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Prevalence of childhood maltreatment among people with opioid use disorder: A Systematic Review and Meta-analysis

Thomas Santo Jr.^a, Gabrielle Campbell^{a,b}, Natasa Gisev^a, Lucy Tran^a, Samantha Colledge^a, Gian Luca Di Tanna^{c,d}, Louisa Degenhardt^a

^aNational Drug and Alcohol Research Centre, UNSW Sydney, 22-32 King Street, Randwick NSW 2031, Australia

^bSchool of Health and Sports Sciences, University of the Sunshine Coast, Sunshine Coast QLD 4556, Australia

^cThe George Institute for Global Health, UNSW Sydney, 1 King Street, Newtown NSW 2042, Australia

^dFaculty of Medicine, UNSW Sydney, Wallace Wurth Building, 18 High Street, Kensington NSW 2052, Australia

Abstract

Background: Experience of childhood maltreatment (CM) is a risk factor for opioid use disorder (OUD). CM is also associated with comorbid mental disorders and poor treatment outcomes among people with OUD. To our knowledge, this is the first systematic review and meta-analysis to estimate the prevalence of CM among people with OUD.

Methods: We searched MEDLINE, EMBASE, and PsycINFO to identify observational studies that evaluated CM among people with OUD from January 1990 to June 2020. Prevalence of each CM type, sample characteristics, and methodological factors were extracted from each eligible study. Random-effects meta-analyses were used to pool prevalence estimates. Stratified meta-analyses were used to assess heterogeneity.

Results: Of the 6,438 publications identified, 113 studies reported quantitative CM data among people with OUD and 62 studies (k=62; N=21,871) were included in primary analyses. Among

Corresponding author: Thomas Santo, Jr., National Drug and Alcohol Research Centre, UNSW Sydney, 22-32 King Street, Randwick NSW 2031, Australia, t.santojr@unsw.edu.au, T: +61 2 9385 0333.

Contributors

Conflicts of Interest

LD has received investigator-initiated untied educational grants for studies of opioid medications in Australia from Indivior and Seqirus. GC has received investigator-initiated untied educational grants for studies of opioid medications in Australia from Indivior. GLDT has received a consultancy fee for methodological support from Amgen Inc. outside the scope of this work.

TS formed the scope of the review and search strategy with LD, NG, and GC. TS, NG, GC, LD, SC, and LT contributed to the screening, study selection, data extraction, and double-checking processes. TS and GL DT produced the methods and code for the data analysis. TS conceived the first draft of the manuscript with assistance from GC, NG, and LD. All authors contributed to multiple rounds of critical review by editing and revising the manuscript. All authors met criteria for authorship as recommended by ICMJE and approved the final version of the manuscript prior to submission.

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people with OUD, the estimated prevalence of sexual abuse was 41% (95% CI 36–47%; k=38) among women and 16% (95% CI 12–20%; k=25) among men. Among all people with OUD, prevalence estimates were 38% (95% CI 33–44%; k=48) for physical abuse, 43% (95% CI 38–49%; k=31) for emotional abuse, 38% (95% CI 30–46%; k=17) for physical neglect, and 42% (95% CI 32–51%; k=17) for emotional neglect. Sex, history of injecting drug use, recruitment methods, and method of assessing CM were associated with substantial heterogeneity.

Conclusions: People with OUD frequently report CM, supporting the need for trauma-informed interventions among this population. Future research should consider the impact of CM on OUD presentations and when assessment is appropriate, use of validated instruments.

Keywords

Opioid use disorders; Opioid dependence; Childhood maltreatment; Childhood abuse; Prevalence; Meta-analysis

1. Introduction

Globally, an estimated 40.5 million people live with opioid use disorder (OUD) (GBD 2017 causes of death collaborators, 2018). OUD is a chronic relapsing disorder that increases risk of blood borne virus transmission (Camacho et al., 1996), non-fatal overdose (Brady et al., 2017), and mortality (Degenhardt et al., 2019; Larney et al., 2020). The mortality rate of people with OUD is ten times that of comparable general population samples (Larney et al., 2020) and deaths attributable to OUD have increased exponentially over the past four decades (Hall et al., 2020). Risk factors for OUD include socioeconomic disadvantage (Needle et al., 1990), peer illicit substance use (Tucker et al., 2020), mental disorders (Martins et al., 2009), and the experience of childhood maltreatment (CM; Conroy et al., 2009).

CM is defined as the experience of sexual abuse, physical abuse, emotional abuse, or neglect of an individual under 18 years old (World Health Organization, 2006). Definitions for each type of CM are provided in Panel 1. Associations between CM and psychopathology related to substance use disorder are well-documented (Cicchetti and Handley, 2019). CM increases risk of behavioural disorders during childhood (Jones et al., 2004; Kendall-Tackett, 2004), youth mental health issues (Cicchetti and Valentino, 2006), and earlier onset of opioid and injection drug use (Kerr et al., 2009; Larance et al., 2018; Taplin et al., 2014). CM increases both risk of OUD (Conroy et al., 2009) and OUD severity. Among people with OUD, people who report experience of CM have higher rates of comorbid mental and substance use disorders (Darke, 2013; Maloney et al., 2007), engagement in risky injecting (McCurdy et al., 2010; Stein et al., 2017) and sexual behaviour (Engstrom et al., 2016), non-fatal overdose (Lake et al., 2015; Stein et al., 2017), and suicidal behaviour (Darke and Ross, 2002).

Although studies of people with OUD report higher rates of CM than control groups (Conroy et al., 2009) and general population samples (Afifi et al., 2012; Evans et al., 2020), estimates vary widely (Conroy et al., 2009; Kumar et al., 2016).

To our knowledge, there has not yet been a systematic review and meta-analysis of the prevalence of any type of CM among people with OUD. Systematic reviews and meta-analyses of prevalence of CM exist for community samples (Stoltenborgh et al., 2015) and certain clinical populations, for example, people with psychosis (Bonoldi et al., 2013). These reviews have found that definitions of each type of CM are subject to cultural-geographical interpretation (Elliott and Urquiza, 2006; Stoltenborgh et al., 2013b, 2015), evolve over time (Miller-Perrin and Perrin, 2013), and vary by the methodology and instrument used to assess the experience (Baldwin et al., 2019).

We aimed to:

- 1. Estimate the prevalence of each major type of CM among people with OUD;
- **2.** Examine sample characteristics and methodological factors associated with heterogeneity for each prevalence estimate;
- 3. Compare estimates of CM among people with OUD to global prevalence estimates of CM from a series of global reviews by Stoltenborgh et al (Stoltenborgh et al., 2015).

2. Methods

This review followed the PRISMA reporting guidelines (eAppendix 1; Moher, 2009) and was registered with PROSPERO (registration number: <u>CRD42018094623</u>).

2.1 Search strategy and study selection

Search terms were tailored for MEDLINE, Embase and PsycINFO databases using the OVID interface. Searches identified citations that reported any type of CM data among people with OUD published from January 1st, 1990 to June 18th, 2020. We aimed to estimate global prevalence of CM among people with OUD, therefore we did not restrict by language and used Google Translate to translate non-English studies. More details on the search strategy are provided in the supplementary material (eAppendix 2).

