Drug Use Disorders and Violence: Associations With Individual Drug Categories

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ABSTRACT

Although drug use disorders are among the most important modifiable factors for violence perpetration, previous reviews have not investigated links with individual categories of drug use disorders or explored sources of variation in risk estimates between studies. We conducted a systematic review and meta-analysis of studies that examined the link between individual drug categories and violent outcomes. We searched for primary case-control and cohort investigations that reported risk of violence against others in individuals diagnosed with drug use disorders using validated clinical criteria, and followed PRISMA guidelines. We identified 18 studies published from 1990 to 2019 reporting data from 591,411 individuals with drug use disorders. We reported odds ratios (OR) of the violence risk in different categories of drug use disorders compared with those without. We found ORs ranged from 0.8 to 25.0 for most individual drug categories, with generally higher ORs in individuals with polydrug use disorders. In addition, we explored sources of between-study heterogeneity by subgroup and meta-regression analyses. Cohort investigations reported a lower risk of violence than case-control reports (OR = 2.7 [2.1-3.5] vs 6.6 [5.1-8.6]), and associations were stronger when the outcome was any violence rather than intimate partner violence (OR = 5.7 [3.8-8.6] vs 1.7 [1.4-2.1]), which was consistent with results from the meta-regression. Overall, these findings highlight the potential impact of preventing and treating drug use disorders on reducing violence risk and associated morbidities.

Keywords: substance use disorder; substance misuse; violence; crime; meta-analysis; opioid; stimulant; sedative
Abbreviations: CI, confidence interval; DSM, Diagnostic and Statistical Manual of Mental Disorders; ICD, International Classification of Diseases; MOOSE, Meta-analyses of Observational Studies in Epidemiology; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis; RCTs, randomized controlled trials; WHO-CIDI, World Health Organization’s Composite International Diagnostic Interview.
INTRODUCTION

Drug misuse is a global public health concern (1, 2). Worldwide, around 70 million individuals were diagnosed with drug use disorder (1). Drug use disorders have been associated with a wide range of adverse outcomes, including suicide, comorbid mental illness, and premature mortality (3-5). In addition, drug use disorders increase risk of violence against others (3, 6-9). Further, the prevalence of drug use disorder in prison ranges from 10% to 48% in men and 30% to 60% in women (10), which is substantially elevated compared to the prevalence, ranging from 0.6% to 4.0% in men and 0.3% to 2.9% in women, in the general population (11).

The prevalence differs between individual categories of drug use disorders. The rate per 100 000 people is 65 for stimulants such as amphetamines, 78 for cocaine use disorders, 290 for cannabis use disorders, 353 for opioid use disorders, and less than 52 for other drugs including hallucinogen and sedatives globally in 2016 (12). Although research has consistently found increased violence risk in drug use disorders, there are individual studies that have shown that the magnitude of this increased risk varies depending on the drug category. For example, when compared to general population, odds ratios of violence in cannabis use have ranged from 1 to 7 (13-17), and in cocaine, they have varied from 2 to 11 (18-21). This might be due to different methodologies adopted and specific outcomes used in different studies. Furthermore, it has been suggested that certain type of stimulants, such as crack cocaine that are associated with irritability and aggressiveness (7, 22), might have a higher risk of criminal behaviour than others, including less strong forms of cannabis that may reduce risks due to sedative and calming effects (23, 24). This is important to clarify further as more precise estimates would allow for risk stratification, better treatment allocation (especially if liaison with criminal justice agencies is required), and allow for more evidence-based estimates of the population impact of certain drug policies. Overall, the
relative risk of violence in different categories of drug use disorders is uncertain, which would inform the assessment and management of individuals at risk of violence, and possibly service development.

