

## Supplementary Materials

### **How the Review Was Conducted**

We began this review with a systematic literature search to supplement the literature library collected by one of the authors (MHT) over the past 20 years. We examined Pubmed for key words or abstract terms of child abuse, maltreatment, early life stress, sexual abuse, physical abuse, witnessing domestic violence crossed with psychiatric illness, mental illness, depression, PTSD, substance abuse, bipolar disorder, anxiety disorders, panic disorder, generalized anxiety disorder, specific phobias, social phobia, eating disorders, personality disorders, borderline personality disorder, antisocial personality disorder and psychosis. The primary focus was on the last 5 years. Based on the large and varied number of references retrieved we then selected criteria for inclusion in meta-analyses.

First, we limited the exposure criteria to either childhood sexual abuse, as a particularly potent and well-studied form of maltreatment, or a composite exposure measure, such as an ACE score, that included CSA. Second, we required that the sample be large (N greater than 800 for cross-sectional studies, N greater than 500 for longitudinal studies). Third, we required that the subjects were drawn from a non-psychiatric sample. Fourth, that the study was published in English, and finally that the study provided odds ratios with confidence intervals, or sufficient data to calculate these parameters for inclusion in

the meta-analysis statistics. When these parameters were set we extended the search backwards, and included additional studies found in citations from the collected articles. Initially we covered the entire array of DSM diagnosis reported to be associated with childhood abuse. Then, upon the recommendation of a reviewer we focused on the array of common and moderately heritable disorders selected (major depressive disorder, substance abuse, anxiety disorders and posttraumatic stress). Key aspects of the selected studies are summarized in Supplementary Tables 1-3 for depression, PTSD and anxiety disorders and drug and alcohol use disorders, respectively.

Altogether, we identified 36 cross-sectional studies (N= 155,837 excluding overlap between studies examining the same sample) that met criteria for inclusion in the major depression category (Table S1). Similarly, 25 cross-sectional studies met criteria in the PTSD and anxiety disorder category (N= 104,322) (Table S2), and 37 cross-sectional studies (N= 244,887) met criteria for inclusion in drug or alcohol use and abuse category (Table S3).

The number of prospective studies was substantially smaller, though the study by Spataro (173) markedly increased the recorded sample size. This study assessed risk by examining confirmed cases of sexual abuse through the Victorian (Australia) Institute of Forensic Medicine records, which rendered all such decisions, and subsequent psychiatric diagnoses listed in the Victorian Psychiatric Case Registrar that recorded all contacts with public in-patient and community mental health services and contained over 500,000 names. This information was coupled with Australian Bureau of Statistics

records for this region over the same time period to provide a population-based prospective assessment of risk for 3,141,357 individuals.

Altogether, 8 prospective studies (N = 3,149,066) met criteria for depression, 5 met criteria (N = 9,014) for drug or alcohol abuse, and 7 met criteria (N = 3,151,351) for posttraumatic stress or anxiety disorders.

We created Forest plots to compare results from studies providing adjusted and unadjusted odds ratios. As the paper further progressed, we were encouraged to focus on the emerging theory of ecophenotypes and to consider placing supporting statistical tables in an on-line supplement. The final literature review that the submission was based upon was current as of April 1, 2013.

We also crossed the array of maltreatment descriptors with imaging, MRI, hippocampus, corpus callosum, amygdala, cortex, gray matter, white matter. Additional searches were run crossing the array of maltreatment categories with family history and with treatment. These reviews covered all years.

### **Meta-Analyses**

Odds ratios were analyzed using mixed-effect models with both fixed effect and random effect outcomes. Fixed effect outcomes provide composite results specific to the selected group of studies and assume that the studies are assessing the same effect. Random effect models provide composite results that assume heterogeneity between

studies, which is certainly the case as the studies differed in severity of exposure, outcome measures and methodology. There is considerable debate between statisticians on which is the better model to use as they both involve tradeoffs. Hence, results from both models are presented. For many of the comparisons the results are nearly identical suggesting that statistical heterogeneity was not a serious problem in these cases. Results differed most strongly in the analysis of prospective studies on alcohol use and abuse, which is understandable given the small number of studies available and marked differences in effect measures for Widom et al (174) versus Cutajar et al (175). Cutajar et al (175) is perhaps the more reliable given the much greater number of exposed cases (N = 2,759 versus N = 85) with confirmed childhood sexual abuse.

Studies often provided results broken down by exposure severity levels (e.g., non-consensual touch versus forced intercourse). Odds ratios were pooled across severity levels to provide an effect measure commensurate with the broadest definition of sexual abuse. If different types of exposure were reported we selected the category most specifically related to sexual abuse (e.g., presence or absence of sexual abuse versus ACE score). If multiple outcomes were presented we included the most serious result in the meta-analysis (e.g., drug abuse versus use of illicit drugs). For the Forest plots we included up to 2 outcomes, if one represented a current outcome measure (color-coded red) and the other a lifetime outcome (color-coded blue) on Figure 1. Odds ratios for these two outcomes within each study were pooled for the meta-analysis, and only included once in the sample size determination. Separate results for males and

females were also pooled for the sake of simplicity.