Study screening was conducted in Covidence, a web-based systematic review management tool (Veritas Health Innovation, 2016). After removing duplicates, we conducted title and abstract screening to identify observational studies of participants with OUD or proxy measures. Proxy measures for OUD included receiving treatment for opioid use (e.g. Opioid Agonist Therapy (OAT), detoxification, etc.), daily illicit opioid use, or frequent opioid use among people who inject drugs (PWID). Evaluation of CM was not considered at title and abstract screening stage to avoid selection bias. Relevant reviews were noted at title and abstract screening and citations were screened for eligibility. At the full-text screening stage, studies were excluded if the authors did not report any type of quantitative CM data among people with OUD (or proxy characteristics). Studies with less than 40 participants with OUD were also excluded. Full-text screening was conducted by two team members.

Authors were contacted if CM data and assessment of OUD (or proxy) were reported separately among the sample. Authors of citations that reported only continuous or

aggregate types of CM data and those that did not report sexual abuse by sex were also contacted. eAppendix 3 includes details regarding the study selection process.

2.2 Data extraction

Data were extracted into a Microsoft Access database and double-checked by a second team member. Conflicts were resolved by discussion and referred to a third reviewer if necessary. eAppendix 4 includes details on the variables extracted and double-checking process.

- **2.2.1 CM Prevalence**—The number and proportion of participants reporting each type of CM were extracted. Details on the instrument utilised and definition of maltreatment were collected. Details on the definition of CM included the instrument or scale utilised, cut-off used for continuous measurements, description of the event(s) or experience, and age cut-off for "childhood".
- **2.2.2 Study characteristics**—Sample characteristics, publication year, and recruitment method details were collected. Sample characteristics included age, proportion of men, proportion of people with a history of injecting drug use (IDU), description of opioid use patterns (i.e. details for 'proxy' OUD), childhood socio-economic status (SES) of the sample, history of parental SUD, and study location. Recruitment method details included setting and details on the participant inclusion and exclusion criteria. Recruitment setting of each study was stratified by four categories: sub-samples of general population studies, samples of people prescribed opioids for chronic non-cancer pain (CNCP), people with OUD recruited from OUD treatment settings (i.e. OAT, rehabilitation programs, supervised detoxification, and other in-patient services), and people recruited from non-treatment settings (i.e. community samples of PWID out of OAT, harm reduction services, and prisons).
- 2.2.3 Risk of bias and study quality—Study risk of bias was assessed by three domains: study inclusion or exclusion criteria, definition of OUD, and definition of CM, according to definitions described in Panel 1 (Leeb et al., 2008; World Health Organization, 2006). Risk of bias measures were adapted from published systematic reviews of people with OUD (Larney et al., 2020) and those with CM (Stoltenborgh et al., 2015). Risk of inclusion or exclusion criteria bias was a qualitative measure based on associations between CM and pre-defined risk of bias variables (e.g. studies that excluded participants with comorbid substance use or mental disorders were "high risk of underestimate"). These categorisations are not indicative of study quality, as the aims of included studies were not necessarily aligned with the aims of the current study. Each of the three domains was assessed by two independent reviewers and conflicts were resolved by a third party if necessary. Further details are provided in the supplementary material.

Statistical analyses were conducted in STATA 16.1 (StataCorp, 2017) using the *metaprop_one* command (Nyaga et al., 2014). Stratified random-effects meta-analyses were conducted by subgroup according to sex, history of IDU, recruitment setting, region, language of publication and language of survey administration. Random-effects meta-analyses were used as studies of retrospective CM data often report substantial heterogeneity

(Baldwin et al., 2019). Stratified meta-analyses and meta-regressions were repeated by sex given that sex is a confounding variable in the experience of CM (Stoltenborgh et al., 2011). Sensitivity analyses were conducted by excluding studies at high risk of any form of bias, studies of adolescents, studies requiring translation, and studies before 2010.

Meta-regression analyses were conducted using the *metareg* function (Harbord and Higgins, 2009) to determine associations with continuous study-level variables, such as average sample age, percentage of men in the samples, and publication year.

3. Results

3.1 Included studies

Of the 113 studies (k=113) eligible for inclusion, 62 were included in one of the six primary analyses. Of the studies omitted from the primary analyses, 15 reported only continuous CM data, 8 reported only aggregate types of CM (i.e. 'childhood adversity'), and 28 were secondary publications (i.e. participant overlap with primary studies). The PRISMA Flow diagram (Figure 1) provides further detail on the study inclusion and exclusion decisions. eAppendix 5 presents information on eligible studies excluded from the primary analyses.

Of the k=62 studies included in the primary analyses, there were samples from 18 different countries. Most studies recruited participants from North America (k=36; 58%) and evaluated CM among people in treatment for illicit OUD (e.g. heroin; k=45; 73%). Only one study evaluated history of CM among people with OUD who were prescribed opioids for CNCP. Over half of the included studies were published in 2010 or later (k=32; 52%) and 38 studies reported results among both men and women (61%). All estimates were self-report from observational studies, and most were published in English (94%). Table 1 presents detailed study-level descriptions.

3.2 Prevalence of CM

Studies of people with OUD most commonly report frequency of childhood sexual abuse (k=53; n=20,522). Among samples of people with OUD, 41% of women reported a history of childhood sexual abuse (95%CI: 36–47%; k=38; n=8,478), compared to 16% of men (95%CI: 12–20%; k=25; n=9,940). A history of childhood physical abuse was reported by 38% of all people with OUD (95%CI: 33–44%; k=48; n=18,324) and 43% reported a history of emotional abuse (95%CI: 38–49%; k=31; n=11,8030). Prevalence of physical neglect was reported in 17 studies (n=7,504; 38%, 95%CI: 30–46%) and prevalence of emotional neglect was reported in 17 studies (n=6,964; 42%, 95%CI: 32–51%) among people with OUD. Every pooled estimate of CM reported substantial heterogeneity (Table 2). eAppendix 7 presents forest plots by study for each analysis.

3.3 Sample characteristic associations

In stratified sub-analyses (Table 2), women reported significantly higher rates of childhood sexual and emotional abuse than men with OUD. Samples of people with a history of IDU and OUD had substantially higher rates of all types of CM, excluding emotional abuse, than samples with lower rates of history of IDU and OUD. Prevalence rates of sexual abuse

among men, emotional abuse, physical neglect, and emotional neglect varied substantially in stratified analyses of recruitment setting. Meta-regressions of average sample age and CM prevalence did not produce significant results, however, in stratified meta-analyses of age, studies of adolescents reported significantly lower rates of sexual abuse among women and men and emotional abuse among all people with OUD. Further information is presented in eAppendix 7 of the supplementary material. There was insufficient information to examine childhood SES and parental SUD as potential sources of heterogeneity.

3.4 Quality and risk of bias of included studies

Table 3 displays results from stratified analyses of each prevalence estimate according to risk of bias. Study inclusion or exclusion criteria was associated with substantial variance for prevalence estimates of sexual abuse among men and emotional abuse among women. The method of assessment of OUD (i.e. evaluation assessed via structured interviews versus proxy measures) did not affect prevalence estimates of any type of CM. Studies that used similar definitions to the "gold standard" WHO or CDC definitions reported significantly higher prevalence rates of sexual abuse among men, physical abuse, and physical neglect compared to less rigorous measures. eAppendix 6 provides further detail on risk of bias measures and classifications by study.

Publication year was associated with lower prevalence of physical and emotional neglect in meta-regressions. In stratified meta-analyses, studies published after 2010 reported higher rates of sexual abuse among men and significantly lower rates of emotional neglect among all people with OUD. Studies published in English reported higher rates of sexual abuse among men, physical neglect, and emotional neglect, however, only two non-English studies were included in these analyses. More detail is provided in eAppendix 7.

