

# Influence of the type of childhood violence on cannabis abuse and dependence among adolescents: a systematic review and meta-analysis

## *Tipos de violencia en la infancia que inciden en el abuso y dependencia de cannabis entre adolescentes: una revisión sistemática y metaanálisis*

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### Abstract

The use of cannabis for recreational purposes has increased worldwide, and the proportion of cannabis users in the adolescent population is high. Susceptibility to cannabis use involves various factors, including childhood adversity; however, the effects of different types of violence on cannabis use have not been evaluated. The aim of this review was to analyze the effects of different types of violence on cannabis use in adolescence. We searched electronic databases (PubMed, Science Direct, Web of Science, Ovid and CONRICyT) using the following algorithm: ((“Cannabis” OR “Marijuana Smoking” OR “Marijuana Abuse”) AND (“Child Abuse” OR “Domestic Violence” AND “Adolescent”)), considering all articles published up to November 3th, 2017. Odds ratios (ORs) were calculated for the effects of experiencing different types of violence during childhood on cannabis use. Six studies, representing 10 843 adolescents of both sexes, were ultimately included in the systematic review and meta-analysis. Three types of early-life adversity were associated with cannabis abuse/dependence: physical abuse (OR: 1.58, 95% CI [1.01-2.46]), sexual abuse (OR: 2.35, 95% CI [1.64-3.35]), and witnessing violence (OR: 3.22, 95% CI [0.63-16.54]). The results indicated that two specific types of child maltreatment, sexual and physical abuse, were critical factors affecting vulnerability to cannabis use in adolescence. The number of studies examining other types of violence was limited. The results highlighted the importance of enhancing efforts to prevent violence, particularly sexual abuse, as part of integral programs designed to prevent cannabis abuse and dependence.

**Keywords:** Cannabis abuse; Child abuse; Childhood; Adolescents; Violence.

### Resumen

El uso recreativo de cannabis ha incrementado en todo el mundo, principalmente en la población adolescente. Se ha propuesto que la adversidad en la infancia contribuye al consumo de esta droga. El objetivo de esta revisión sistemática y metaanálisis fue analizar el efecto de diferentes tipos de violencia en la infancia sobre el consumo de cannabis en la adolescencia. Se realizó una búsqueda en diferentes bases de datos (PubMed, Science Direct, Web of Science, Ovid y CONRICyT) usando los términos de búsqueda: ((“Cannabis” OR “Marijuana Smoking” OR “Marijuana Abuse”) AND (“Child Abuse” OR “Domestic Violence” AND “Adolescent”)), considerando todos los artículos publicados hasta el 3 de noviembre de 2017. Se calcularon los Odds Ratio (OR) del consumo de cannabis en adolescentes, para los diferentes tipos de abuso infantil, así como sus intervalos de confianza del 95% (IC 95%). Se identificaron seis estudios, que incluyeron 10 843 adolescentes de ambos sexos. Las siguientes adversidades fueron asociadas con abuso/dependencia de cannabis en la adolescencia: abuso físico (OR: 1,58, IC 95% [1,01-2,46]), abuso sexual (OR: 2,35, IC 95% [1,64-3,35]), y ser testigo de violencia (OR: 3,22, IC 95% [0,63-16,54]). Los resultados sugieren que el abuso sexual o físico durante etapas tempranas de la vida aumenta el riesgo de consumo de cannabis en la adolescencia. Los estudios que evaluaron otras formas de violencia fueron escasos. Los resultados destacan la importancia de diseñar programas integrales para reducir el uso y la dependencia de cannabis mediante estrategias enfocadas a la prevención de la violencia en la infancia.

**Palabras clave:** Uso de cannabis; Abuso infantil; Infancia; Adolescencia; Violencia.

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The use of cannabis for recreational purposes has increased worldwide (United Nations Office on Drugs and Crime, 2015). Eleven million cases of dependence were reported globally in 1990, and this figure had increased to 13 million in 2010 (Degenhardt et al., 2013). For example, prevalence rates of 15.2% and 13.7% have been reported for cannabis use in the general populations of the Czech Republic and United States, respectively (Villatoro-Velázquez et al., 2012; United Nations Office on Drugs and Crime, 2015). Remarkably, the proportion of cannabis users in the adolescent population is high. In the United States, the Youth Risk Behavior Survey showed an increase, from 19.7% in 2007 to 23.4% in 2013, in prevalence rate for cannabis use in high school students aged between 14 and 18 years (Substance Abuse and Mental Health Services Administration, 2015).

Enhancement of social behavior, risk taking, and novelty seeking is observed during adolescence. This period of life is also a critical period for brain development, during which the efficiency and velocity of neuronal communication are enhanced via synaptic pruning and increased myelination (Spear, 2000; Spear, 2013). Cannabis use during this stage of increased neurodevelopment could lead to aberrant connections and failure in cerebral cortex remodeling, with consequent alterations in behavior (de la Fuente et al., 2015). Users who initiate cannabis use during adolescence are likely to exhibit deficits in memory, verbal fluency, decision making, and cognitive flexibility (de la Fuente et al., 2015), and chronic consumption could lead to the deterioration of general intelligence, short-term memory, executive function, judgment, and major motor impulsivity (Meier et al., 2012; Ramaekers et al., 2006). In addition, the social consequences of cannabis abuse during late adolescence have been associated with poor academic performance and a lack of opportunity to secure stable employment and build a family (Substance Abuse and Mental Health Services Administration, 2015).