As illustrated in Figure 1A we identified 13 large N cross-sectional studies that provided unadjusted odds ratios for the association between childhood sexual abuse or composite exposure measures and risk for various types of depression-related outcomes. The fixed and random effect models provided very similar composite odds ratio estimates of 2.6 and 2.7 respectively. The 95% confidence intervals were slightly larger for the random effects model. Estimated odds were lower, though still highly significant, in the group of studies that adjusted odds ratios for additional risk factors such as sociodemographics and family history. These 23 studies provided a composite estimated odds ratio of 2.1 or 2.2, with 95% confidence intervals of 2.0 – 2.5 for the random effects model. Similarly, analysis of the 8 prospective studies provided an estimated composite odds ratio of 2.1 (95% CI, 1.7 – 2.6, random effects model). Hence, meta-analysis shows that broadly-defined childhood sexual abuse doubles the odds of developing a depressive disorder outcome. While some of the individual studies showed a non-significant difference (as indicated by a lower 95% confidence interval less than 1), the overall results were highly significant and no study showed a significant protective effect (i.e., upper 95% confidence interval less than 1).

Figures 1B and 1C provide the Forest Plot for the association between exposure and odds of developing PTSD and other anxiety disorders. In this case the studies were delineated by the nature of the reported outcome, and adjusted, unadjusted and prospective studies within a diagnostic category were combined into a single composite

measure. We identified 14 studies that assessed the association between exposure and risk for current or lifetime PTSD. These studies provided a composite odds ratio of 4.4 for both the fixed and random effects models. Confidence intervals were wider for the random effects model and ranged from 3.6 – 5.2. Overall, exposure to sexual abuse broadly defined (or multiple exposure measure including sexual abuse) more than quadrupled the odds of developing posttraumatic stress disorder, and these were the highest odds for the different outcomes we examined.

Altogether, 17 studies reported the association between exposure to childhood sexual abuse and development of any anxiety disorder, or a suprathreshold anxiety score on a rating instrument (Fig 1C). The composite random effects odd ratio was 2.4 (95% CI 2.1 – 2.8). Random effects odds ratios were 1.8 (95% CI 1.3–2.5) for generalized anxiety disorder, 2.4 (95% CI 1.7-3.5) for panic disorder and 1.9 (95% CI 1.3–2.9) for simple or social phobias.

The Forest Plot for alcohol use disorders is illustrated in Figure 1D. Reported outcomes included heavy episodic (binge) drinking, alcohol abuse and dependence. Altogether, analyzable data was extracted from 8 large N cross-sectional studies with unadjusted odds ratios, 20 cross-sectional studies with adjusted odds ratios, and 3 prospective studies. Random effect odds ratios and 95% confidence intervals were 1.9 (1.5–2.3), 1.7 (1.5–1.9) and 2.0 (0.8–4.9), respectively.

Figure 1E shows the Forest Plot for the association between exposure and risk for

substance use disorders (excluding alcohol abuse). We identified 10 cross-sectional studies that provided unadjusted odds ratios, 16 cross-sectional studies with adjusted odds ratios and 4 prospective studies. Most of the studies reporting odds ratios for drug use and abuse had also reported odds ratios for alcohol use disorders. Random effect odds ratios and 95% confidence intervals were 2.8 (1.9–4.2), 2.0 (1.8–2.4) and 2.3 (1.3–4.3), respectively.

### **Maltreatment Ecophenotypes Versus Developmental Trauma Disorder**

Developmental trauma disorder has been advanced as an integrated and developmentally-sensitive strategy for the diagnosis and treatment of individuals with maltreatment-related psychopathology (52). This approach emerged from Judy Herman's groundbreaking work on the long-lasting effects of exposure to prolonged interpersonal trauma in situations such as entrapment or captivity (176). Symptoms seen following prolonged trauma include a sense of loss of control, helplessness, impaired emotion regulation, somatization, disturbed self-perception and perception of others, as well as dissociation. This type of complex posttraumatic stress reaction was also recognized to be present in many individuals with chronic maltreatment histories (52, 54). Complex PTSD, also referred to as Disorders of Extreme Stress Not Otherwise Specified, was considered for inclusion in DSM-IV but was not included as 92% of individuals with complex PTSD met established diagnostic criteria for PTSD (60).