3.5 Sensitivity analyses

We performed sensitivity analyses by pooling CM estimates of studies with low risk of inclusion or exclusion criteria bias, studies excluding adolescents, studies with "gold-standard" definitions of CM, studies published in English, and studies published after 2010. Results from sensitivity analyses were similar to those presented in Table 1, however, I² values remained significant. We present the results of sensitivity analyses in eAppendix 8.

3.6 Comparison to community samples

Figure 2 presents prevalence estimates for each type of CM among people with OUD alongside global, self-report estimates of each CM type from a series of reviews by Stoltenborgh et al. (Stoltenborgh et al., 2015, 2013a, 2013b, 2012, 2011). Similar to the current review, studies included in the pooled estimates from Stoltenborgh et al were predominantly from North America (Stoltenborgh et al., 2015). Although it is difficult to formally compare the pooled estimates of CM prevalence from the different reviews, all pooled self-report estimates of CM prevalence are higher among people with OUD compared to community samples. Excluding emotional abuse, the 95% CIs of the two random-effects meta-analyses do not overlap.

4. Discussion

4.1 Major findings and implications

The experience of CM among people with OUD was common, ranging between 16–43% across different types of CM. With the exception of emotional abuse, people with OUD report significantly higher rates of all types of CM when compared to community samples (Stoltenborgh et al., 2015). Our findings provide further evidence for CM as a risk factor for OUD (Conroy et al., 2009; Darke, 2013; Rossow and Lauritzen, 2001). Children who are abused or neglected often experience adversity and stress, which can increase risk of OUD later in life (Cicchetti and Handley, 2019). Additionally, CM and OUD share common environmental risk factors, including low SES (Young et al., 2007; Zielinski and Bradshaw, 2006) and parental SUD (Chatterjee et al., 2018), contributing to the elevated prevalence rates of CM among people with OUD.

There is clearly an integral relationship between a history of CM and OUD in adolescence and adulthood. Findings from the current review provide further evidence that prevention efforts of OUD may consider the long-term impact of CM. Policies that aim to reduce the overall prevalence of CM and opioid use following experience of CM, particularly during adolescence (Davis et al., 2019a), could help to reduce the burden of OUD in the general population (Afifi et al., 2012). Findings from the current review also have implications for interventions for people with OUD. Evidence suggests that experience of CM may affect an individual's cognitions, beliefs, and feelings about their opioid use (Cicchetti and Handley, 2019). Additionally, there is strong evidence to support the relationship between CM and externalising disorders (Darke, 2011), which can play an important role in the frequency of opioid use (Cicchetti and Handley, 2019). The associations between CM and harms related to OUD, including overdose (Lake et al., 2015), alongside the extensive prevalence of CM among people with OUD reported in the current review, provides further evidence for interventions that aim to integrate CM experiences into OUD treatment.

Our findings underscore recommendations in clinical guidelines (Center for Substance Abuse Treatment, 2000) and research (Davis et al., 2019a, 2019b) for greater screening for CM among people in treatment for OUD. The high prevalence of CM within this population emphasises the importance of providing trauma-informed care for people with OUD, including the education of treatment providers around the sensitivities and complexities regarding disclosure of potentially traumatic experiences (Center for Substance Abuse Treatment, 2000; Elwyn and Smith, 2013). Trauma-informed care is critical for people with OUD because negative experiences with disclosure of victimisation is a significant treatment barrier, especially among women with OUD (Davis et al., 2019b; Green, 2006). Appropriate screening for experience of CM may also help to identify signs and symptoms of comorbid mental disorders, including depression (Center for Substance Abuse Treatment, 2000), post-traumatic stress disorder (Darke, 2013), and other anxiety-related disorders (Lawson et al., 2013). Since people with OUD and CM are more likely to present to treatment with comorbid mental disorders (Maloney et al., 2007); the findings of this review may have implications on the availability of treatment for comorbid mental disorders and OUD.

OAT is the most effective treatment for OUD (Degenhardt et al., 2019; Mattick et al., 2009; Sordo et al., 2017), including individuals with comorbid mental disorders (Trafton et al., 2006). However, people receiving OAT for OUD with a history of CM or comorbid mental disorders have higher levels of non-fatal overdose (Caudarella et al., 2016; Kang et al., 2002) and OAT treatment dropout (Hassan et al., 2017; Schiff et al., 2006), respectively. Adjunct psychosocial services have demonstrated mixed effectiveness in increasing retention in OAT and reducing psychological distress for people with OUD (Amato et al., 2011). There is some evidence that adjunct mental health and behavioural services may reduce symptoms of mental disorders among people with OUD (Fingleton et al., 2015; Hassan et al., 2017), including those who have experienced CM (Alexander, 2018). Examples of such services include psychopharmacological management of mental disorders (Hassan et al., 2017), cognitive behavioural therapy (Langdon et al., 2019; McHugh et al., 2017), and contingency management (Ainscough et al., 2017; Carroll and Weiss, 2017). Clinicians providing mental health treatment to people with OUD (Adams J.M. and Giroir B.P., 2019) may explore how experiences of CM can be integrated into comprehensive treatment plans for OUD and mental disorders (Davis et al., 2019b). Associations between inclusion or exclusion of participants with comorbid mental or substance use disorders and CM provides further evidence for the relationship between CM, polydrug use and mental health comorbidities. However, further research on the effective management of OUD among people with complex medical histories that include trauma and comorbid mental disorders is necessary.

Subgroup analyses of CM prevalence among different groups of people with OUD demonstrated that some groups of people with OUD have been exposed to higher rates of CM than others. Women with OUD reported significantly higher rates of childhood sexual abuse compared to men with OUD. Multiple studies included in our review report associations between CM and experience of revictimization and intimate partner violence among women with OUD (Engstrom et al., 2012, 2008; Green, 2006). People with a history of IDU and OUD, a clinical sample that commonly reports mental health comorbidities (Darke, 2011), reported elevated rates of multiple forms of CM. Finally, low rates of sexual abuse reported by adolescents are likely because these samples have not yet experienced the entire childhood period (Stoltenborgh et al., 2011) and fear of disclosure (Paine and Hansen, 2002) rather than true prevalence rates. Findings from the current review support further research on trauma-informed interventions (Alexander, 2018; Davis et al., 2019b) tailored to the needs and experiences of subgroups of people with OUD.

4.2 Limitations

Limitations of studies that assess CM prevalence among people with OUD are similar to limitations described in the wider literature on CM prevalence. For example, studies specific to people with OUD assess physical and sexual abuse most frequently (Stoltenborgh et al., 2015), despite evidence that all types of CM may have similar adverse health and social effects (Darke, 2011; Vachon et al., 2015). Several studies used questions that provided little detail on the experience of CM, which is critical to defining each CM type (Baldwin et al., 2019). The current review identified higher rates of CM in studies that used validated scales or definitions similar to the "gold standard" definitions for three of six pooled estimates,

which implies that questions that require participant interpretation may be underestimating the true prevalence of CM.

Additionally, as all studies reported retrospective CM data, issues with memory and recall bias need to be considered when interpreting CM data (Baldwin et al., 2019). There is some concern that retrospective measures may identify a different group of people than prospective measurements of CM, particularly for individuals with substance use disorders (Elwyn and Smith, 2013). Despite these issues, use of retrospective measures do not necessarily indicate poor validity (Baldwin et al., 2019).