It should be noted that the risk of initiating cannabis use and developing dependence differs between individuals. The etiology of these differences involves a combination of biological, genetic, and environmental factors, which enhances vulnerability (Buisman-Pijlman et al., 2014). The development of risk behaviors, such as cannabis use and the development of dependence, has been associated with events that occur during the early stages of development (i.e., childhood and early adolescence; Benjet, Borges & Medina-Mora, 2010). This is the main reason why interventions designed to prevent drug use should focus on children.

Childhood adversity, including physical abuse, sexual abuse, neglect, poverty, and parental loss or separation, is highly prevalent worldwide (38.4% to 39.1%; World Health Organization, 2016) and has been associated

with increased risk of psychiatric disorders (Kessler et al., 2010). Analysis of data clustering by adversities show that family dysfunction and abuse adversities (i.e., physical abuse) are the strongest and most consistent predictors of psychopathologies such as substance abuse and externalizing behaviors, influencing the onset of these disorders throughout of childhood, adolescence or even adulthood (Benjet et al., 2010). Enduring effects of chronic stress on brain structures (Benjet et al., 2010), dysfunctional coping mechanisms (Folkman & Lazarus, 1988; Folkman, Lazarus, Gruen & DeLongis, 1986) or poor emotional regulation (Zimmermann et al., 2017) seem explain the impact of adversity throughout of life course.

Children's exposure to violence covers a broad range of community, family and media violence (Osofsky, 1999). This exposure can be direct in form of victimization or indirect in the form of witnessing (Foster & Brooks-Gunn, 2009). Being exposed to violence in childhood leads to higher rates of posttraumatic stress disorder, depression and behavioral problems (Jester, Steinberg, Heitzeg & Zucker, 2015). Furthermore, exposure to violence during early stages of life has been identified as risk factor for development of substance abuse (Benjet et al., 2010; Jester et al., 2015; Kuhar, 2012). For instance, children witnessing of violence are more vulnerable to develop substance abuse in adulthood (OR 2.84, 95% CI [1.53–5.26]) (Kuhar, 2012; Benjet et al., 2010). Furthermore, severe sexual abuse in childhood has been related to increased risk to alcohol abuse/dependence (OR 3.3, 95% CI [1.7-6.6]) or other drugs abuse/dependence (OR 5.1, 95% CI [2.5-10.2]) at 18 years old (Fergusson, Horwood & Lynskey, 1996). Additionally, childhood maltreatment history (including sexual abuse, physical abuse, emotional abuse and neglect) has been described as important predictor of cannabis problems among young adults (Vilhena-Churchill & Goldstein, 2014). However, the relationships between the type of violence during childhood and cannabis use in adolescence have not been evaluated systematically in the literature. Altogether, the main aims of this systematic review and meta-analysis were to examine the relationships between exposure to various types of violence during childhood and cannabis abuse or dependence in adolescence and determine the main risk factors for the development of cannabis abuse and dependence.

## Methods

### Study types

We included all studies involving case-control, cross-sectional, or longitudinal study designs and data regarding the relationship between childhood exposure to violence and use of cannabis prior to adulthood. Childhood abuse (or childhood violence) was defined as violence perpetrated by parents, primary caregivers or community members

in any environment. Physical abuse was assessed with questions about being hit, kicked, throttled, or attacked with a gun, knife, or some other weapon, by any person, or about being spanked by parents until to induce marks. Sexual abuse is defined as different extents of sexual approaches between adult and children. Sexual abuse was assessed with questions about noncontact episodes including indecent exposure, public masturbation, sexual propositions, and incidents involving sexual contact attempted or completed intercourse. Witnessing was defined as exposure to violence directed against another family member or any person, in any environment (home, community). Witnessed violence was assessed with questions about witnessing interparental slap, hit, kick, grasp or threaten any person with a knife, gun or other weapon. Adolescence was defined the period between the ages of 12 and 17 years. Use (or abuse) of cannabis included all forms of consumption including use on a single occasion, infrequent or intermittent use, and chronic use. We excluded studies in which cannabis use was reported during adulthood or via prenatal exposure.

### **Participants**

Participants included persons who were incorporated in the samples of national studies that included adolescents or young adults and used various types of data analysis. All participants gave informed consent prior to being interviewed, and approval of Institutional Review Boards is mentioned in each study.

### **Types of exposure**

Studies examining exposure to all types of violence perpetrated by adults during childhood were included.

### **Outcome measures**

The outcome measures included the use or abuse of cannabis during adolescence, and sex differences were analyzed where possible.

### **Search methods for study identification**

Studies suitable for inclusion were identified via a search of the following electronic databases: PubMed (MEDLINE), Science Direct, Web of Science, Ovid (MEDLINE), and CONRICyT (database of the National Council for Science and Technology). Studies conducted prior to November 3<sup>th</sup> 2017 were included. We performed a broad search using the following Medical Subject Headings and Boolean terms: ((“Cannabis” OR “Marijuana Smoking” OR “Marijuana Abuse”) AND (“Child Abuse” OR “Domestic Violence” AND “Adolescent”)). Entry terms for Cannabis included: Marihuana; Marijuana; Hashish; Cannabis sativa. Terms for Marijuana Abuse included: Cannabis-related Disorder; Cannabis Abuse; Marijuana Dependence; Marihuana Abuse; Hashish Abuse. Terms for Marijuana Smok-

ing included: Marihuana Smoking; Hashish Smoking; Cannabis Smoking. Entry terms for child abuse include: Abuse, Child; Child Mistreatment; Mistreatment, Child; Child Maltreatment; Maltreatment, Child; Child Neglect; Neglect, Child. Domestic violence includes terms: Violence, Domestic; Family Violence; Violence, Family. There were no restrictions with respect to language or publication status.

### **Searching other resources**

The reference lists of all included studies were analyzed to identify further studies of interest that were not retrieved via the database search.