Developmental trauma disorder evolved from complex PTSD by focusing on chronic

maltreatment as the necessary stressor and coupling this with many of the clinical features of complex PTSD (e.g., affective dysregulation, somatic symptoms, and altered attributions and expectancies). The advantage of focusing on maltreatment as the stressor is that the majority of maltreated children do not meet diagnostic criteria for PTSD, providing a *raison d'être* for inclusion in the DSM that complex PTSD lacks. However, there are three major reasons why chronically maltreated individuals with significant psychopathology do not meet criteria for PTSD. First, some maltreated individuals show all the symptoms of PTSD but fail to meet criteria as the type of maltreatment they experienced (e.g., emotional abuse) does not fulfill the DSM A1 criteria for a traumatic event. This problem is most readily addressed by expanding the A1 criteria to include events that turn out to be traumatizing to children. Second, some maltreated children fail to meet criteria, as they may show symptoms in only two of three DSM-IV category clusters, but are as impaired as children meeting full criteria (51). Again, this is easily addressed by modifying the required number of symptom clusters for children. Finally, most maltreated individuals with psychopathology fail to meet criteria for PTSD because the symptoms they manifest are simply not the symptoms of PTSD. These individuals are better characterized as suffering from major depression, social anxiety disorder, alcohol use disorder, etc. Although maltreatment may be an important consideration in all of these cases there are good reasons for not lumping them together.

Developmental trauma disorder makes the assumption that there is basically one overarching psychiatric reaction to chronic childhood maltreatment. What we see

instead is that childhood maltreatment is a major risk factor for a host of different psychiatric disorders. There is not a single developmental trauma disorder but an array of developmental trauma disorders, or more accurately maltreatment-related psychiatric disorders. As we described in the article, these different outcomes likely depend on type, timing, severity and multiplicity of exposure, coupled with genetic and interpersonal risk and resilience factors.

From this perspective developmental trauma disorder overlaps extensively with the maltreatment-related PTSD ecophenotype, particularly if diagnostic criteria for PTSD are modified to make them more developmentally sensitive. However, there are several other maltreatment-related ecophenotypes with distinctly different clinical presentations. Hence, we propose that these maltreatment-related ecophenotypes continue to be labeled by the best fitting and most appropriate current DSM diagnostic codes, with the addition of a specifier to denote the individual's prior history of significant childhood maltreatment.

### **Strategies for Subgrouping by Ecophenotype**

There are two viable methods for identifying and delineating patients with ecophenotypic variants within the DSM-5 for each of the reviewed disorders and maybe others depending on what future research reveals.

The simplest, and least controversial would be to denote the ecophenotype by adding it

a specifier to the different disorders. For major depression current specifiers include: With Mixed Features; Catatonic Features; Melancholic Features; Atypical Features; Seasonal Pattern; and Postpartum Onset. It would be relatively easy to include as another specifier – With ‘Maltreatment History’ or perhaps more euphemistically – With ‘Early Life Stress’. Similarly, ‘With Maltreatment History’ could be added as a specifier to Substance Use Disorder, Alcohol Use Disorder, Posttraumatic Stress Disorder, etc. A specifier in DSM-5 serves to define a more homogeneous subgrouping of individuals with the disorder who share common features. Maltreated individuals certainly share a history of early life stress and important clinical features such as earlier onset, more severe course, poorer response to certain treatments, heightened risk for comorbidities and increase risk for suicide attempts.

The second alternative would be to designate "with childhood maltreatment" as a specific subtype within each DSM category. A good example is the DSM-5 PTSD category, which lists the following subtypes: Subtype: Posttraumatic Stress Disorder in Preschool Children and Subtype: Posttraumatic Stress Disorder – With Prominent Dissociative (Depersonalization/Derealization) Symptoms. Hence, within the different category clusters there could be Subtype: Major Depression in Individuals with Childhood Maltreatment, Subtype: Substance Use Disorder in Individuals with Childhood Maltreatment. DSM-5 subtypes define mutually exclusive and jointly exhaustive phenomenological subgroupings within a diagnosis.

At the present time we believe that there is ample evidence to justify adding ‘With

Maltreatment History' or 'With Early Life Stress' as a specifier to: major depressive disorder, dysthymia, generalized anxiety disorder, panic disorder, simple phobias, social anxiety disorder, obsessive compulsive disorder, posttraumatic stress disorder and drug and alcohol use disorders.

Determining whether or not they are distinct subtypes would follow the strategy outlined by Robins and Guze (177). They described a method for achieving diagnostic validity in psychiatric illness, which consisted of 5 phases: clinical description, laboratory study, exclusion of other disorders, follow-up study, and family study. This is the approach we followed in providing the initial evidence base for these ecophenotypes. This approach was expanded on by DSM-5 members, which recommended organizing supporting data for diagnostic categories or subtypes into antecedent validators (family history, sociodemographic and cultural factors, environmental risk factors, prior psychiatric history), concurrent validators (cognitive, emotional, temperament, and personality correlates unrelated to diagnostic criteria, biological markers, comorbidities) and predictive validators (diagnostic stability, course of illness, response to treatment) (178).