Previous reviews have explored associations between general drug misuse and violence against others but have mostly investigated selected samples, such as prisoners (25) or psychiatric patients (26-29). In addition, most existing reviews have not used standardized clinical criteria to identify drug use disorders (22, 30). This could introduce bias as self-report of the extent of drug use is often unreliable (31). Validated diagnostic tools based on validated criteria (such as International Classification of Diseases, Diagnostic and Statistical Manual of Mental Disorders or International Classification of Diseases) can identify individuals with a severe form of drug misuse, which may present to clinical and addiction services, and for which there is evidence-based treatment available. In addition, diagnostic categories enable consistent communication between clinicians and researchers as the criteria are widely known, validated cross-culturally, and with decent reliability measures (32, 33). Furthermore, the most recent review that did examine the link between general drug use disorders and violence was conducted more than two decades ago (34) and did not explore potential source of between-study heterogeneity or differences between individual categories of drug use.

However, the link between drug use and violent outcomes is complex as a wide range of factors such as experiences of violence including both as victim and perpetrator, the comorbidity of other mental disorders, and social determinants such as gender, ethnicity, and poverty may moderate and mediate this link. For instance, previous violence victimization might trigger development of drug use disorders which might in turn lead to later perpetration of violence (35-39). Moreover, structural causes of drug use problems are relevant as they have been linked to criminalization (23), and factors such as poverty (40), poor mental
health (4, 41), treatment availability (42) and homelessness (43). In addition, physical and psychological effects of drugs can lead to agitation, aggression, and cognitive impairment that may in turn heighten risk of violence. Individuals with drug use disorders might also turn to violence to finance their drug use and disputes within illegal drug markets might associated with violence (44). To address these gaps in the evidence, in this review, we aimed to synthesize the odds of violence in individual drug use disorders and explore sources of heterogeneity between studies.

METHODS

We conducted this review following the Meta-analyses of Observational Studies in Epidemiology (MOOSE) (45) and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (46). The study was registered with an international prospective register of systematic reviews (PROSPERO CRD42019119533).

Search strategy

We conducted searches in the following digital databases from the inception of the databases (dated to 1 January 1927) to 18 February, 2019: PubMed, Web of Science, Embase, Ovid MEDLINE, PsycINFO, Global Health, and US National Criminal Justice Reference Service Abstract Database. We used a combination of search terms related to drug misuse (i.e., illegal drug OR illegal substance OR marijuana OR cocaine OR cannabis OR opioid OR heroin OR methamphetamine OR stimulant*), AND violence (i.e., violen* OR crim* OR homicide OR aggress* OR offen*), AND study design (i.e., cohort OR longitudinal OR follow-up OR prospective OR case-control). We included studies on both illegally and legally obtained drugs. There were no language restrictions and non-English language articles were translated. We also scanned reference lists in attempt to identify additional articles. We searched for
unpublished literature including conference proceedings, theses and dissertations. The first 
author (S.Z) conducted the initial screening of the titles and abstracts for inclusion and 
exclusion. S.Z and R.Y screened full-text publications for eligibility. Any uncertainties were 
discussed with S.F.

**Study selection**

Inclusion criteria were: Inclusion criteria were: 1) cohort and case-control studies that 
examined link between individual categories of drug use disorders and violent outcomes and 
provided data for calculation of odds ratio between individuals with and without the studied 
drug use disorder. Eligible case-control studies were those that reported prevalence of drug 
use disorders in cases with and without violence perpetration; 2) investigations that reported 
drug use disorders (or, in older studies, equivalent diagnostic categories of drug misuse or 
dependence) meeting diagnostic criteria for Diagnostic and Statistical Manual of Mental 
Disorders and International Classification of Diseases; 3) studies that reported violent 
outcomes, including any violence and not being limited to context (e.g. community, domestic, 
intimate partner), type of crime (e.g. homicide, assault, threat or intimidation and all sexual 
offenses) and measures (self-report, family report or official/criminal records).