### **Data collection**

Two authors performed independent reviews of all of the titles, abstracts, and potentially relevant full-text reports according to the established inclusion and exclusion criteria. Disagreements were resolved via discussion or consultation with a third judge (Figure 1).

A predesigned data abstraction form was used to extract relevant information. Data extracted from each study included the name of the first author, year of publication, study type, participant details, sample size, type of childhood abuse examined, cannabis use during adolescence, study findings, and odds ratios (ORs). The studies' key findings were summarized descriptively in the first instance, and the feasibility for quantitative meta-analysis was considered.

### **Statistical methods**

Measurement of effects and assessment of heterogeneity ORs with 95% confidence intervals (CIs) were calculated for dichotomous outcomes (e.g., cannabis use) in case-control and cross-sectional studies, and relative risk was calculated for longitudinal studies (e.g., cohort studies). The results of the analyses were presented as forest plots.

The statistical heterogeneity of each meta-analysis was assessed using  $I^2$  and  $\chi^2$  (with P values). We regarded heterogeneity as substantial if  $I^2$  values were higher than 50%. Data were analyzed using random- or fixed-effects models as appropriate.

### **Data synthesis**

Data were analyzed using Review Manager Software 5.3.

## **Results**

The literature search yielded 190 articles. Of these, 135 were excluded based on their abstracts, and 36 were excluded following full-text analysis, as they did not fulfill the inclusion criteria. Ultimately, only six studies accomplished all of the inclusion criteria (Figure 1).

### Description of the studies

All types of violence were included in the database research; however, frequencies of cases for childhood violence and cannabis abuse were reported only in six articles. These publications reported frequencies for sexual, physical and witnessing violence in childhood and cannabis abuse in adolescence. Five studies were referred to as cohort studies involving cross-sectional evaluation within specific periods during the lifespan (Dubowitz et al., 2016; Duncan et al., 2008; Fergusson & Horwood, 1998; Fergusson & Lynskey, 1997; Sartor et al., 2015) and one study included a National Household Survey probability sample (Kilpatrick et al., 2000). Although two studies, which were conducted by Fergusson & Horwood (1998) and Fergusson & Lynskey (1997), involved the same sample, they were both included in the systematic review, as they analyzed different types of violence (Table 1).

The studies conducted by Fergusson & Horwood (1998) and Fergusson & Lynskey (1997) were conducted in New Zealand (Fergusson, Horwood, Shannon & Lawton, 1989), while those conducted by Kilpatrick et al. (2000), Duncan et al. (2008), Sartor et al. (2015) and Dubowitz et al. (2016) were conducted in the United States.

Three studies evaluated violence using structured, personal interviews and questionnaires to collect data regarding the characteristics of abuse experienced during child-

hood (Dubowitz et al., 2016; Fergusson & Horwood, 1998; Fergusson & Lynskey, 1997). In addition, in Dubowitz et al. (2016) study the data was collected from multiple informants: reports from the Child Protective Services (CPS), and later from parents and children interviewed. One study obtained data via ad-hoc, structured, telephone-based interview designed by the authors (Kilpatrick et al., 2000), while two studies evaluated the characteristics of abuse with the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA) via telephone (Duncan et al., 2008; Sartor et al., 2015) (Table 2). Therefore, the evaluation of exposure to types of abuse examined (i.e., sexual abuse, physical abuse, and witnessing violence) included heterogeneous interviews.

Physical abuse was identified four studies (Dubowitz et al., 2016; Duncan et al., 2008; Fergusson & Lynskey, 1997; Kilpatrick et al., 2000). Additionally, Dubowitz and co-workers reported information of other forms of abuse, as neglect and emotional abuse, in the studied population. All articles, with exception of Fergusson & Lynskey (1997), reported data of sexual abuse in children, while two reports showed data of witnessing violence in childhood (Fergusson & Horwood, 1998; Kilpatrick et al., 2000). Duncan et al. (2008) and Kilpatrick et al. (2000) included three and six interview questions pertaining to sexual abuse, respectively. Questions for physical abuse fluctuated from three to ten. Finally, for witness of violence Kilpatrick et al. (2000) asked one general question and Fergusson and Horwood (1998) consisted of eight questions (i.e., type of incident and frequency of occurrence). Dubowitz et al. (2016) followed the LONGSCAN protocol (English, Bangdiwala & Runyan, 2005; Runyan et al., 1998) consisting in collection of data from reports from the CPS, and interviews from parents and children, in order to categorize five forms of maltreatment (Table 1).

The main outcome of the analysis (Table 2), use or abuse of cannabis during the preceding year or before 18 years old, was determined via personal interviews (three studies), two of them by the administration of the World Health Organization Composite International Diagnostic Interview (Cottler & Compton, 1993), or by telephone-based interviews (three studies). Instruments of five studies were based on the criteria for the diagnosis of substance abuse disorder in the Diagnostic and Statistical Manual of Mental Disorders (DSM, American Psychiatric Association, 1994). One study identified use of cannabis by a dichotomous question at any of the age 12, 14, 16 and 18 interviews. If participants answered positively they were further questioned about the heavy or occasional consume (Dubowitz et al., 2016).