To fully establish the evidence base for these ecophenotypes as distinct subtypes will require the following types of studies. To satisfy the *clinical description* and *exclusion of other disorders* criteria we need more studies identifying the clinical characteristic of the maltreated ecophenotype with the specific delineation of clinical features that differentiate between maltreated and non-maltreated individuals with the same primary diagnosis. For the *laboratory studies criteria* we need additional neuroimaging and

other types of neurobiological investigations (e.g., neuroendocrine, epigenetic) comparing the ecophenotype to the non-maltreated variant. Ideally, these studies would also include unexposed controls and resilient maltreated individuals without psychopathology. The goal would be to identify potential biomarkers for the ecophenotype. Similarly, *family studies* would focus on gene by maltreatment interactions that differentiate the ecophenotype from the non-maltreated subtype. Finally, the *follow-up study* criteria would include treatment trials comparing maltreated and non-maltreated patients with the same primary diagnosis that may elucidate important differences in therapeutic response, course of illness and diagnostic stability.

**TABLE S1. Odds of developing depressive disorders in individuals exposed to childhood sexual abuse or multiple forms of maltreatment including sexual abuse**

First Author (Reference)	Types of Maltreatment	Clinical Outcome	Method	N	Age Range	Restrictions Location	Odds Ratio (95% CI)*	Model
<b>Cross-sectional Studies</b>								
Fergusson (179)	1 Non-contact sexual activity 2 Contact w/o penetration 3 Penetration or attempt. All < 16 y	a Major depression between ages 16-18	Interview (CIDI)	1019	18	Christchurch, NZ Longitudinal evaluation	3.6 (1.3–9.6) 1a 3.0 (1.4–6.1) 2a 5.4 (2.4–12.3) 3a <i>Pooled CSA</i> 3.59 (2.24–5.75)	aOR
Wilsnack (180)	Unwanted familial sexual activity < 18 y or w ≥ 5 y older individual or unwanted extrafamilial sexual activity < 18 y or < 13 y w ≥ 5 y older person	Lifetime Major depressive disorder	Interview (DIS)	1099	21-UUA	Females US National	2.51 (1.69-3.74)	aOR
McCauley (181)	Ever sexually abused and/or physically abused < 18 y but not after 18 years	High v. low depression score	SR Survey SCL-22	1931	18-UUA	Females Baltimore primary care sample	2.73 (1.87–3.98)	OR
Dinwiddie (182)	Forced into sexual activity, including intercourse < 18 y	Lifetime Major depressive disorder	Telephone Interview (SSAGA)	5959	27-90	Female twins Australia National	2.68 (2.08-3.44)	OR
Kendler (8)	1 Non-genital 2 Genital touch or view 3 Intercourse or attempt. All < 16 y	a Lifetime Major depressive disorder	Interview (SCID DSMIIIR)	1411	17-55	F twins Virginia population	1.12 (0.69-1.80) 1a 1.53 (1.06–2.19) 2a 2.80 (1.69–4.64) 3a <i>Any CSA</i> 1.72 (1.30–2.26) a	aOR
Molnar (183)	1 Raped or molested < 18 years	a Lifetime MDD b Lifetime dysthymia	Interview (CIDI)	5866	15-54	US National Comorbidity Study	1.80 (1.42–2.28) 1a 1.80 (1.29–2.53) 1b <i>Pooled M and F</i>	aOR
MacMillan (34)	Unwanted exposure, threats, touching attempted sex or attack w adult while “growing up”	Lifetime Major depressive disorder	Interview (CIDI)	7016	15-64	Ontario Canada probability sample (OHS)	3.4 (2.3–4.8)	aOR
Hanson (184)	1 Rape ± aggravated assault < 18 y v neither	a Lifetime MDD b Current MDD	Telephone interview SCID-depr	4008	18-UUA	Females US National Survey	2.89 (2.31–3.63) 1a 3.27 (2.18–4.90) 1b	OR
Chapman (185)	1 Touch, attempt or penetration < 18 y with person ≥ 5 yrs older from ACE	a Lifetime b Current MDD or dysthymia	SR (2 items DIS, 6 items CES-D)	9460	19-94	San Diego HMO sample	1.74 (1.54–1.96) 1a 1.90 (1.66–2.17) 1b <i>Pooled M and F</i>	aOR
Tanskanen (186)	CSA (incest, pedophilia) by family member(s) or stranger(s) during your childhood	Persistent depression, 2 years	BDI medication or diagnosis	1405	25-64	Finland stratified population sample	2.63 (1.40–4.93)	OR