We excluded: 1) animal investigations; 2) experimental, cross-sectional, qualitative 
studies, or randomized controlled trials (RCTs); 3) investigations with within-individual 
designs; 4) studies that used self-report (47) (e.g. Addiction Severity Index) or urine tests to 
identify drug use, or did not separate drug misuse from alcohol and nicotine misuse; 5) 
reports with recidivism or re-offending as outcomes (48); 6) studies in only selected samples 
(e.g. offenders, cohorts with mental disorders) to increase the generalizability of risk 
estimates to the general population; 7) investigations that used the non-specific outcome of 
all criminal behavior, antisocial behavior or delinquency, which was not broken down for 
vviolence specifically; 8) studies that reported selected participants under medication (e.g.,
antidepressant, antipsychotic drugs, or other prescription drugs) or individuals undergoing other interventions for drug use disorders; or 9) case-series studies or reviews.

In case of duplicate samples, we included the study which was the most recent, used the most common outcome, or with the largest sample. If a study reported outcomes at multiple time points, outcomes with the longest follow-up period were included.

Data extraction

We used a standardized form to extract data. The following information was recorded: study design, country, sample characteristics, diagnostic criteria, category of drug use disorders, type of drugs, comparison group, gender, age, years of follow-up, and study period. SZ conducted the initial data extraction. In case of uncertainties, RY and SF were consulted.

Statistical analysis

Quality of the individual study was assessed using the Newcastle-Ottawa Quality Assessment Scale (49). Heterogeneity was estimated using $I^2$. $I^2$ is reported as a percentage out of 100%, where 0-40% represents low heterogeneity, 30% to 60% may indicate moderate heterogeneity, 50%-90% may denote substantial heterogeneity and 75% to 100% may indicate considerable heterogeneity (50)-(51). All effect sizes were converted into odds ratios (OR), and converted from Pearson’s $r$ and Cohen’s $d$ using standard approaches (52). Sources of heterogeneity were explored using subgroup analyses and meta-regression analyses. Meta-regression was conducted to estimate the extent to which one or more measured covariates (the same variables as used in the subgroup analysis) explained the observed heterogeneity in risk estimates between primary studies (50). The same variables were used in the subgroup and meta-regression analyses and only non-overlapping samples were included in the analyses. When testing the association of sample size, we excluded two studies as they were disproportionately large (53, 54). We set the years of follow-up as a continuous variable and
also a dichotomous variable using the median period as the cut-off. Other analyses included estimating associations while excluding studies published before 2000 and subgroup analyses by different comparison groups. We tested publication bias using Egger’s test (55), with p<0.05 indicating publication bias. Analyses were conducted in STATA (version 13, StataCorp LLC, Texas).

RESULTS

We identified eighteen eligible studies (for details, see Figure 1 and Table 1) that included 591,411 individuals with drug use disorders. Studies were from 5 countries: 14 from the US (n=542,393, 91.7%) (53, 54, 56-67), one each from New Zealand (n=182, 0.03%) (68), Denmark (n=43,403, 7.3%) (69), the Netherlands (n=5303, 0.9%) (70), and Turkey (n=130, 0.02%) (71). Eight studies used case-control designs (53, 54, 56, 58, 63, 66, 67, 71) and others were longitudinal cohorts with a median follow-up of 9.5 years.

In 16 investigations, diagnosis was made using the Diagnostic and Statistical Manual of Mental Disorders (version 3 onwards). One study adopted the International Classification of Diseases -8 (69) and one provided both International Classification of Diseases -10 and Diagnostic and Statistical Manual of Mental Disorders -IV diagnoses (63).

For outcome measurement, two studies used violent conviction from official records (65, 69) and one reported intimate partner violence from the partner’s report (62). Most used self-report items in Diagnostic Interview Schedule (56), the PPC Delinquency and Criminal Behavior inventory (57), Aggression Questionnaire (58), Conflict Tactics Scale (63), physical aggression subscale in Buss-Perry Scale (71), and specially developed questionnaires (53, 54, 60, 61, 66, 67, 70). A combination of several measures (e.g., official records and self-report) was applied in three studies (59, 64, 68).
Any/poly drug use disorder

We identified seven cohort investigations (57, 60, 64, 65, 69, 70) and six case-control reports (53, 54, 56, 63, 66, 67) that examined the risk of violence in any or poly drug use disorder (Figure 2). ORs ranged from 0.1 and 55.1. The ORs ranged from 1.3 (95% 0.1-13.0) to 25.0 (16.1-39.0). When excluding the two studies that were published prior to 2000, the OR was 4.1 (3.0-5.7).