One notable limitation of existing evidence concerns sparse evidence on people with OUD whose primary opioid of concern is a pharmaceutical opioid, primarily because studies reporting on CM in such populations did not assess OUD as required for this review (Bouvier et al., 2019; Merrick et al., 2020; Williams J.R. et al., 2020). Given the widespread concerns over OUD among people prescribed opioids, more evidence on this population is needed.

Finally, there was substantial heterogeneity for each CM estimate. Heterogeneity is a common limitation in meta-analyses of retrospective CM data (Baldwin et al., 2019; Stoltenborgh et al., 2015), and inherent of many epidemiological reviews. Despite the heterogeneity, patterns identified in community samples (Stoltenborgh et al., 2015) were also identified in the current study, demonstrating consistency with the broader literature related to CM. For example, emotional abuse was the most prevalent type of CM reported by people with OUD and in community samples (Stoltenborgh et al., 2015; Vachon et al., 2015). Due to limited data, we were unable to control for potential sources of heterogeneity including childhood SES and parental SUD. However, we accounted for inclusion or exclusion of participants with comorbid mental or substance use disorders, language and year of publication, measurement of CM type, and geographic location in sensitivity analyses. Sensitivity analyses did not produce significantly different results to the pooled estimates of all studies of people with OUD that assessed CM.

4.3 Conclusions

This is the first systematic review and meta-analysis of CM prevalence among people with OUD. People with OUD commonly experience CM, and the prevalence of CM history is much higher than community samples. As such, comorbid mental health and SUD treatment providers should ensure that trauma-informed care for people with OUD is accessible, particularly for women and people with a history of IDU. Research on interventions that mitigate the long-term health and social consequences of CM among people with OUD is critical, and when appropriate, researchers should utilise validated instruments to assess history of CM.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

 Childhood maltreatment (CM) is common among people with opioid use disorder (OUD)

- Women with OUD experience childhood sexual abuse (41%) more often than men (16%)
- People with OUD often report childhood physical abuse (43%) and neglect (40%)
- Most studies evaluate childhood sexual or physical abuse among OUD treatment samples
- "Gold standard" definitions of CM produce the highest prevalence rates of CM

Panel 1:

Definitions of each type of childhood maltreatment

Sexual abuse

An attempted or completed sexual act or exploitation of a child (World Health Organization, 2006). Perpetrators of sexual abuse may be adults or other children in positions of power over the victim (World Health Organization, 2006). Examples include penetrative sexual abuse, sexual contact, and noncontact sexual abuse (e.g. child pornography) (Leeb et al., 2008).

Physical abuse

An intentional physical act by a caregiver that causes, or potentially causes, harm to a child's health, survival, development, or dignity (World Health Organization, 2006). Examples include hitting, beating, kicking, and burning. Often inflicted with the object of punishment (World Health Organization, 2006) and recognised by physical injury (e.g. bruises) (Leeb et al., 2008).

Emotional abuse

An act or pattern of non-physical acts by a caregiver that have the potential to damage a child's mental, physical, or social health and development (World Health Organization, 2006). Acts of emotional abuse may convey rejection and produce a hostile environment (World Health Organization, 2006). Examples include belittling, blaming, threating, ridiculing, terrorizing, and isolating (Leeb et al., 2008; World Health Organization, 2006). Also described as 'psychological abuse' (Leeb et al., 2008).

Physical neglect

Failure of a caregiver to provide for the child's physical development and well-being, when they are in a position to do so (Leeb et al., 2008; World Health Organization, 2006). Examples include failure to provide adequate nutrition, appropriate clothing, hygiene, or shelter (Barnett et al., 1993; World Health Organization, 2006). The most commonly reported form of neglect (Stoltenborgh et al., 2015).

Emotional neglect

A caregiver's failure to seek care for mental, emotional, or behavioural health problems and/or the omission of adequate affection (Barnett et al., 1993; Leeb et al., 2008). Examples include ignoring a younger child's cry or an older child's attempt to interact (Barnett et al., 1993; Leeb et al., 2008).

Panel notes:

Definitions derived from the World Health Organization (WHO) and United States Centers for Disease Control and Prevention (CDC)

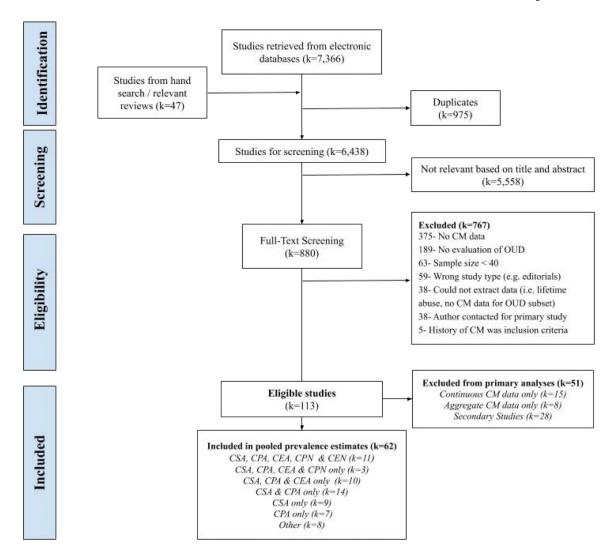


Figure 1: PRISMA flowchart for included studies in the current review

Notes: k=number of studies; OUD=Opioid Use Disorder; CM=Childhood Maltreatment;

CSA= Childhood Sexual Abuse, CPA= Childhood Physical Abuse, CEA= Childhood

Emotional Abuse, CPN=Childhood Physical Neglect, CEN=Childhood Emotional Neglect

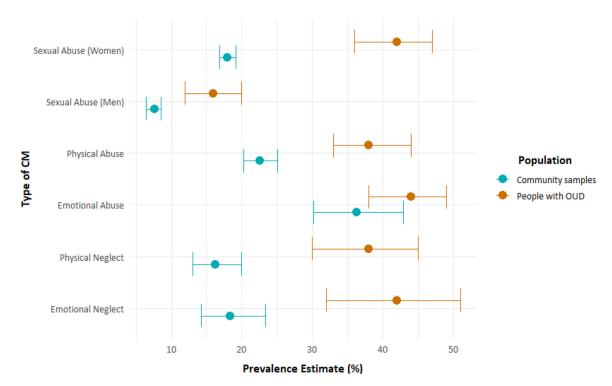


Figure 2: Prevalence estimates of childhood maltreatment (CM) among people with opioid use disorder (OUD) versus community samples

Table 1:

Description of studies included in primary analyses

Study Author, Year	Location	Total (N)	Men (n)	Women (n)	Setting	Description	OUD Definition	Inclusion / Exclusion Criteria	IDU Status	CSA- Women	CSA- Men	CPA	CEA	CPN	CEN
Afifi et al., 2012	USA (National)	700	350	268	General Population	Subset from representative population of USA adults. The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)-II.	DSM-4 OUD	Excl: Institutionalised	ı	40%	14%	38%	20%	43%	18%
Alexander, 2018 (Alexander et al., 2019)	Philadelphia, Pennsylvania, USA	175	1	175	OAT	Women receiving methadone with a child or pregnant enrolled in a mindfulness intervention trial.	OAT	Incl: Women with children < 3 years or pregnant		ı	ı	1	30%	ı	ı
Bailey et al., 1994	Norco, Califomia, USA	354	354		Prison	Men in the Civil Addict Program, a rehabilitation 'alternative' to prison for 'narcotic addicts'.	Other treatment	Excl: LTFU 24 years after recruitment	1	1	2%	1	1	1	1
Bartholomew et al., 2005	Texas, USA (One city)	137	1	137	OAT	Women in a nofee methadone program at a private clinic.	OAT	1	ı	39%	1	1		1	ı
Blatchley et al., 2000	Baltimore & Washington- DC, USA	248	1	248	OAT	Women in OAT with adolescent children. Children enrolled in a psycho-educational program.	OAT	Incl: Mothers with custody of children	1	32%	ı	1	ı	ı	ı
SAMHSA, 2009 (From Bohnert et al., 2011)	USA (National)	1275	892	393	OAT, Rehabilitation	Adults surveyed as part of the National Treatment Improvement Evaluation Study	Other treatment	Incl: Admitted to treatment for heroin or 'street' methadone use	75%- Ever	22%	5%	36%		1	