The analysis of biases showed that only the cohort study (Kilpatrick et al., 2000) selected a randomly representative community sample of adolescents, while the other five studies did not randomize the selection of their popula-

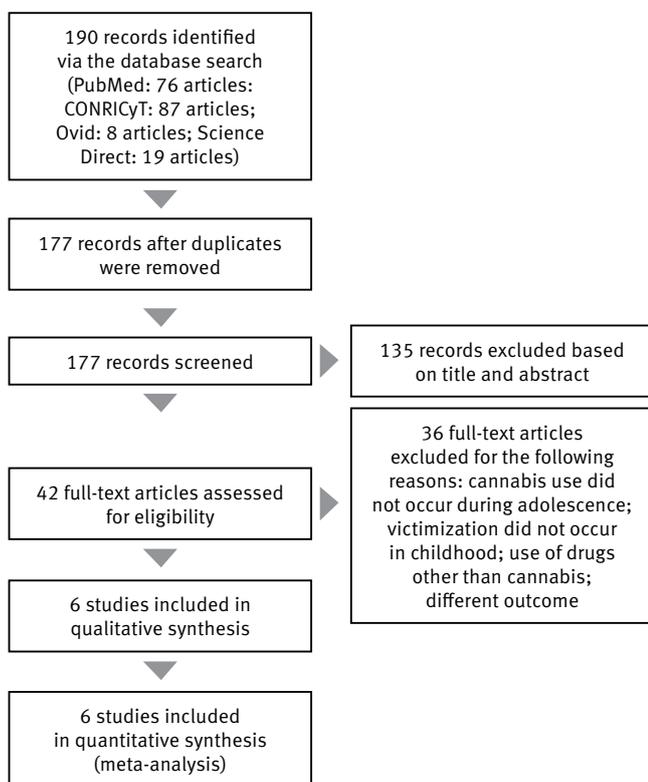


Figure 1. Flow chart of the identification and selection of studies for systematic review.

Table 1. *Characteristics of epidemiological studies of childhood exposure to violence on use, consume or dependence of cannabis.*

Authors, Year	Country	Study	TE	Exposure definition	Instrument/ Evaluation	Outcome/ Diagnosis	Sample size/ Demographics	Age exposure	Age evaluation	Estimated/Note
Fergusson & Lynskey, 1997	NZ	CHDS	T	PA	F-to-FA, I, Q	Cannabis abuse or dependence DSM-IV	N = 1265	<16 y. o.	<18 y. o.	Rates of substance abuse by extent of intraparental violence
Fergusson & Horwood, 1998	NZ	CHDS	T	IA SA	F-to-FA, I, Q	Cannabis abuse or dependence DSM-IV	N = 1265 Male and female	<16 y. o.	<18 y. o.	Rates of substance abuse by extent of intraparental violence
Kilpatrick et al., 2000	USA	NSA	T	PAS SAS WV	Structured TI	Cannabis abuse or dependence DSM-IV	N = 3907 Male and female	Past year	12-17 y. o.	PA: OR 4.84 SA: OR 3.80 WV: OR 8.42 95% CI were no reported
Duncan et al., 2008	USA	VETR	T	SA PA	TI-SSAGA	Cannabis abuse or dependence DSM-IV	N = 819 Male and female	<16 y. o.	Adolescent or Young adult	HR 2,16 (95% CI 1.48-3.16)
Sartor et al., 2015	USA	MOAFTS MOFAM	T	SA	TI-SSAGA	Cannabis abuse or dependence DSM-IV	N = 4150 Female twings and siblings	<16 y. o.	18-29 y. o.	Eur American HR 1.57 (95% CI 1.37-1.79) African American HR 2.52 (95% CI 1.52-4.18)
Dubowitz et al., 2016	USA	LONG-SCAN	T	SA PA N EM	MMCS	Dichotomous response: Never use cannabis or use of cannabis	N = 702; 332 males and 370 women	From birth to 18 y. o.	18 y. o.	EM OR 1.32 (95% CI 0.98-1.78) N OR 0.78 (95% CI 0.49-1.25)

*Note.* NZ: New Zeland; USA: United States of America. Studies: CHDS Christchurch Health & Development Study; NSA: National Survey of Adolescents; VETR: The Vietnam Era Twin Registry (registers from offsprings); MOAFTS: Missouri Adolescent Female Twin Study; MOFAM: Missouri Family Study; LONGSCAN: Longitudinal Studies of Child Abuse and Neglect project; F-to-F A: Face to face assessment for parents and children; obtained from Fergusson et al., 1989; T: Transversal evaluation; I: Interview; Q: Questionnaire; PA: Physical abuse; IA: Intraparental abuse; SA: Sexual abuse; PAS: Physical assault; SAS: Sexual assault; WV: Witnessed violence; N: Neglect; EM: Emotional maltreatment; SSAGA: Semi-Structured Assessment for the Genetics of Alcoholism, for telephone interview (TI); MMCS: Maltreatment Coding Scheme Modified version of Barnett et al., 1993.

tions. As the studies included cohorts, no allocation concealment or blinding procedures were used in any of the studies. On the contrary, the collection of data regarding demographic characteristics and the establishment of one or more clinical diagnoses occurred on separate occasions. All six studies, including those involving structured telephonic interviews, reported acceptable compliance. The baseline age of exposure to abuse was almost uniform, as four studies reported that participants were younger than 16 years of age when the abuse occurred, one study reported occurrence during the year preceding evaluation, and one study reported information of abuse from birth to 18 years old. The timing of evaluations varied between studies, with the exception of those conducted by Fergusson & Horwood (1998) and Fergusson & Lynskey (1997), as they included the same population. All studies reported participant withdrawal and evaluated the main outcomes via personal or telephone-based interviews, five of them based on the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 1994). The validity of the telephone-based evaluations performed by Kilpatrick et al. (2000), Duncan et al. (2008), and Sartor et al. (2015)

was of concern, as if adolescents discussed their childhood and substance abuse freely. In addition, there was an increased risk of bias in these studies, because of high levels of variation in sampling procedures and the evaluation of comorbidity during adolescence and early adulthood.