Cannabis/Marijuana use disorder

Six cohort studies (57, 59, 61, 62, 64, 68) and five case-control investigations (53, 54, 56, 67, 71) examined the link between cannabis/marijuana use disorder and violence. The ORs ranged from 1.3 (1.1-1.7) to 11.5 (7.8-17.2). When excluding studies prior to 2000, the OR ranged from 1.3 (1.1-1.7) to 9.1 (8.5, 9.7).

Hallucinogen use disorder

Two cohort investigations (59, 62) and one case-control report (54) tested the association between hallucinogen use disorder and violence. The ORs varied from 1.4 (1.3-1.4) to 18.3 (14.9-22.5).

Stimulant use disorder

We identified four studies that reported risk estimates for violence in stimulant use disorder, with three studies (59, 61, 62) using a cohort study design and two (54, 58) utilizing a case-control study design. All of these studies were conducted in the US. The ORs ranged from 1.9 (1.4-2.6) to 10.8 (9.3-12.5).
**Opioid use disorder**

Three cohort investigations \((59, 61, 62)\) and two case-control studies \((54, 67)\) reported the risk of violence in opioid use disorder, all of which were conducted in the US. The risk estimates ranged from an odds ratio of \(0.8 (0.5-1.1)\) to \(9.5 (8.7-10.4)\).

**Sedative use disorder**

Two cohort investigations \((59, 62)\) and one case-control study \((54)\) examined the association between sedative use disorder and violence. ORs varied from \(1.1 (1.1-1.2)\) to \(10.5 (9.1-12.2)\).

**Heterogeneity**

No significant differences were found in risk estimates by gender, country, measures of outcomes, study design, years of follow-up and sample size in subgroup analyses (Table 2). The risk estimates in cohort investigations \((\text{OR}=2.7, 95\% \text{CI}: 2.1-3.5)\) were lower than in the case-control reports \((\text{OR}=6.6, 95\% \text{CI}: 5.1-8.6)\). Studies from studies in which drug use occurred before violence reported an OR of \(3.2 (2.0-5.3)\). No differences were found between violence by official records \((\text{OR} = 4.5 [1.1, 18.6])\) and self-report \((4.3 [2.8-6.5])\).

The ORs of intimate partner violence \((\text{OR}=1.7, 95\% \text{CI}: 1.4-2.1)\) were lower than general violence \((\text{OR}=5.7, 95\% \text{CI}: 3.8-8.6)\). When further exploring the associations of the comparison groups in intimate partner violence studies, no significant differences were found.

In the meta-regression analysis, we also found that study design (cohort vs. case-control study) was associated with heterogeneity \((\beta = 0.8, t=2.3, p=.04)\), as was the violent outcome (intimate partner violence vs general violence; \(\beta=-1.2, t=-3.3, p<.05\)). No other variables examined explained the heterogeneity among studies. Egger’s test did not clearly suggest publication bias \((t = 1.32, p = 0.20)\).
DISCUSSION

Main findings

This systematic review and meta-analysis examined the association between drug use disorders and violence. We identified 18 eligible studies from five countries with 591,411 individuals meeting diagnostic criteria for drug use disorders. There were two main findings. First, we found that individuals with a diagnosed drug use disorder have a four- to ten-fold higher risk of perpetrating violence compared with general population or individuals without the studied drug use disorder. All of the examined categories of drug use disorders, including cannabis, hallucinogen, stimulant, opioid, and sedative, were associated with elevated violence risks. We found all studies increased risk with 34 out of the 37 studies with confidence intervals that did not cross one. The odds need to be seen in the context of absolute rates of these disorders – which vary from 52 cases (per 100 000) of hallucinogen use disorders to 353 cases of opioid use disorders (12). Second, there was a substantial heterogeneity between studies, which was partially explained by study design and the type of outcome. Violence risk in drug use disorders was lower in cohort than in case-control studies, and when intimate partner violence was the outcome rather than general violence.