CEA CPN CEN						
		- 23% -		22% 43% 55%	43% %81	18%
Status Wollien				38%- Ever		
Exclusion Criteria				Excl: Only prescribed opioids for OAT or cancer pain		
Definition		OAT		ICD-10 Dependence		
,	(NTIES), a survey of publicly funded treatment centres in the USA	Consecutive patients admitted for methadone detoxification (n=19). Patients referred by GPs, addiction councillors, or	selfreferral.	Subset of people with pharmaceutical opioid dependence prescribed opioids for CNCP. Recruited from community pharmacies in Australia.	Subset of people with pharmaceutical opioid dependence prescribed opioids for CNCP. Recruited from community pharmacies in Australia. Subset of mothers from the DATOS study. Recruited from drug treatment programs, hospitals, and criminal justice programs.	Subset of people with with popolid dependence prescribed opioids for CNCP. Recruited from community pharmacies in Australia. Subset of mothers from the DATOS study. Recruited from computers from the programs. Recruited from drug treatment programs. Sexually active women enrolled in one of seven OAT programs participating in a mational multisite clinical trial for HIV/STD interventions.
0		OAT		Prescribed for CNCP	Prescribed for CNCP CNCP Rehabilitation, Detoxification	Prescribed for CNCP CNCP Rehabilitation, Detoxification
(n)		24		178	178	336
(n)		78		1 203		
(N)		Dublin, 52 Ireland		Australia (National)		onal) onal)
Study Author, Year		Browne et al., 1998		Campbell et al., 2016		6

CEN	1	40%	1		1	19%	
CPN	1	ı	ı	ı	1	54%	1
CEA	42%	45%	1	1	1	30%	1
CPA	61%	1	22%	38%	38%	38%	24%
CSA- Men	3%	1	7%		1	12%	
CSA- Women	30%	1	ı	31%	28%	36%	ı
DU Status	1	1	16%- Ever	1	1		ı
Inclusion / Exclusion Criteria	Incl: Adolescents only	1		Incl: 2 HIV- risk behaviours	Incl: Sexually active with men	Excl: Institutionalised	1
OUD Definition	DSM-4 OUD	OAT	Frequent Illicit Use	OAT	OAT	DSM-5 OUD	ICD-10 Dependence
Description	Subset of adolescents with OUD in Chestnut Health Systems, a substance use treatment provider in Illinois.	Medical chart review of a rural clinic providing OAT and counselling.	Male inmates in prison for drug related offenses. 98% past-month heroin use, mean use: 13 years.	Women recruited from OAT clinics in Harlem through outreach and staff referrals (1995– 96), 32% sex workers	Women recruited from OAT clinics in a sexual relationship. Subset of random sample from OAT sites in NYC.	Subset of participants with lifetime illicit OUD from a 2012–13 representative USA household survey (NESARC-III)	Sample of people with opioid
Setting	Rehabilitation, Detoxification	OAT	Prison	OAT	OAT	General Population	OAT
Women (n)	694	12	1	28-	390	388	71
Men (n)	1373	65	278	1		390	169
Total (N)	2067	87	278	280	390	778	240
Location	Illinois, USA	Tennessee, USA	Kandy, Sri Lanka	NYC, USA	NYC, USA	USA (National)	Warsaw, Poland
Study Author, Year	Davis et al., 2019a	Derefinko et al., 2019	Dissabandara et al., 2009	El-Bassel et al., 2001 (El-Bassel et al., 2000)	Engstrom et al., 2012 (El-Bassel N. et al., 2019; Engstrom et al., 2016; Panchanadeswaran et al., 2008; Rojas, 2006)	Evans et al., 2020 (Blanco C. et al., 2020; Hassan and Le Foll, 2019)	Fudalej et al., 2015

Study Author, Year	Location	Total (N)	Men (n)	Women (n)	Setting	Description	OUD Definition	Inclusion / Exclusion Criteria	IDU Status	CSA- Women	CSA- Men	CPA	CEA	CPN	CEN
						dependence from an OAT Clinic.									
Gardner S.M. et al., 2020	Columbus, Ohio, USA	40	16	24	Rehabilitation, Detoxification	Adolescents, young adults receiving outpatient treatment for OUD.	Any OUD	,				35%	57%	35%	43%
Garfield et al., 2017	Melbourne, Australia	121	87	34	OAT, Rehabilitation, Detoxification	People receiving OAT (n=90) and recently abstinent people (n=31) from residential services.	DSM-4 Dependence	Excl: Psychosis, bipolar, major depression	ı	1	28%	45%	20%	36%	49%
Gilbert et al., 1997 (Gilbert et al., 2000)	NYC, USA	151	1	151	OAT	Women enrolled in OAT programs in Bronx/ Harlem, recruited through staff referrals and printed announcements in 1994.	OAT		1	27%	1	39%	1		
Golden, 2018	Alaska, USA	43	1	43	OAT	Sample of 43 Alaskan women seeking opioid- treatment without PTSD from a dissertation.	OAT	Excl: Comorbid PTSD	ı	40%	1	30%	25%	1	ı
Grella et al., 1995	Los Angeles, Califomia, USA	209	1	209	Snowballing, Harm Reduction	Subset of women recruited to an OAT trial by outreach and snowballing. Targeted sex workers.	OAT	Excl: LTFU (13%)	100%- Ever	38%	1	40%	57%		1
Heffernan et al., 2000	NYC, USA	136	84	52	Hospital	Subset of opiate users (> daily use) from a sample of consecutive admissions to a psychiatric hospital.	Frequent Illicit Use		1	27%	1	46%	ı		ı
Hien et al., 2000	Long Island, NY, USA	96	47	49	OAT	People at a rehabilitation	OAT	1	ı	29%	4%	23%	1		