## Populations studied

Overall, the number of participants included in the reviewed studies was 10,843 (3,395 men and 7,448 women). Half of the studies collected data via telephone-based and the other by means of personal interviews. The types of childhood violence included in the studies were sexual abuse, physical abuse, and witnessing violence, for instance the evaluation of exposure to violence was heterogeneous, as the number of interview questions used in the studies ranged from one to ten. In the Dubowitz's study violence identified by reports from the CPS was categorized by the Maltreatment Coding Scheme (MMCS, Barnett, Manly & Cicchetti, 1993) in a modified version for LONGSCAN (Table 2).

Table 2. *Items used for defining childhood abuse or dependence of cannabis.*

Authors/year	Exposure violence	Items for establishing abuse exposure	Outcome/diagnosis criterion for abuse/dependence of cannabis
Fergusson & Lynskey 1997	PA	Subjects were questioned about: <ul style="list-style-type: none"> <li>– Being frequently smacking</li> <li>– Being hit around head of body with fists</li> <li>– Being frequently hit on the button with a cane, strap or similar object</li> <li>– Being hit around head or body with a cane, strap or similar objects</li> <li>– Receiving severe beating</li> <li>– Being kicked, choked or throttled,</li> <li>– Being locked in a cupboard or shed</li> <li>– Being burnt or being injured as results of physical abuse.</li> </ul>	Instrument Composite International Diagnostic Interview DSM-IV
Fergusson & Horwood 1998	IPA (being a witness of violence)	Report of rating of: <ul style="list-style-type: none"> <li>– Threaten to hit or throw something at partner</li> <li>– Push, grab or shove partner</li> <li>– Slap, hit or punch partner</li> <li>– Throw, hit or smash something</li> <li>– Kick partner choke or strangle partner</li> <li>– Threaten partner with knife, gun or other weapon</li> <li>– Call partner names, criticize partner</li> <li>– At least one of the above</li> </ul>	Instrument Composite International Diagnostic Interview DSM-IV
	PA	Items referred in Fergusson & Lynskey, 1997	
	SA	Items referred in Fergusson et al., 1996 Face-to-face interview which participants were questioned about occurrence of SA before 16 y.o. Questions established 15 sexual activities comprising: 1) noncontact episodes including indecent exposure, public masturbation by others, and unwanted sexual propositions or lewd suggestions; 2) incidents involving sexual contact including sexual fondling, genital contact, and attempts to undress the respondent; and 3) incidents involving attempted or completed oral, anal, or vaginal intercourse.	
Kilpatrick et al., 2000	SA	Questionnaire <ul style="list-style-type: none"> <li>– Has a man or boy ever put a sexual part of his body inside your private sexual part, inside your rear end, or inside your mouth when you didn't want them to?</li> <li>– Has anyone, male or female, ever put fingers or objects inside your private sexual parts or inside your rear end when you didn't want them to?</li> <li>– Has anyone, male or female, ever put their mouth on your private sexual parts when you didn't want them to?</li> <li>– Has anyone, male or female, ever touched your private sexual parts when you didn't want them to?</li> <li>– Has anyone ever made you touch their private sexual parts when you didn't want them to?</li> <li>– [For boys] Has a woman or girl ever put your private sexual part in her mouth or inside her body when you didn't want her to?</li> </ul>	Structured interview based on DSM-IV
	PA	Questionnaire <ul style="list-style-type: none"> <li>– Has anyone—including family members or friends—ever attacked you with a gun, knife or some other weapon, regardless of when it happened or whether you ever reported it or not?</li> <li>– Has anyone—including family members and friends—ever attacked you without a weapon, but you thought they were trying to kill or seriously injure you?</li> <li>– Has anyone—including family members and friends—ever threatened you with a gun or knife but didn't actually shoot or cut you?</li> <li>– Has anyone—including family members and friends—ever beat you up, attacked you, or hit you with something like a stick, club, or bottle so hard that you were hurt pretty bad?</li> <li>– Has anyone—including family members and friends—ever beat you up with their fists so hard that you were hurt pretty bad?</li> <li>– Families have different ways of punishing young people if they think they have done something wrong.</li> <li>– Some families spank young people as a form of punishment. Has a parent or some adult in charge of you ever spanked you so hard that you had to see a doctor because you were hurt so bad?</li> <li>– Has a parent or someone in charge of you ever spanked you so hard that you got bad marks, bruises, cuts, or welts?</li> <li>– Has a parent or someone in charge of you ever punished you by burning you, cutting you, or tying you up?</li> <li>– Adolescents who responded affirmatively to any of these questions were classified as having experienced a PAs.</li> </ul>	

Duncan et al., 2008	PA  SA	An individual was considered to have experienced PA in childhood (6-12 y.o.) if he or she: a) reported having been physically abused before the age of 16 in the traumatic events section of the interview or b) answered “yes” to “When you were 6 to 12, did any adult ever physically injure or hurt you on purpose? or c) reported “often” being “punched or hit with a belt or stick or something like that by your mother or father CSA was considered to have occurred if an individual reported having been: a) raped or b) sexually molested before age 16 or c) forced to have sex before age 16	Structured interview based on DSM-IV Abuse diagnosis, if he or she endorsed any of the four DSM-IV cannabis abuse Dependence, if he or she endorsed three or more of seven cannabis dependence symptoms, including withdrawal
Sartor et al., 2015	SA	First questionnaire: Raped, sexually molested at 15 years or younger Second questionnaire: Has anyone ever forced you to have sexual intercourse at 15 years or younger Third questionnaire: Before you turned 16, was there any forced sexual contact between you and any family member? And, Before you turned 16, was there any forced sexual contact between you and anyone who was 5 or more years older than you (other than a family member)?	Semi-structured interview based on DSM-IV Individuals who endorsed to one or more symptoms of abuse or dependence of cannabis
Dubowitz et al., 2016	SA  PA	Subjects were questioned: Exposure, exploitation, molest and penetration. Once they received blows in: Head, torso, buttocks, limbs, violent handling, choking Burns, shaking, nondescript.	Dichotomous response: never use cannabis or use of cannabis

Note. PA: Physical abuse; SA: sexual abuse; IPA: intraparental abuse.