Implications

Although the odds are not dissimilar to other neuropsychiatric conditions (72), their importance is greater from a public health perspective as drug use disorders are more prevalent than mental illnesses, such as schizophrenia or bipolar disorder. In addition, although drug use disorders are not more prevalent than disorders such as depression and anxiety, their risk of violence is usually higher (67, 73). Therefore, drug use disorders have greater population impact when taking into account both prevalence and relative risk. This underscores the importance of treating drug use disorders as part of any public health
approach to violence prevention. Notably, long-term methadone maintenance programs and behavioural treatments can reduce crime (74). In addition, there are studies that demonstrate reduced crimes after drug treatment (e.g. opioid maintenance treatment (OMT), methadone, buprenorphine and naltrexone) and non-medical treatment (e.g. Therapeutic Communities (TC), drug courts), in individuals using cocaine (75), opioid (76-79), and with general drug use disorders (80-83). Moreover, prison-based interventions, such as TC, opiate maintenance treatment and pharmacotherapies for drug use disorders, are effective in reducing recidivism in prisoners (84-86). Despite this, most individuals with drug use disorders do not receive treatment. In the US, only 13.5% and 24.6% received treatment among individuals with 12-month and lifetime drug use disorders, respectively (87). Thus, more efforts should be taken to improve accessibility of treatment for individuals with drug use disorders. Together, the treatability of drug use disorders, unmet needs and risk of adverse outcomes present an opportunity to improve public health and safety.

A second implication is that two aspects of study design explained some of the between-study heterogeneity. Cohort studies had lower risk estimates than case-control investigations. This difference is likely because cohort studies are more likely to account for the temporal sequence between drug use disorders and violent outcome. This allowed for a more accurate estimation of the associations than case-control studies. Future observational research should prioritize cohort designs to longitudinally follow up individuals with drug use disorders and examine their violent outcome. We also found that the associations with intimate partner violence was less strong than for general violence. This may be because individuals with drug use disorders are less likely to have partners (87, 88) and those who have partners might present with less severe symptoms of drug use disorders (89).
**Strengths, Limitations, and Future Directions**

This review has several strengths. First, we only included studies which used validated diagnostic criteria to identify drug use disorders and excluded studies using self- or other measures that may reflect short-term or recreational use. Second, we carefully explored heterogeneity using two methods (subgroup analyses and meta-regression). Third, we excluded studies examining drug use disorders and violent outcomes in selected samples such as offenders, cohorts with mental disorders, and individuals under treatment for drug use disorders, as not all individuals with drug use disorders were offenders or having other mental disorders and the majority will not be subject to treatment. This likely increases the generalizability of our findings.

However, a number of limitations should be noted. First, all included studies were conducted in high-income countries. We found one investigation in middle-income, namely Turkey but no others, and none in Central Latin America, Tropical Latin America, and Southern sub-Saharan Africa, where violence is among the top 10 leading causes of disability-adjusted life-years (DALYs) (90). Many countries in these regions account for the majority of global drug manufacture, trafficking, and consumption (91, 92). Therefore, more research on the link in these settings is needed. The second limitation was the amount of information on individual categories was not sufficient to draw definite conclusions about differences by drug class. We identified three studies (54, 59, 62) in sedative use disorder and five each for stimulant use disorder (54, 58, 59, 61, 62) and opioid use disorder (54, 59, 61, 62, 67). Furthermore, we found a limited literature on polydrug use, although it is common and linked to poorer treatment outcomes, social maladjustment and overdose lethality (93-95).