Libby (187)	CSA, rape, unwanted sex, forced touch < 13 y	Lifetime Depression or dysthymia	Interview (CIDI)	3084	15-54	American Indians, 2 tribes	4.07 (2.77–5.99) <i>Pooled across tribes</i>	aOR
Hussey (188)	Touched, forced to touch or forced sex by parents or other adult-care givers < 6 <sup>th</sup> grade	Current Major depressive disorder	SR (CES-D cutoff 22/24)	10828	18-26	US National (Add Health)	1.58 (1.25–2.01)	OR
Schneider (189)	Unwanted sexual activity force or threat < 18 years	Frequent sadness past 30 days	Telephone interview Healthy Days Screen	3936	18-94	Females California (CWHS)	2.56 (2.02–3.26)	aOR
Afifi (190)	Intercourse or penetration w force or threat or unwanted touch < 16 years	Any mood disorder lifetime	Interview (CIDI)	9291	18-UUA	US (NCS-R)	1.87 (1.51–2.31)	aOR
Zlotnick (191)	1 Potentially traumatic childhood event including rape < 15 y v no exposure	a Lifetime MDD b Lifetime dysthymia	Interview (DIS) (CIDI)	2390	15-UUA	Chile National	1.4 (0.9-2.2) 1a 2.1 (1.3-3.3) 1b	aOR
Bonomi (192)	Unwanted touch or made to touch < 18 years ± CPA	Current severe depressive symptoms	Telephone Interview (CES-D 5 item ≥ 6)	3568	18-64	Females northern Idaho and Washington State GHC	1.89 (1.58–2.26)	aOR
Rohde (193)	Unwanted touch or made to touch or forced threatened sex < 18 y (modified CTQ)	Current moderately severe depressive symptoms	Telephone Interview (PHQ-9 ≥ 10)	4641 overlaps w (192)	40-65	Females northern Idaho and Washington State GHC	2.14 (1.62–2.83)	aOR
Draper (194)	Victim of any sexual abuse ± physical abuse < 15 years	Current depression	Postal survey (PHQ -9 ≥ 15)	21822	60-UUA	Australia, general medical practice	3.49 (2.82–4.33)	aOR
Fletcher (195)	Touched, forced to touch or forced sex by parents or other adult-care givers < 6 <sup>th</sup> grade	Current depression at age 17 or 22	SR (CES-D cutoff 22/24)	14240 14228 overlaps w (188)	~ 17 (7 <sup>th</sup> -12 <sup>th</sup> grade) ~ 22 (18-26)	US National (Add Health Waves I, III)	1.77 (1.20–2.62) 17 1.88 (1.29–2.72) 22 <i>Pooled across age</i> 1.83 (1.39–2.39)	aOR
Ritchie (196)	CSA and/or CPA unspecified criteria	Current late-life Major depressive disorder	Interview (MINI)	942	65-92	Montpellier France random sample	2.67 (0.9–7.90)	OR
Polanczyk (197)	1 Childhood maltreatment (CTQ) none v moderate + severe	a Current MDD (past yr) b Recurrent MDD	Interview (DIS)	924	26-55	Mothers of twins UK National (E-risk)	3.49 (2.41–5.06) 1a 4.05 (2.76–5.95) 1b	OR
Brezo (198)	Touch, attempt or penetration < 18 years from ACE	Lifetime DSM-III-R Mood disorder	Interview (DIS)	1121	27	Quebec French speaking population	3.11 (2.05–4.72)	OR
Green (3)	Repeated fondling, attempted rape, and rape < 18 years	Lifetime DSM-IV Mood disorder	Interview (CIDI)	9282 overlaps w (190)	18~ UUA	US National (NCS-R)	1.8 (1.6-2.0) bivariate	aOR

Cannon (199)	Unwanted touch or made to touch < 18 y and/or CPA ± WDV	Current Severe Major depressive disorder	SR (abbreviated CES-D cutoff ≥ 6)	3568	18-64	Females northern Idaho and Washington State GHC	1.99 (1.66–2.39) <i>Pooled across WDV exposure</i>	aOR
Gal (200)	1 CSA raped or molested < 13 years or 13-17 years	a Lifetime depressive DO b Current depressive DO (past year)	Interview (CIDI)	3978	21-UUA	Israel National Health Service Jewish sample	1.92 (1.30–2.84) 1a 1.60 (0.95–2.70) 1b <i>Pooled preteen and teen CSA</i>	OR
Ramiro (201)	ACE Score > 0 v = 0	Depression	SR (ACE Survey)	1068	35-92	Metro Manila, Philippines	2.47 (1.82–3.33)	aOR
King (202)	Exposure, touch ± force, penetration or intercourse < 18 years	Affective disorder past 6 month	Interview (DISC)	1735	10-18	Cook County IL. Juvenile Detention Center stratified	2.26 (1.35-3.77) <i>Pooled sexual abuse ± severe physical abuse</i>	OR
Jonas (203)	1 Non-consensual touch 2 Non-consensual intercourse	a Depressive episode past week	Interview (CIS-R)	7403	16~UUA	England National (APMS)	3.08 (2.0–4.8) 1a 5.07 (2.7–9.6) 2a <i>Pooled exposure 3.62 (2.52–5.19)</i>	OR
Teicher (204)	Forced unwanted sexual contact < 18 y, controlling for other forms of maltreatment	Current severe depressive symptoms	Online survey, Kellner SQ Depression ≥ 12	1412	18-25	Boston, convenience sample	1.85 (1.33–2.57)	aOR
Fujiwara (205)	Rape, attempt or repeated fondling < 18 y controlling for other forms of adversity	First onset mood disorder	Interview (CIDI)	1722	20-UUA	Japan, National Survey	1.5 (0.3–5.2)	aOR
Chou (206)	1 Non-consensual touch or intercourse < 16 years	a Depressive episode b Mixed depression anxiety past week	Computer-assisted self interview	3493 overlaps with (203)	50-UUA	Middle-age or older England National (APMS)	1.88 (0.8–4.2) 1a 1.85 (1.2–2.8) 1b	OR
Sartor (207)	Hi-risk exposure (eg CSA, physical abuse, severe neglect) v. no risk	Lifetime major depressive disorder	Interview (SSAGA)	2568	38.6 ±4.7	Twins and siblings Australia National	3.04 (2.34–3.95)	OR
Dunn (208)	1 Sexual assault 2 Rape < 18 years	a Adolescent onset depression (exposure year or later)	Interview (CIDI)	5498 overlaps w (3, 190)	18-99	US National (NCS-R)	3.33 (2.6–4.3) 1a 3.50 (2.6–4.7) 2a <i>Pooled exposure 3.40 (2.81–4.12)</i>	aOR
Gonzalez (209)	1 Sexual contact, attempt or forced < 16 years	Depression ± pain condition last 12 months	Interview (CIDI-SF)	1475	21-35	Ontario CA population (OCHS)	2.60 (1.41–4.80)	aOR
Li (210)	Exposure, peeping, touch, touching or intercourse < 14 years	Depression – single scale item past 6 months	Interview and computer-assisted self-interview	4084	15-24	Taipei representative sample	2.06 (1.46–2.91)	aOR

