the association. Fourth, since most data was cross-sectional and retrospective, evidence is limited as a basis for concluding any causal relations. Literature necessitates more longitudinal studies.

With the upcoming policy changes on cannabis internationally such as the 2018 Canadian legalization of cannabis, it is of high importance to better investigate its potential harmful effects on violence mostly in more vulnerable psychiatric populations to devise effective interventions. Cannabis use should be considered in violence risk prevention and management. Hitherto, this meta-analysis highlights the point that current research and practice have devoted insufficient attention to examining and addressing cannabis use among SMI in relation with violence compared to other substances such as alcohol use. Larger, better quality studies should be conducted to clarify the cannabis-

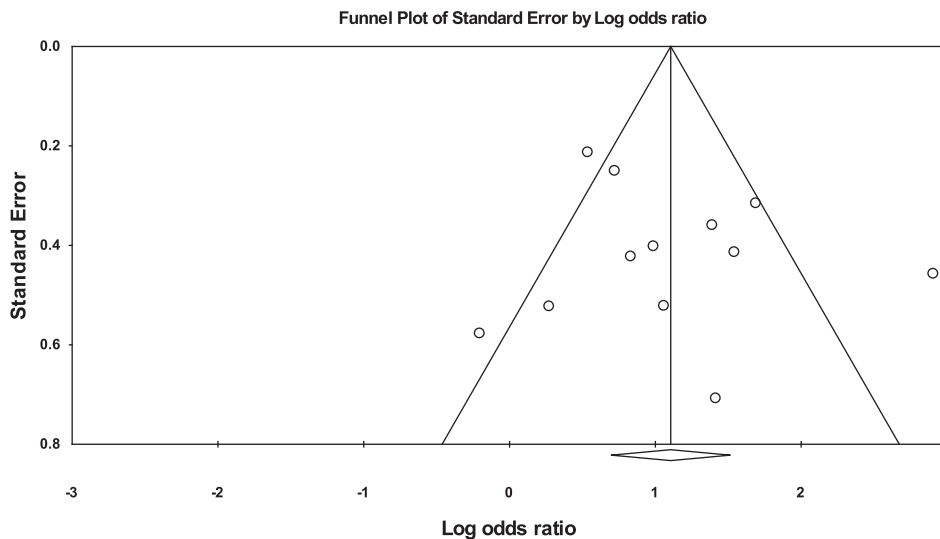


Fig. 2. Egger's test for publication bias.

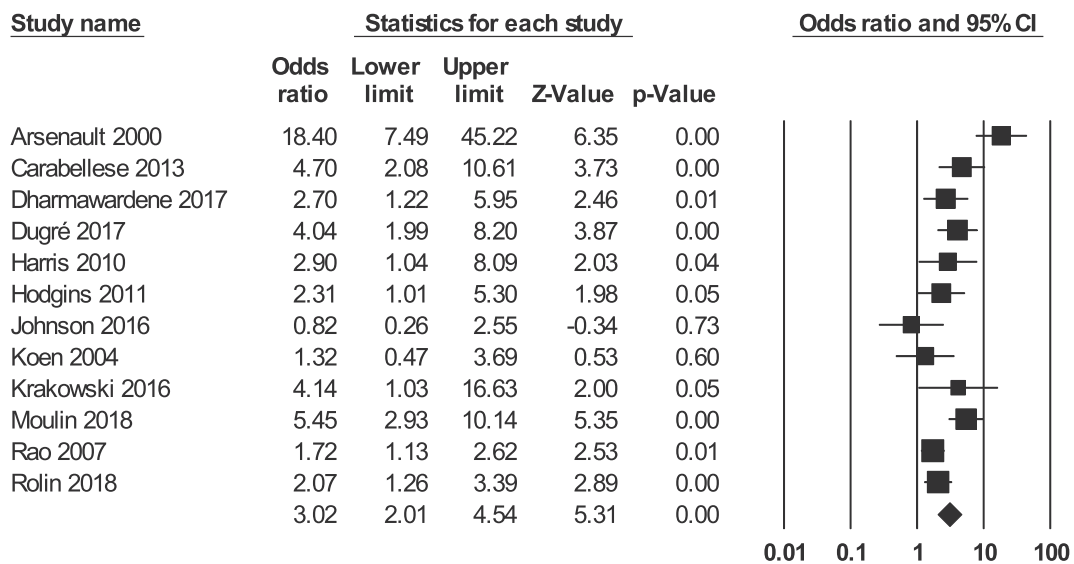


Fig. 3. Forest plot of the association between cannabis use and violence in patients with severe mental illnesses.

Table. 3

Sub-analyses included in the meta-analysis.

Sub-analysis	Number of studies (k)	Effect size (OR)	95% confidence interval	p-value	Q	Heterogeneity p-value	I ²
% of severe mental illness							
100% sample	9	3.01	1.8–5.04	0.0001	29.5	0.0001	72.9%
< 100% sample	3	3.05	1.35–6.91	0.0007	7.1	0.029	71.8%
Type of cannabis use							
Misuse	4	5.8	3.27–10.28	0.0001	10.2	0.017	70.5%
Mixed	1	4.7	1.56–14.18	0.006	–	–	–
Use	7	2.04	1.36–3.05	0.001	7.9	0.24	24.3%
Adjustments for confounding factors							
Adjustments ^a	12	2.82	1.89–4.23	0.0001	35.0	0.0001	68.5%
Without outlier							
Without Arsenault et al. (2000)	11	2.6	1.88–3.58	0.0001	19.6	0.034	48.9%

^a Studies adjusting for confounding factors included: Carabellese et al. (2013) (psychiatric disorder, sex, age); Dugré et al. (2017) (effects of time, other substances used, age, age at first hospitalization, sex, ethnicity, schizophrenia spectrum disorders, affective disorders, psychopathic traits, impulsivity); Moulin et al. (2018) (main diagnosis, comorbid personality disorder); Rolin et al. (2018) (age, gender and health insurance).

violence relationship in SMI.

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Declaration of interest

The authors declare no potential conflicts of interest.

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