Future studies should investigate more carefully the different categories of drug use disorders, polydrug use and the links with novel psychoactive substances. Third, it is difficult to meta-analyse studies of selected populations as the effects of mediators cannot be modelled.
Therefore, our findings are not necessarily risk estimates in specific subpopulations such as prisoners or individuals who are participating in treatment programmes. For example, our estimates might be overestimates as we excluded studies individuals under drug treatment, which could decrease risk of violence (96, 97). Fourth, we found links between hallucinogen use and violence in the general population, but they appear to be heterogeneity in their associations by population. For example, in criminal justice populations, recent work has found decreased associations between hallucinogen use and repeated offending in substance-involved offenders under community corrections supervision (48), which is also reported in intimate partner violence perpetrators (47, 98). In individuals with schizophrenia, there is an increased risk (99). Finally, due to lack for data, we only identified a few factors that might explain heterogeneity between studies. For example, we were not able to examine whether some factors moderate the link between drug use disorders and violence, such as being subjected to violence, comorbidity of other substance use disorders (including alcohol) and mental health conditions, time between onset of drug use and violent outcome, and other social determinants (including poverty and access to services). In addition, the heterogeneity analyses were based on different drug categories and limited by variations in primary study settings. The results should therefore be interpreted with caution and read in the context of implications for future research rather than clinical practice.

However, these factors could be either associated, mediate or modify links between drug misuse and violence. For instance, an umbrella review of 22 meta-analyses based on over 120 000 individuals have shown that a range of neuropsychiatric disorders including schizophrenia, personality disorders, and bipolar disorders and perpetration, witness, or victim of violence during childhood are linked to increased risk of violence (72), suggesting that all of these comorbidities can be confounds. In addition, individuals who are victims of
violence may use drugs as a coping mechanism and victimization itself might in turn lead to later violence (35-39). Therefore, more research accounting for these factors is necessary.

Conclusions

This systematic review and meta-analysis have synthesized the evidence on associations between individual categories of drug use disorder and violent outcomes. The findings suggest that all categories of drug use disorders have an elevated risk of violence, and that study design and type of violent outcome partly explain variation in risk estimates between studies.