Warner (211)	Sexual assault or rape < 18 years	Lifetime major depressive episode or dysthymia	Interview (CIDI)	1427	18-UUA	Hispanic Females US National (NLAAS)	1.62 (0.91–2.87)	aOR
<b>Prospective Studies</b>								
Brown (212)	1 CSA, Central Registry Abuse and Neglect or SR of $\geq 2$ of the following touched, touching or sex play < 18	a Dysthymia b Major depression	Interview (DISC)	639	18-25	Upstate NY Followed 15 years	9.74 (2.79-34.3) 1a 3.22 (0.88-11.8) 1b	OR
Thornberry (213)	Substantiated maltreatment CPS (including physical and sexual abuse; neglect; lack of supervision; moral, legal, and educational neglect; and emotional abuse)	Depressive symptoms > 1 SD from mean	SR (14 item scale)	881 Early Adol 818 Late Adol	~13 18	Rochester NY stratified high-risk study  Early Adol Late Adol 3 yr follow-up	1.40 (0.99–1.95) Early Adol 0.86 (0.59–1.25) Late Adol  <i>Pooled outcome 1.12 (0.87–1.45)</i>	aOR
Spataro (173)	Confirmed CSA < 16 by records of the Victorian Institute of Forensic Medicine	Major affective disorders lifetime	Diagnoses from the Victorian Psych-iatric Case Registrar	314135 <sup>7</sup>	27.1 $\pm$ 13.3	Victoria, Australia 9 year follow-up	3.18 (2.23–4.54)	OR
Widom (5)	Court substantiated abuse or neglect < 12	Current Major depressive disorder	Interview (DIS)	1196	19–40	US, metropolitan Midwest, 22 yr follow-up	1.75 (1.01-3.02)	aOR
Fergusson (214)	1 Non-contact sexual activity 2 Contact wo penetration 3 Penetration or attempt. All < 16 y	a Major depressive disorder at 21-25 years	Interview (CIDI)	1001 overlaps with (179)	21-25	Christchurch, NZ 3 year follow-up	2.47 (1.12-5.45) 1a 3.52 (1.99-6.26) 2a 3.08 (1.83-5.18) 3a <i>Pooled CSA 3.10 (2.19–4.38)</i>	OR
Polanczyk (197)	1 Prospective caring, discipline + retrospective CSA CPA < 18 y	a Current MDD (past y) b Recurrent MDD	Interview (DIS)	918	32	Dunedin sample, 30 yr follow-up	1.61 (1.12–2.29) 1a 1.91 (1.35–2.71) 1b	OR
Cutajar (175)	Confirmed CSA < 16 y by records of the Victorian Institute of Forensic Medicine	Affective DO (ICD)	Diagnoses from the Victorian Psych-iatric Case Registry	5365 part of (173)	33.8 $\pm$ 11.0	Victoria, Australia 12-43 year follow-up	2.07 (1.59–2.70)	OR
Scott (2)	Primary client in CPS database plus retrospective assessment of sexual abuse, physical abuse or WDV < 17 y	Lifetime major depressive disorder	Interview (CIDI)	2144	16-27	New Zealand National Survey 10 year follow-up	2.10 (1.32-3.35)	aOR

\*The number indicates which type of maltreatment and the letter indicates which clinical outcome the odds ratio applies to within a given study with multiple types of maltreatment or outcomes (e.g., Fergusson (179) 1a, 1 = Non-contact sexual activity, a = Major depression between ages 16-18).