### **Effect of exposure to violence**

The statistical analysis of associations showed that the three types of childhood violence contributed to the likelihood that cannabis abuse or dependence would occur during adolescence (physical abuse: OR: 1.58, 95% CI [1.01–2.46], Figure 2, panel A; sexual abuse: OR: 2.35, 95% CI [1.64–3.35], Figure 2, panel B; witnessing violence: OR: 3.22, 95% CI [0.63–16.54], Figure 2, panel C), to varying degrees. It was not possible to perform an analysis of physical abuse or witnessing violence according to sex. However, data from two articles were used to obtain an association between sexual abuse in childhood and cannabis use in adolescent girls, OR 2.22 (95% CI [1.86–2.66], Figure 2, panel D).

## **Discussion**

The main finding of the systematic review and meta-analysis was that adolescents who had been physically or sexually victimized or witnessed violence during childhood were at increased risk of cannabis abuse or dependence. Although a great number of studies in the literature have the focus in the addictive capacity of the substance itself there is lack of evidence on the causality of the use of drugs in youth. Present results support the notion that sexual abuse appeared to be a stronger predictor of cannabis abuse or dependence during adolescence, relative to the other two types of adversities.

The results also showed that violence in childhood played a variable role in the development of cannabis abuse or dependence. Participants who had experienced sexual

abuse were at higher risk of cannabis use, relative to those who had experienced physical abuse or witnessed violence. In contrast, physical abuse exerted a marginally significant effect on the development of cannabis abuse or dependence, and witnessing violence exerted a weak effect, inducing only a tendency toward this outcome. The increases in the risk of cannabis use following these types of violence observed in the current review were smaller relative to those reported by Kilpatrick et al. (2000) (physical abuse: OR: 4.84, sexual abuse: OR: 3.80, witnessing violence: OR: 8.42; Table 1). However, outcomes were assessed during the year preceding the evaluation, and 95% CIs were not provided for the ORs in Kilpatrick et al.'s study (2000); therefore, it was difficult to compare the results directly. In addition, the heterogeneity of the definitions of violence in the studies included in the review could have limited the appropriate risk values for these items.

A study conducted by Caravaca, Navarro, Luna Ruiz-Cabello, Falcon & Luna (2017) in college students in Spain showed similar results to our present work. This study including men and women with an average of 22.6 years old showed high rates of physical abuse OR 2.00 (95% CI [1.12-3.58]) and sexual abuse OR 2.72 (95% CI [1.06-6.95]) among users of cannabis. However, this study is a transversal design then causality and direction of this relationship (i.e., sexual victimization increases the risk of cannabis use) cannot be established. Findings showed by Caravaca et al. (2017) further support the notion that abuse has an impact on the vulnerability for use of drugs in young population, and highlight the importance of investigate this association in other population worldwide.