Study Author, Year	Location	Total (N)	Men (n)	Women (n)	Setting	Description	OUD Definition	Inclusion / Exclusion Criteria	IDU Status	CSA- Women	CSA- Men	CPA	CEA	CPN	CEN
						centre seeking methadone for OUD.									
Isralowitz et al., 2002; Isralowitz and Bar Hamburger, 2002	Negev, Israel	152	86	54	OAT, Detoxification	Israeli-born patients in an outpatient drug treatment program.	OAT		ı	26%	%5	32%	1		1
Isralowitz, 2001	Negev, Israel	154	93	61	OAT, Detoxification	Russia/Ukraine- born patients in an outpatient drug treatment program.	OAT, other treatment		ı	43%	12%	40%	1		1
Kaboski, 2013	Chicago, Illinois, USA	205	ı	205	OAT	Mothers of infants and preschoolers at one of seven public OAT clinics.	OAT		1	35%	ı	33%	1	1	1
Kang et al., 2002	NYC, USA	432	294	138	Snowballing, Harm Reduction	Participants recruited from a list of OAT treatment dropouts and by local outreach workers from 1997–1999.	OAT	Incl: Only people who left OAT	1	48%	31%	%09	58%	%99	
Khosravani et al., 2019 (Ghorbani et al., 2019)	Tehran, Iran	350	350	1	Detoxification	Men with heroin dependence at a treatment centre in Tehran (N=450), Survey 2 weeks post detoxification.	DSM-4 Heroin Dependence	Excl: Health comorbidity, refusal, women	50%- Ever				74%	1	29%
Koyuncu et al., 2003	Istanbul, Turkey	100	68	=	Detoxification	People with heroin dependence at an inpatient hospital detoxification centre.	DSM-4 Heroin Dependence	Excl: Comorbid psychiatric diagnosis			1	%65	62%	1	ı
Kumar et al., 2016	Little Rock, Arkansas, USA	113	63	50	OAT	Chart review of adults receiving buprenorphine at an outpatient clinic.	OAT	1	27%- Ever	16%	18%	19%	25%	23%	18%
Lake et al., 2015 (Braitstein et al.,	Vancouver, Canada	2393	1489	903	Snowballing, Harm Reduction	People with a history of OAT or daily illicit	OAT, Frequent Illicit Use	1	100%- Ever	46%	21%	36%	51%	32%	53%

CEA CPN CEN		15%			47% 64% 79%	- 64%	58%	58%
CPA		18%						
				1		27%		
Status Women		,		2 25%	l o	1.0)		
		100%- Ever		100%- Past 2 days				
Exclusion Criteria				Incl: Current IDU Excl: LTFU at 5 months (44%)	Incl: Current IDU Excl: LTFU at 5 months (44%) Excl: Past month drug treatment	Incl: Current IDU Excl: LTFU at 5 months (44%) Excl: Past month drug treatment treatment Excl: Active psychosis	Incl: Current IDU Excl: LTFU at 5 months (44%) Excl: Past month drug treatment Excl: Active psychosis Excl: Other illicit substance use, Alcohol SUD, psychosis, trauma	
Definition		Frequent Illicit Use		Frequent Illicit Use				
	opioid use from the VIDUS/ ARYS/ACCESS cohorts.	People with past year IDU recruited from 3 areas in Marseille. > 82% on OAT and injecting duration 10	years.	Women injected recently and had sex in the month prior. Of 559 screened, 249 remained at 5-month FU.	Women injected recently and had sex in the month prior. Of 559 screened, 249 remained at 5-month FU. Subset of participants that primarily use opioids from women recruited to an AIDS prevention program.	Women injected recently and had sex in the month prior. Of 559 screened, 249 remained at 5-month FU. Subset of participants that primarily use opioids from women recruited to an AIDS prevention prevention prevention. Participants with lifetime SUD, identified opioids as primary substance. 29% had received OAT.	Women injected recently and had sex in the month prior. Of 559 screened, 249 remained at 5-month FU. Subset of participants that participants that primarily use opioids from women recruited to an AIDS prevention program. Participants with lifetime SUD, identified opioids as primary, substance, 29% had received OAT. Outpatient attendees at a derug treatment attendees at a derug treatment service without mental or SUD comorbidities.	Women injected recently and had sex in the month prior. Of 559 screened, 249 remained at 5-month FU. Subset of participants that participants that primarily use opioids from women recruited to an AIDS prevention prevention prevention prevention prevention prevention program. Participants with lifetime SUD, identified on AIDS prevention prevention prevention prevention prevention prevention as a primary substance. 29% had received OAT. Outpatient attendees at a drug treatment service without mental or SUD comorbidities. People who visited one of four drug treatment centres
		Snowballing, Harm Reduction		Snowballing, Harm Reduction	Snowballing, Harm Reduction Snowballing, Harm Reduction	Snowballing, Harm Reduction Snowballing, Harm Reduction Snowballing, Harm Reduction	Snowballing, Harm Reduction Reduction Reduction Reduction Reduction Rebabilitation, Detoxification	Snowballing, Harm Reduction Harm Reduction Harm Reduction Reduction Rebabilitation, Detoxification Rehabilitation,
(n)		1		169	80	80 80	30 80 80	33 30 80 19
		Ξ						
		Ξ		, 169				
		Marseille, France		Dar es Salaam, Tanzania	Dar es Salaam, Tanzania San Antonio, Texas, USA	Dar es Salaam, Tanzania San Antonio, Texas, USA Northern New England, USA	Dar es Salaam, Tanzania San Antonio, Texas, USA Texas, USA Northern New England, USA Birmingham, United Kingdom	Dar es Salaam, Tanzania San Antonio, Texas, USA Northern New England, USA Birmingham, United Kingdom
Year	2003; Cheng et al., 2018)	Lovell, 2002		McCurdy et al., 2010		:	;	

		1	43%		
	1	ı	40%	ı	
	1	1	70%	ı	
	25%	ı	48%	1	%65
		34%	29%	24%	
	1	1	67%	%68	72%
		1	100%- Ever	1	
	Incl: Moderateheavy alcohol use	Incl: OAT > 3 months; Past year sexual partner	Incl: 5 years use, 1 OAT attempt	Incl: Daily heroin use for 1 year Excl: LTFU (19%)	Incl: Past 6- month
	OAT	OAT	OAT	DSM-4 OUD	DSM-4 Dependence
Twin Register. Participants with OUD born 1964—71. Substance use resembled general population.	People in OAT with moderate-heavy alcohol use at five sites promoting HAV/HBV vaccinations.	Males in heterosexual relationships in OAT. Parent study was a sample of males enrolled in at seven sites.	Participants used opioids chronically from GeMa trial (5 years use, chronic use 6 months prior to survey, 1 OAT attempt). Recruited through snowballing and community.	People at OAT clinic and the CSA prevalence determined. Of initial group, 79 patients after LTFU. Next wave, invited all women in OAT to participate: 46 agreed.	Women with > sub-threshold PTSD from six
	OAT	OAT	Snowballing, Harm Reduction	OAT	Rehabilitation, Detoxification
	104		96	76	137
	152	356	96	49	
	256	356	172	125	137
	Los Angeles, Califomia, USA	NYC, USA	Vancouver, Canada	Tel Aviv, Israel	USA (Multisite)
	Nyamathi et al., 2010	Orellana et al., 2014 (Orellana, 2010)	Palis et al., 2016	Peles et al., 2016 (Peles et al., 2012)	Pinto et al., 2011
	14 1 /-	Twin Register. Participants with OUD born 1964— 71. Substance use resembled general population. People in OAT with moderate- heavy alcohol USA Los Angeles, California, 256 152 104 OAT use at five sites of T Moderateheavy 25% Promoting HAV/HBV vaccinations.	Twin Register. Participants with OUD born 1964- 71. Substance 21. Substance 22. Subs	Purple Register. Purple Register. Purple Register. Purple Register. Purple Register.	The Neglect The Neglect