Abbreviations: aOR – Odds ratio adjusted for covariates, Adol - Adolescence, APMS - Adult Psychiatric Morbidity Survey, CES-D - Center for Epidemiologic Studies Depression Scale, CIDI - World Health Organization Composite International Diagnostic Interview,

CIS-R - Clinical Interview Schedule – Revised, CPA - Childhood Physical Abuse, CPS – Child Protective Service or similar agency, CSA - Childhood Sexual Abuse, CTQ - Childhood Trauma Questionnaire, DIS - Diagnostic Interview Schedule, DISC - Diagnostic Interview Schedule for Children, DO - Disorder, DSM - Diagnostic and Statistical Manual of Mental Disorders, EA - Emotional Abuse, F - Female, GHC - Group Health Cooperative, ICD - International Classification of Disease, M - Male, MDD - Major Depressive Disorder, MINI - Mini-International Neuropsychiatric Interview, NCS-R – National Comorbidity Survey – Replication, NLAAS - National Latino and Asian American Survey, Negl - Neglect, OCHS – Ontario Child Health Study, OHS – Ontario Health Survey, OR – raw odds ratio, PHQ - Patient Health Questionnaire, PVA - Parental Verbal Abuse, RR - Relative Risk, SCID - Structured Clinical Interview for DSM Disorders, SR - Self-Report, SSAGA - Semi-Structured Assessment for the Genetics of Alcoholism, Sx - Symptoms, UUA - Unspecified Upper Age, WDV - Witnessing Interparental Violence, y – year.

**TABLE S2. Odds of developing anxiety disorders or PTSD in individuals exposed to childhood sexual abuse or multiple forms of maltreatment including sexual abuse**

First Author (Reference)	Types of Maltreatment	Clinical Outcome	Method	N	Age Range	Restrictions Location	Odds Ratio (95% CI)*	Model
<b>Cross-sectional Studies</b>								
Fergusson (179)	1 Non-contact sexual activity 2 Contact w/o penetration 3 Penetration or attempt. All < 16 years	a Any anxiety disorder (excluding PTSD) between ages 16-18	Interview (CIDI)	1019	18	Christchurch, NZ Longitudinal evaluation	2.8 (1.1–7.1) 1a 3.0 (1.5–6.1) 2a 3.2 (1.5–6.7) 3a <i>Pooled CSA</i> 3.02 (1.93–4.73)	aOR
Wilsnack (180)	Unwanted familial sexual activity < 18 y or w ≥ 5 y older individual or unwanted extrafamilial sexual activity < 18 y or < 13 y w ≥ 5 y older person	Current anxiety (single item)	Interview (DIS)	1099	21-UUA	Females US National	1.56 (1.02–2.40)	aOR
McCauley (181)	Ever sexually abused and/or physically abused < 18 y but not after 18	High v low anxiety score	SCL-22	1931	18-UUA	Females Baltimore primary care sample	2.99 (2.00–4.46)	OR
Dinwiddie (182)	1 Forced into sexual activity, including intercourse < 18 y	a Lifetime Social Phobia b Lifetime Panic / Agoraphobia	Telephone Interview (SSAGA)	3868	27-90	Female twins Australia National	3.10 (1.81-5.31) 1a 4.22 (2.85-6.26) 1b	OR
Kendler (8)	1 Non-genital 2 Genital touch or view 3 Intercourse or attempt All < 16 years	a Lifetime Panic / Agoraphobia b Lifetime GAD	Interview (SCID - DSMIIIR)	1411	17-55	Female twins Virginia population	1.21 (0.45-3.41) 1a 1.92 (0.93–3.94) 2a 2.62 (1.08–6.34) 3a 1.13 (0.6–2.1) 1b 1.32 (0.81–2.14) 2b 2.62 (1.67–4.65) 3b <i>Pooled any CSA</i> 1.99 (1.12–3.52) a 1.62 (1.12–2.34) b	aOR
Molnar (183)	1 Raped or molested < 18 years	a PTSD b Panic disorder c GAD d Simple Phobia e Social Phobia All lifetime history	Interview (CIDI)	5866	15-54	US National Comorbidity Study	9.23 (6.65–12.8) 1a 1.34 (0.94–1.92) 1b 1.22 (0.87–1.69) 1c 1.26 (0.90–1.77) 1d 1.43 (1.02–2.01) 1e <i>pooled results for males and females</i>	aOR
MacMillan (34)	Unwanted exposure, threats, touching attempted sex or attack w adult while “growing up”	Lifetime any anxiety disorder	Interview (CIDI)	7016	15-64	Ontario Canada probability sample	2.0 (1.5–2.7)	aOR
Hanson (184)	1 Rape ± aggravated assault < 18 y v neither	a Lifetime PTSD b Current PTSD	Telephone interview NWS PTSD module	4008	18-UUA	Females US National Survey	4.42 (3.43–5.69) 1a 4.48 (3.12–6.44) 1b	OR