Acknowledgments

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| First Author, Year (Reference no.) | Country | Source of Population | Diagnosis Criteria | Design | Type of drugs | Comparison Groups | Sample Size | Age | Gender | Year | Follow up (year) | Outcome | Source of Outcome | Assessed Alcohol Use |
|------------------------------------|---------|----------------------|-------------------|-------|--------------|------------------|-------------|-----|--------|------|-----------------|----------|-----------------|----------------------|
| Swanson, 1990 (56)                | US      | The Epidemiologic Catchment Area Surveys | DSM-III² | case-control | cannabis use dependence/other drugs | non-drug use disorder | 8061 | ≥18 | mixed | 1985 |  | violence | self-report | yes |
| Friedman, 1996 (57)               | US      | A longitudinal study of the National Collaborative Perinatal Project | DSM-III | cohort | marijuana use/drug abuse | non-marijuana use/non-drug abuse | 380 | 25.5±6.1 | mixed | 1985 | 2.5 | violent offence | self-report | yes |
| Arseneault, 2000 (68)             | New Zealand | The Dunedin Study | DSM-III-R | cohort | marijuana dependence disorder | non-marijuana dependence disorder | 182 | mean 21 | mixed | 1994 | 21 | violence | court convictions and/or self-report | yes |
| Corrigan, 2005 (66)               | US      | The National Comorbidity Survey (NCS) | DSM-III-R | case-control | any drug use disorder | non-drug use | 5865 | 18-54 | 18-54 | 1990-1992 | 9 | violent behaviour | self-report | yes |
| Payer, 2011 (58)                  | US      | Participants diagnosed with methamphetamine dependence | DSM-IV | case-control | methamphetamine dependence | healthy controls without drug use disorder | 44 | 32.8±8.8 | female | not stated |  | aggression | self-report | yes |
| Christoffersen, 2003 (69)         | Denmark | The 1966 birth cohort in Denmark | ICD-8⁶ | cohort | drug addicts | non-drug addicts | 43403 | 15-47 | male | 1993 | 13 | violence crimes | official records | no |
| Feingold, 2008 (59)               | US      | The Couple Study associated with the Oregon Youth Study | DSM-IV | cohort | cannabis/hallucinogen/cocaine/opiates/amphetamines/sedatives | non-cannabis/hallucinogen/cocaine/opiates/amphetamines/sedatives | 150 | 19-28 | male | not stated | 9 | intimate partner violence | self-report, other's report, interview ratings | yes |
| Van Dorn, 2012 (60)               | US      | National Epidemiologic Survey on Alcohol and Related Conditions | DSM-IV | cohort | drug use disorder | non-drug use disorder | 36019 | ≥18 | mixed | 2005 | 3 | any violence | self-report | yes |
| Smith, 2014 (61)                  | US      | National Epidemiologic Survey on Alcohol and Related Conditions | DSM-IV | cohort | cocaine/cannabis/opioid use disorder | non-cocaine use disorder/non-opioid use disorder | 25633 | mean 46.4 | mixed | 2005 | 3 | intimate violence | self-report | yes |
| Study                                      | Country | Design/Method                                                                 | DSM-IV/III-R | Drug Use Disorders                                                                 | Sample Size | Age | Gender | Time Period | Violence Measure                                                                 | Reporting Method | Notes   |
|-------------------------------------------|---------|-------------------------------------------------------------------------------|---------------|-----------------------------------------------------------------------------------|-------------|------|--------|------------|---------------------------------------------------------------------------------|-----------------|---------|
| Feingold, 2014 (62)                       | US      | The Couple Study associated with the Oregon Youth Study                        | DSM-IV-TR    | cannabis/hallucinogen/cocaine/opiates/amphetamines/sedatives                      | 146         | mean 35 | female | not stated | intimate partner violence                                                         | others' report   | yes     |
| Have, 2014 (70)                           | Netherlands | A cohort study of the Dutch general population                               | DSM-IV       | drug dependence                                                                   | 5303        | 18-64 | mixed  | 2012       | physical violence                                                                | self-report      | yes     |
| McCauley, 2015 (63)                       | US      | The National Comorbidity Survey Replication                                 | WHO-CIDI     | drug abuse                                                                        | 5692        | 21-99 | mixed  | 2003       | physical dating violence                                                          | self-report      | yes     |
| Harford, 2016 (53)                        | US      | National Survey on Drug Use and Health                                        | DSM-IV       | drug use disorder                                                                 | 108560      | 12-17 | mixed  | 2008-2013 | other-directed violence                                                          | self-report      | yes     |
| White, 2015 (64)                          | US      | A cohort of the Pittsburgh Youth Study                                        | DSM-IV       | cannabis/hard drug use disorder                                                   | 240         | 35.8±0.8 | male   | 2010       | persistent violence                                                               | self-reports and official records | yes     |
| Trauffer, 2017 (65)                       | US      | A cohort study in which children were followed into adulthood                | DSM-III-R    | drug abuse and/or dependence                                                       | 413         | 29.6±3.9 | female | 2014       | violent offender                                                                  | self-report      | yes     |
| Harford, 2018a (54)                       | US      | National Survey on Drug Use and Health                                        | DSM-IV       | any drug use disorder                                                              | 314881      | ≥18   | mixed  | 2008-2015 | other-directed violence                                                          | self-report      | yes     |
| Harford, 2018b (67)                       | US      | The National Epidemiologic Survey on Alcohol Related Conditions- III         | DSM-V        | cannabis/opiod/other drug use disorder                                             | 36309       | ≥18   | mixed  | 2012-2013 | other-directed violence                                                          | self-report      | yes     |
| Altintas, 2019 (71)                       | Turkey  | Outpatients synthetic cannabinoid use disorders                              | DSM-IV       | synthetic cannabinoid use disorders                                               | 130         | 28.2±7.6 | mixed  | not stated | aggression                                                        | self-report      | no      |

Abbreviations: DSM, The Diagnostic and Statistical Manual of Mental Disorders; ICD: International Classification of Diseases; WHO-CIDI, World Health Organization’s Composite International Diagnostic Interview. – not applicable.
Table 2. Sources of heterogeneity in included studies of the odds ratio for violence in drug use disorder.