Study Author, Year	Location	Total (N)	Men (n)	Women (n)	Setting	Description	OUD Definition	Inclusion / Exclusion Criteria	IDU Status	CSA- Women	CSA- Men	CPA	CEA	CPN	CEN
						community- based treatment sites in different US regions from Women and Trauma Study (WTS).		substance use; DSM-4 PTSD							
Plotzker et al., 2007	Philadelphia, Pennsylvania, USA	113	ı	113	Snowballing, Harm Reduction	Women recruited from two needle and syringe programs.	Frequent Illicit Use	ı	100%- Past 3 month	%95	ı	%89		1	1
Rodriguez et al., 2017	Tulsa, Oklahoma, USA	48	1		OAT	Receiving buprenorphine at an addiction centre medicine practice. Patients approached during regular clinic visit with their physician.	OAT		1			1	52%	1	48%
Rovis D. et al., 2019	Rijeka, Croatia, Koper, Slovenia	167	129	38	Rehabilitation, Detoxification	Participants recruited from two in-treatment Rehab. Programs in Croatia and Slovenia. OAT (86%)	DSM-5 OUD				%9	13%	12%	%8	7%
Sansone et al., 2009	Dayton, Ohio, USA	113	61	52	Rehabilitation, Detoxification	Participants presented for admission to sub-acute detoxification detoxification that uses buprenorphine.	Other Treatment	Excl: Withdrawal or psychosis	ı	ı		40%	%09	23%	1
Santos Goni et al., 2010	Castilla & León, Spain	50	1	50	Rehabilitation, Detoxification	Subset of women with opiate dependence from a sample of women at 27 residential centres.	ICD-10 Dependence	Excl: Severe depression, psychosis		33% *	ı	47%	%65	1	ı
Sartor et al., 2014	USA (Multisite)	3513	2178	1335	General Population	Sub-set of clinical and general community samples of people with OUD. Recruited	DSM-4 Dependence	Excl: Major psychotic illness		32%	11%	13%		1	

	_					
CEN		ı	61%	1		42%
CPN		ı	37%		42%	18%
CEA		ı	53%	20%	1	%84
CPA		ı	62%	30%	28%	36%
CSA- Men		ı	36%	1	30%	11%
CSA- Women		72%	71%	39%		42%
DU Status		ı	1	1		
Inclusion / Exclusion Criteria		Excl: Participant, social worker refused (25%)		Incl: Pregnant	Excl: < 3 weeks in program -	
OUD Definition		OAT	OAT	OAT, other treatment	OAT	Other
Description	by family pairs from five east coast university medical schools for case-control studies.	Women from methadone clinics in Israel were approached for their consent to participate.	Participants from CATS Study were receiving OAT for heroin dependence at 34 of 35 OAT clinics in Sydney.	Pregnant women entered unit to receive methadone- supervised detoxification or OAT.	Receiving treatment in main heroin recovery program of northern Israel. Detoxification (n=49), outpatient treatment (n=48), OAT (n=52).	Sample of patients seeking and admitted to inpatient opioid detoxification at 24-hour medically supervised detoxification facility.
Setting		OAT	OAT	Rehabilitation, Detoxification	OAT, Rehabilitation, Detoxification	Rehabilitation, Detoxification
Women (n)		144	599	89	≣	131
Men (n)		1	914	1	1	326
Total (N)		144	1513	89	149	457
Location		Israel (Multisite)	Sydney, NSW, Australia	Lexington, Kentucky, USA	Northern Israel	Fall River, Massachusetts, USA
Study Author, Year		Schiff et al., 2010 (Schiff et al., 2006, 2002)	Shand et al., 2011 (Conroy et al., 2009; Larance et al., 2018; Lamey et al., 2016; Maloney et al., 2010, 2009, 2007; Shand et al., 2010)	Shannon, 2007	Somer et al., 2010 (Somer, 2003)	Stein et al., 2017

Study Author, Year	Location	Total (N)	Men (n)	Women (n)	Setting	Description	OUD Definition	Inclusion / Exclusion Criteria	IDU Status	CSA- Women	CSA- Men	CPA	CEA	CPN	CEN
Teegen and Zumbeck, 2000	Northern Germany	122	96	26	Rehabilitation, Detoxification	Participants were recruited from 10 addiction therapy facilities, all of whom use opioids. 53% in OAT.	Other treatment		1		%4	16%	ı	T	ı
Vogel et al., 2011	Basel, Switzerland	193	128	65	OAT	People from OAT, diacetylmorphine outpatient treatment centres.	OAT	ı	1	40%	20%	31%	34%	40%	41%
Walker et al., 2014	Dallas, Texas	72	25	47	Rehabilitation, Detoxification	Adolescents with "cheese" heroin SUD from residential drug remement or juvenile detention programs.	Other treatment	Excl: Psychosis, withdrawal, suicidal/ homicidal ideation	13%- Ever	17%		17%	11%	ı	
Wang et al., 2010	Shanghai, China	341	123	218	Rehabilitation, Detoxification	Participants were currently injecting and recruited through convenience sampling from three government operated drug rehabilitation facilities.	DSM-4 Heroin Dependence	Excl: Cardiovascular, ineurological issues	100%- Past Month	29%	20%	26%	36%		
Weiss et al., 2019	Tel Aviv, Israel	51	33	18	OAT	Patients at an OAT clinic. All clients approached (81% participation).	OAT	Incl: OAT > 3 months	63% - Ever		1	53%		1	
Wickersham et al., 2016	Kuala Lumpur, Malaysia	09	1	09	Snowballing, Harm Reduction	Sub-set of women in OAT recruited from community sites and shelters.	ОАТ	Incl: Past year other illicit substance use	1	27%	ı	47%	1		

Table Notes: Secondary studies cited in parentheses; Abbreviations: OAT=Opioid Agonist Therapy, IDU=Injecting Drug Use, OUD=Opioid Use Disorder; CM=Childhood Maltreatment, CSA= Childhood Sexual Abuse, CPA= Childhood Physical Abuse, CPA= Childhood Physical Neglect, CEN=Childhood Emotional Neglect, LTFU: Lost to follow-up, PTSD: posttraumatic stress disorder, Incl= Key inclusion criteria for study, Excl= Key exclusion criteria for study

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Table 2:

Pooled prevalence estimates for each type of childhood maltreatment in people with opioid use disorder stratified by sample characteristics