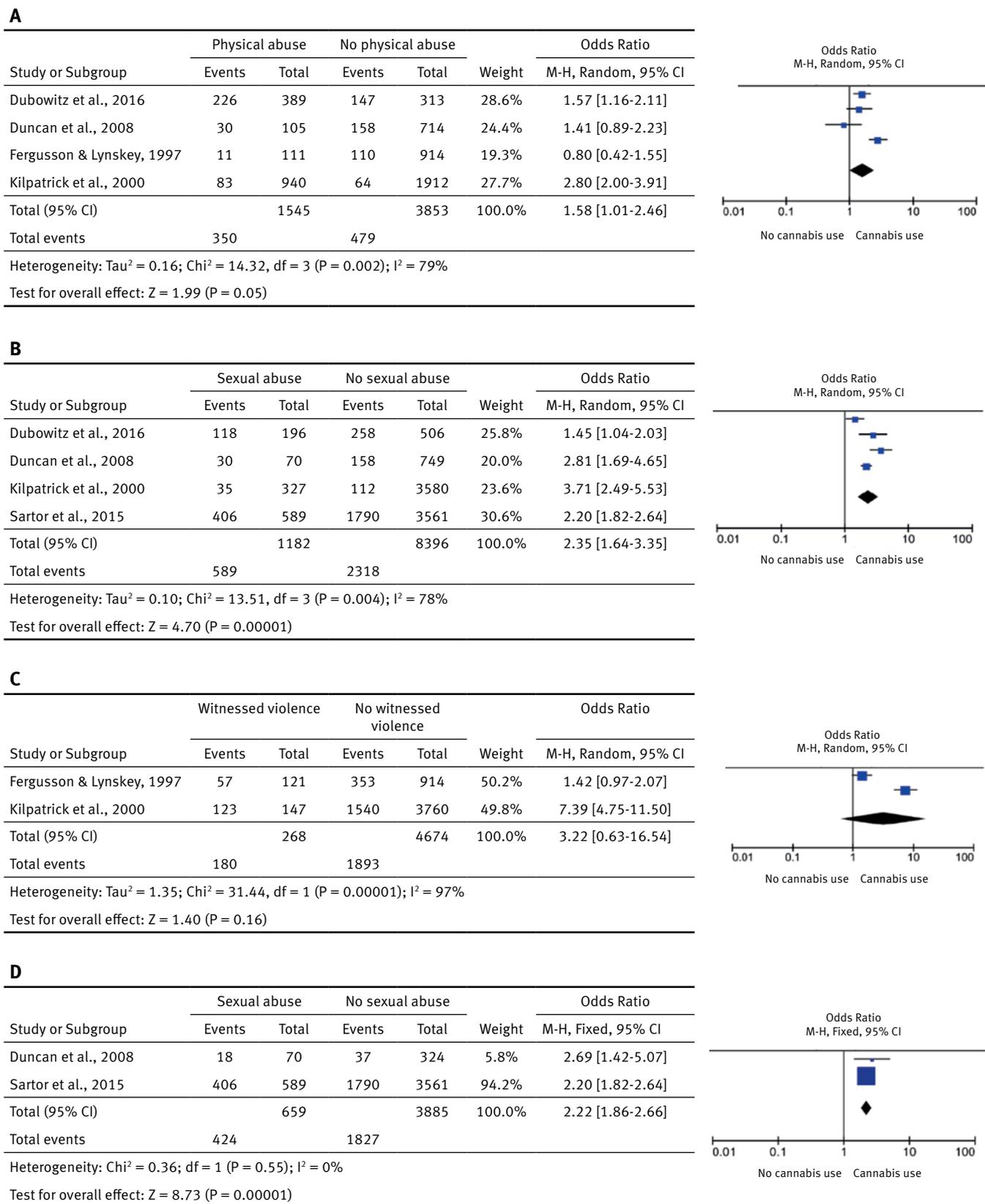


Figure 2. Odds ratios and 95% CI for cannabis use in female and male population who experienced physical abuse (panel A), sexual abuse (panel B) or witnessed violence (panel C) during childhood. Odds ratios and 95% CI for cannabis use in females who experienced sexual abuse (panel D) in childhood.

Note. Odds ratios were calculated using the number of events involving cannabis use recorded in the adolescence. Data were analyzed using random- or fixed-effects models, depending on the heterogeneity of the studies. CI = confidence interval. Overall effect for each forest plot was estimated with the Z test.

The results of the four studies that evaluated the effects of sexual abuse on cannabis abuse or dependence were consistent, in that the 95% CI values were similar and exceeded the unity value, which suggested an association between exposure and the outcome and indicated that the results were reliable. The analysis of these four studies showed that sexual abuse in childhood doubled the risk of cannabis abuse or dependence in adolescence for both sexes. Interestingly, sexual abuse in girls was an important factor in the development of cannabis use, even though the numbers of studies (two) and subjects (3 885 girls) included in the analysis were relatively low. This was also indicated in the results regarding the homogeneity of reports, narrow CIs, and statistical significance of the association. With respect to physical abuse, four studies reported a relationship between physical abuse and cannabis abuse or dependence, and the 95% CI values exceeded the unity value in the forest plot; however, the CIs were sufficiently high to indicate that the difference was barely significant. The relationship between witnessing violence and cannabis use was difficult to interpret because only two studies examined this association. Furthermore, one of the two studies included a small sample, and the OR for the other was high, leading to a wide 95% CI. This finding was supported by the results of the heterogeneity test, which were statistically significant for the comparison of physical abuse and witnessing violence.

The mild effect of physical abuse and the marginal effect of witnessing violence and their relationships with cannabis use could be explained by higher rates of dependence on other substances such as alcohol (physical abuse: OR: 3.93; witnessing violence: OR: 4.87) and hard drugs (physical abuse: OR: 12.35; witnessing violence: OR: 13.22) (Kilpatrick et al., 2000). Furthermore, levels of consumption of other drugs have been found to be higher in users who initiated cannabis use at an early age or used the drug frequently, relative to those observed in other users (de la Fuente et al., 2015).

Ecological studies examining contextual factors involved in substance use have identified multiple social and economic disadvantages as factors affecting substance use in individuals exposed to violence. In addition, marital discord, poor parent-child attachment, and parental substance use have been identified as risk factors for children, and living in impoverished, disorganized neighborhoods in which drugs are obtained easily increased their vulnerability to drug abuse (Duncan et al., 2008; Fergusson & Lynskey, 1997; Rogosch, Oshri & Cicchetti, 2010). All of these factors contributed to substance use in individuals who had experienced multiple types of child abuse (Rogosch et al., 2010). In this context, coping theory suggests that individuals initiate substance abuse in an attempt to regulate the negative effects of violence (Foster & Brooks-Gunn, 2009; Harrison, Hoffmann & Edwall, 1989; Kilpatrick et al., 2000;

Wright, Fagan & Pinchevsky, 2013). For instance, behaviors observed in girls who had experienced childhood sexual abuse included helplessness, somatic complaints, emotional withdrawal, and posttraumatic stress disorder. Endocannabinoids signaling has been found to be involved in stress regulation and acute effects of cannabinoids such tetrahydrocannabinol include anxiolytic effects (Zimmermann et al., 2017). Cannabis use may thus down-regulate negative effect. Therefore substance use can become an emotion regulation tactic and cannabis use might represent a self-medication with lower emotion regulation efficacy (Khantzian, 1997; Zimmermann et al., 2017).

From another perspective, violence exposure could lead to the development of adjustment difficulties resulting in externalizing behaviors during adolescence; in consequence, behavioral and mental health problems, juvenile delinquency, and substance abuse disorders are commonly observed in maltreated children (Fergusson & Horwood, 1998; Fergusson & Lynskey, 1997; Oshri, Rogosch, Burnette & Cicchetti, 2011). Evaluation of the different types of substance abuse demonstrated two scenarios involving adolescents: those who used alcohol because it was accessible and legal, and those in whom cannabis use resulted from deviant behavior, as it is illegal (Oshri et al., 2011; Sartor et al., 2013). Furthermore, increases in substance use could lead to additional victimization or revictimization, which increased the risk of future substance use, perpetuating the cycle (Kilpatrick et al., 2000).