| Source of heterogeneity               | Number of studies | Number of population | Odds ratio | 95% CI       |
|---------------------------------------|-------------------|----------------------|------------|--------------|
| Gender                                |                   |                      |            |              |
| Males                                 | 4                 | 43976                | 3.9        | 1.7, 8.9     |
| Females                               | 4                 | 800                  | 2.2        | 1.8, 2.7     |
| Mixed                                 | 11                | 546635               | 5.4        | 4.1, 7.0     |
| Study location                         |                   |                      |            |              |
| US                                    | 14                | 542393               | 4.2        | 2.9, 6.1     |
| Other high-income counties            | 3                 | 48888                | 7.1        | 4.1, 12.2    |
| Regions in US                         |                   |                      |            |              |
| National based                        | 8                 | 533339               | 4.4        | 2.9, 6.1     |
| Regional based                        | 6                 | 9054                 | 3.9        | 2.0, 7.6     |
| Measures of outcome                   |                   |                      |            |              |
| Self-reported outcome                 | 12                | 546877               | 4.6        | 3.0, 7.2     |
| Others’ report/official records       | 3                 | 43962                | 3.2        | 1.3, 7.8     |
| Combined measures                     | 3                 | 572                  | 4.4        | 1.3, 14.5    |
| Temporality in cohort studies         |                   |                      |            |              |
| Drug prior to violence                | 4                 | 85105                | 3.8        | 1.6, 9.1     |
| Others                                | 6                 | 26764                | 2.6        | 1.6, 4.3     |
| Study design                          |                   |                      |            |              |
| Cohort study                          | 10                | 111869               | 2.7        | 2.1, 3.5     |
| Case-control study                    | 8                 | 473850               | 6.6        | 5.1, 8.6     |
| Years of follow-up                    |                   |                      |            |              |
| < 9.5 years                           | 5                 | 67485                | 1.9        | 1.5, 2.4     |
|                  |     |         |     |     |
|------------------|-----|---------|-----|-----|
| **≥ 9.5 years**  | 5   | 44384   | 4.5 | 2.2, 9.1 |
| **sample size**  |     |         |     |     |
| < 500            | 8   | 1503    | 2.6 | 2.0, 3.4 |
| ≥ 500            | 8   | 166285  | 5.1 | 2.9, 9.2 |
| **Violent outcome** |     |         |     |     |
| Intimate partner violence | 4   | 31621   | 1.7 | 1.4, 2.1 |
| Intimate partner violence with general controls | 2   | 31325   | 1.8 | 0.8, 4.2 |
| General violence  | 14  | 559790  | 5.7 | 3.8, 8.6 |
| **Clinical criteria** |     |         |     |     |
| DSM-III(-R)      | 5   | 14901   | 5.7 | 2.5, 13.0 |
| DSM-IV(-TR)      | 10  | 491106  | 3.4 | 2.0, 6.0 |

Abbreviation: DSM, The Diagnostic and Statistical Manual of Mental Disorders.
Figure legend/titles:

Figure 1.
Title: Figure 1. Flow-diagram of the systematic search to identify included studies

Figure 2.
Legend: Weights are from random effects analysis
Title: Figure 2. Odds ratio of violent outcomes in drug use disorder
Records Identified Through Database Searches
(n = 6,589)

Additional Records Identified Through Other Sources
(n = 11)

Records After Duplicates Removed
(n = 2,707)

Records Excluded in Title/Abstract Screening
(n = 2,416)

Full-text Articles Assessed for Eligibility
(n = 291)

Full-text Articles Excluded: [n = 273]
Self-report or urine test of drug use (n = 123)
Combined alcohol and drug use (n = 60)
No report of effect size (n = 45)
Selected sample (n = 26)
Combined violence with other offences (n = 16)
Duplicated samples (n = 3)

Studies Included in Meta-analysis
(n = 18)