	Sexual	Sexual Abuse (Women)	len)	Sexual	ual Abuse (Men)	7	Phys	Physical Abuse		Emoti	Emotional Abuse		Physi	Physical Neglect		Emoti	Emotional Neglect	
Strata	Study (k) (Total N)	Estimate (95%CI) p-value	I ₂	Study (k) (Total	Estimate (95%CI) p-value	12	Study (k) (Total	Estimate (95%CI) p-value	12	Study (k) (Total N)	Estimate (95%CI) p-value	12	Study (k) (Total N)	Estimate (95%CI) p-value	Γ_2	Study (k) (Total N)	Estimate (95%CI) p-value	12
Community Sample Estimates (95%CI)	k=193	18 (16– 20)	1	k=104	8 (6–9)		k=157	23 (20– 26)	1	k=42	36 (28– 45)		k=13	16 (12– 22)	1	k=18	18 (13– 25)	
Sex					,													
Total		ı	1	ı		1	48 (18324)	38 (33– 44)	66	33 (11030)	43 (38– 49)	26	17 (7504)	38 (30– 45)	96	17 (6964)	42 (32– 51)	66
		p<0.01*						p=0.40			p=0.04*			p=0.38			p=0.29	
Men		1	ı	25 (9940)	16 (12– 20)	97	23 (9438)	36 (27– 46)	66	15 (5847)	39 (31– 48)	86	12 (4121)	34 (25– 44)	86	11 (3960)	38 (24– 51)	66
Women	38 (8478)	41 (36– 47)	96	i	1		35 (7418)	41 (35– 47)	6	19 (3735)	50 (44- 57)	94	13 (2793)	40 (32– 49)	95	11 (2458)	45 (32– 57)	86
Lifetime injecting history of sample		p=0.01*			p=0.01*			p<0.01*			p=0.68			p<0.01*			p<0.01*	
<100%	4 (658)	25 (12– 39)	92	4 (1429)	12 (6–18)	92	7 (2426)	30 (23– 38)	93	3 (915)	41 (14– 68)	66	2 (513)	18 (15– 21)		2 (463)	44 (40– 49)	
100%	8 (2222)	49 (36– 61)	97	4 (2443)	27 (17– 36)	95	9 (4884)	51 (40– 63)	86	7 (4423)	47 (39– 56)	96	4 (3792)	40 (32– 47)	95	5 (3775)	58 (50– 67)	95
Recruitment Setting		p=0.56			p=0.56			p=0.12			p<0.01*			p<0.01*			p<0.01*	
General population subsample	3 (699)	41 (33– 49)	1	2 (740)	13 (11– 15)	1	2 (1397)	38 (36– 41)	1	2 (1128)	26 (23– 29)	1	2 (1397)	49 (46– 52)	1	2 (1397)	19 (17– 21)	
CNCP patients with OUD	1 (178)	46 (39– 54)	•	1 (203)	22 (16– 28)		1 (381)	43 (38– 48)		1 (380)	55 (50– 60)	1	1 (400)	17 (13–21)	1	1	1	1
OUD treatment settings ²	26 (5971)	39 (32– 47)	97	17 (7120)	14 (10– 18)	86	34 (12780)	35 (28– 42)	66	21 (6308)	42 (36– 49)	96	9 (2783)	30 (20– 39)	96	11 (3092)	41 (28– 54)	86

Sex	Sexual Abuse (Women)	7omen)	_	Sexual	Abuse (Men		Phys	Physical Abuse		Emot	Emotional Abuse		Phys	Physical Neglect		Emot	Emotional Neglec		
Study (k) (Total N)	y Estimate (95%CI) al p-value	.T)	2 2	Study (k) (Total N)	Estimate (95%CI) p-value	\mathbf{I}_2	Study (k) (Total N)	Estimate (95%CI) p-value	12	Study (k) (Total N)	Estimate (95%CI) p-value	I_2	Study (k) (Total N)	Estimate (95%CI) p-value	Γ_2	Study (k) (Total N)	Estimate (95%CI) p-value	Γ^2	
8 (1630)	46 (37– 0) 54)	6)	5 1877)	22 (12– 32)	95	11 (3766)	47 (36– 58)	86	7 (3214)	50 (40– 60)	95	5 (2924)	52 (34– 70)	86	4 (2475)	56 (44– 68)	92	

Table Notes:

Abbreviations:

 $[\]stackrel{*}{\sim}$ =Significant (<0.05) results subgroup comparison from stratified meta-analysis;

 $^{^{}I}$ Estimates from series of meta-analyses by Stoltenborgh et al. I ;

 $^{^2}$ Treatment settings include Opioid Agonist Treatment (OAT), rehabilitation, and other inpatient services;

³ Non-Treatment Settings include harm reduction services, community samples of people who inject drugs, and prisons; k=number of studies, CNCP=Chronic Non-Cancer Pain

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Table 3:

Pooled prevalence estimates for each type of childhood maltreatment in people with opioid use disorder stratified by risk of bias measures

	Sexual ,	Sexual Abuse (Women)	ten)	Sexual	Sexual Abuse (Men)	2	Phys	Physical Abuse		Emol	Emotional Abuse			Physical Neglect		Emoti	Emotional Neglect	
Strata	Study (k) (Total N)	Estimate (95%CI) p-value	12	Study (k) (Total N)	Estimate (95%CI) p-value	I_2	Study (k) (Total N)	Estimate (95%CI) p-value	I_2	Study (k) (Total N)	Estimate (95%CI) p-value	\mathbf{I}_2	Study (k) (Total N)	Estimate (95%CI) p-value	12	Study (k) (Total	Estimate (95%CI) p-value	72
Inclusion/ Exclusion criteria ¹		p=0.17			p<0.01*			p=0.09			p=0.01*			p=0.35			p=0.10	
Low risk of inclusion/ exclusion criteria bias	26 (5637)	39 (32– 46)	97	19 (6399)	15 (11– 19)	96	31 (11756)	35 (28– 41)	86	20 (5554)	40 (32– 48)	97	12 (4543)	34 (25– 43)	86	13 (4452)	37 (25– 49)	66
High risk of underestimate	4 (921)	40 (16– 64)	76	3 (1805)	9 (3–15)		8 (2597)	40 (26– 55)	96	6 (2437)	43 (29– 56)	95	1 (121)	36 (27– 45)	1	1 (121)	49 (40– 58)	1
High risk of overestimate	8 (1920)	50 (41– 59)	94	3 (1736)	26 (19– 34)	1	9 (3971)	49 (38– 60)	86	5 (3039)	57 (50– 64)	88	4 (2840)	50 (30– 71)	66	3 (2391)	58 (43– 73)	
OUD evaluation		b=0.09			p=0.66			p=0.42			p=0.99			p=1.00			p=0.37	
Structured evaluation (DSM, ICD)	10 (3634)	50 (37– 63)	86	10 (5354)	17 (10–24)	86	15 (9485)	42 (29– 55)	66	12 (6219)	40 (32– 49)	86	8 (3667)	38 (26– 50)	86	7 (3405)	36 (18– 55)	66
Proxy measure (i.e. OAT, ~daily use, etc.)	28 (4844)	38 (33– 43)	94	15 (4586)	15 (10-20)	96	33 (8839)	36 (32– 41)	95	19 (4811)	43 (36– 50)	95	9 (3837)	38 (27– 49)	86	10 (3559)	45 (37– 53)	94
CM Definition		p=0.18			p<0.01*			p=0.04*			p=0.60			p<0.01*			1	
Similar to WHO or CDC Definitions ²	16 (3774)	45 (36– 59)	97	16 (6038)	21 (14–27)	86	25 (11298)	44 (38– 49)	86	22 (8237)	43 (37– 50)	97	15 (6991)	43 (35– 50)	76	17 (6694)	42 (32– 51)	66
Specific (e.g. 'severe', <15 year, etc.)	13 (3782)	35 (29– 41)	93	4 (3183)	7 (3–10)	93	8 (4498)	30 (19– 41)	86	8 (2729)	43 (30– 55)	96	1 (113)	23 (16– 32)	1	1	1	ı
Non-specific (e.g. were you abused?)	9 (922)	43 (30– 56)	95	5 (719)	10 (4–15)	85	15 (2044)	34 (27– 40)	91	1 (64)	50 (37– 63)		1 (400)	17 (13–21)	1	1	1	,

Table Notes:

 $I_{\rm Purther}$ information on each study provided in eAppendix 6; :

²See Panel 1 for additional details; **Abbreviations**: k=number of studies, CI= Confidence Intervals, OUD= Opioid Use Disorder, DSM=Diagnostic and Statistical Manual of Mental Disorders, OAT= Opioid Agonist Therapy, ICD=International Classification of Diseases, WHO=World Health Organization, CDC=Centers for Disease Control and Prevention

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