It should be noted that the early onset of cannabis use (i.e., during a critical period of brain development), could have serious, long-lasting consequences (Sartor et al., 2013). Despite empirical evidence for and against the concept, the literature suggests that long-term cannabis use could lead to addiction (Volkow, Compton & Weiss, 2014). Furthermore, cannabis use appears to be a robust risk factor for subsequent consumption of other illicit drugs (Fergusson, Boden & Horwood, 2008).

Empirical evidence shows that long-term cannabis use affects neurocognitive functioning, particularly in those who initiate cannabis use during early adolescence, which results in significant reductions in intelligence quotient and impaired performance in a variety of attention, memory, and executive function tasks. All of these factors contribute to psychosocial difficulties such as academic underachievement and/or school dropout (Ganzer, Broning, Kraft, Sack & Thomasius, 2016; Grant, Gonzalez, Carey, Natarajan & Wolfson, 2003; Volkow et al., 2014). In addition, alterations in motor function (e.g., coordination) have negative consequences, which could lead to motor vehicle accidents (Volkow et al., 2014). Empirical evidence has also shown an increase in the risk of psychosis, including that associated with schizophrenia, mainly in subjects with genetic predisposition (Fergusson, Lynskey & Horwood, 1996; Marconi, Di, Lewis, Murray & Vassos, 2016; Volkow et

al., 2014). Moreover, a longitudinal study showed that cannabis use predicted the development of anxiety disorders, depression, certain personality disorders, and interpersonal violence (Copeland, Rooke & Swift, 2013). Interestingly, results of a recent study indicated that both occasional and chronic cannabis use increased the risk of suicidality in adolescents and young adults. Suicidality is characterized by suicidal ideation and intent (Borges, Bagge & Orozco, 2016) and is considered the most severe symptom of several psychiatric disorders (American Psychiatric Association, 2013). In contrast to the claim that cannabis use involves lower levels of risk of severe mental illness, relative to those observed with tobacco use, the findings described above suggest that cannabis exerts important effects on health, which affects quality of life.

The results of the current review demonstrated the importance of enhancing efforts to prevent childhood violence. In addition, they highlighted the need for early intervention to prevent cannabis abuse or dependence, particularly in children who experience sexual abuse. Cannabis use could exert cumulative effects on health, family life, and social problems. This study highlights the importance of assessing for a history of violence when considering individuals for prevention or intervention strategies pertaining to cannabis use. Individuals with a history of violence in childhood who are seeking treatment to address cannabis problems would benefit from a modality that focuses on establishing strategies for emotion regulation, including exploring more adaptative methods of coping with negative affect (Vilhena-Churchill & Goldstein, 2014). Interventions should include a broad perspective that considers the general social and family contexts in which violence occurs, rather than focusing exclusively on the issue of cannabis abuse/dependence (Fergusson & Horwood, 1998). As policy shifts toward the legalization of cannabis in various countries, the development of such programs is urgent.

### ***Risk of bias and study limitations***

One of the main limitations of the analysis of the impact of childhood abuse on cannabis use in adolescence involved evidence quality from researches, as the results showed an important selection bias, because sampling was not randomized. The other main limitation involved performance bias, as the evaluation of violence in the included studies was heterogeneous, and participants underwent multiple evaluations with different aims (e.g., genetic outcomes) in the examination of cannabis use. Exposure to violence during childhood requires immediate attention; however, ethical considerations should be taking account in the design of prospective studies that would increase the children's vulnerability. For instance, the Dubowitz et al. study's (2016) describes that child in risk of abuse or, those with sustained abuse, were included in protocols for the protection of human subjects, including referrals for sub-

jects in need of services (Runyan et al., 1998). Additionally, most studies included in this systematic review were retrospective, and analysis of the effects of abuse was performed during the final stages of investigation.

Another limitation involved the availability of data from the studies that were evaluated in the review, as we were unable to explore the chronicity or severity of childhood violence. A previous study showed that younger age during sexual abuse enhanced the risk of cannabis use (Sartor et al., 2013); however, it was impossible to perform this type of evaluation in the current review. In addition, we were unable to consider the frequency of consumption, amounts consumed, age at initiation of consumption, or the time lag between interventions and outcomes, with exception of the Dubowitz et al. study's (2016) that included level of cannabis use (never, some or heavy). In addition, it was impossible to perform an analysis of sex differences according to the subtypes of violence, which could have provided important results, as previous research has shown that boys were at greater risk of cannabis use, relative to girls (United Nations Office on Drugs and Crime, 2015).

In conclusion, the results of this review identified specific types of childhood violence, such as sexual and physical abuse, as factors affecting vulnerability to cannabis use. However, the number of studies examining other types of violence is limited. Much of the research in this area focuses on physical or sexual abuse. In spite that, neglect is the most common form of maltreatment and emotional maltreatment has been identified as significant in terms of later development of psychopathologies (Dubowitz et al., 2016; Vilhena-Churchill & Goldstein, 2014). The current results demonstrated the importance of enhancing efforts to prevent violence, particularly sexual abuse, as part of integral programs designed to reduce cannabis abuse and dependence.

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## Authors' contributions

NPM and LMM developed the review protocol, extracted the data, and wrote the first draft of the manuscript. OTHH and GJR performed independent reviews of all of the titles according to the established inclusion and exclusion criteria, and prepared the final figures and tables. All authors read and approved the final version.

## Conflict of interest

The authors have no conflicts of interest to declare.

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