Coid (215)	Unwanted sex ± intercourse < 16 y controlling for other abuse and sexual assault > 16 y	Current PTSD	SR Survey (HADS)	716	16-85	Females UK community practitioner sample	2.48 (1.33–4.64)	aOR
Libby (187)	1 CSA, rape, unwanted sex, forced touch < 13 years	a Lifetime PTSD b Lifetime panic DO	Interview (CIDI)	3084	15-54	American Indians, 2 tribes	10.36 (2.4–45.4) 1a 1.61 (1.25–2.08) 1b <i>Pooled across tribes</i>	OR
Goodwin (216)	1 Contact CSA < 16 years	a Panic attack b Panic disorder	Interview (CIDI)	983 overlap with (179)	18 and 21	Christ-church, NZ longitudinal evaluation	4.1 (2.3–7.2) 1a 2.2 (0.98–5.0) 1b	aOR
Schneider (189)	1 unwanted sexual activity force or threat < 18 year	a Frequent anxiety past 30 days b Probable PTSD	Telephone Interview PTSD Screen	3,936	18-94	Females California (CWHS)	2.64 (2.14–3.25) 1a 5.71 (4.31–7.57) 1b	aOR
Affifi (190)	Intercourse or penetration w force or threat or unwanted touch < 16 y	Any anxiety disorder lifetime	Interview (CIDI)	5142 F 4149 M	18-UUA	US National (NCS-R)	1.57 (1.24-2.00) F 1.52 (NS) M	aOR
Zlotnick (191)	1 Potentially traumatic childhood event including rape < 15 y v no childhood exposure	a Lifetime PTSD b Lifetime Panic / Agoraphobia	Interview (DIS) (CIDI)	2390	15-UUA	Chile National	5.62 (3.75–8.44) 1a 5.80 (3.07–11.0) 1b <i>Pooled no exposure and adult exposure</i>	OR
Draper (194)	Victim of any sexual abuse ± physical abuse < 15 years	Current anxiety	Postal survey (HADS ≥ 11)	21822	60-UUA	Australia, general medical practice	3.54 (3.05–4.10)	aOR
Cougler (7)	1 Raped or molested < 15 years	a Social anxiety DO b Panic DO c GAD d PTSD e Specific phobia Lifetime diagnoses	Interview (CIDI)	4141 overlaps with (190)	18~UUA	US National (NCS-R)	1.85 (1.44–2.39) 1a 2.10 (1.46–3.03) 1b 1.62 (1.28–2.05) 1c 2.83 (2.19–3.65) 1d 0.95 (0.77–1.26) 1e	aOR
Tonmyr (217)	Substantiated CSA < 15 years by CPS	Anxiety and/or depression	Case worker notes	4381	10-15	Canada National Welfare System	2.10 (1.36–3.25)	aOR
Gal (200)	1 Raped or molested < 13 years or 13-17 years	a Lifetime anxiety disorder b 12 month anxiety disorder	Interview (CIDI)	3978	21-UUA	Israel National Health Service Jewish sample	2.43 (1.50–3.93) 1a 1.80 (0.98–3.30) 1b <i>Pooled preteen and teen CSA</i>	OR
King (202)	Exposure, touch ± force, penetration or intercourse < 18 years	Any anxiety disorder past 6 mo	Interview (DISC)	1735	10-18	Cook County IL. Juvenile Detention Center stratified	4.05 (2.47-6.65) <i>Pooled sexual abuse ± severe physical abuse</i>	OR
Jonas (203)	1 Non-consensual touch or intercourse pooled	a Current PTSD b GAD c Panic disorder d Phobias e OCD Past week b-e	SR (TSQ) Interview (CIS-R)	7403	16~UUA	England National (APMS)	4.23 (2.96–6.04) 1a 3.00 (2.24–4.03) 1b 3.19 (1.82–5.58) 1c 4.90 (3.18–7.55) 1d 3.73 (2.17–6.41) 1e	OR

Teicher (204)	Forced unwanted sexual contact < 18 y controlling for other forms of maltreatment	Current severe anxiety symptoms	Online survey, Kellner SQ Anxiety $\geq$ 12	1412	18-25	Boston, convenience sample	1.59 (1.14–2.22)	aOR
Fujiwara (205)	Rape, attempt or repeated fondling < 18 y controlling for other forms of adversity	First onset anxiety disorder	Interview (CID I)	1722	20-UUA	Japan, National Survey	1.4 (0.5–4.2)	aOR
Walsh (218)	1 Forced or drug-related sexual contact, intercourse, or penetration	a Lifetime PTSD b Current PTSD – past 6 months	Telephone survey (NSA-PTSD module)	1763	12-17 adolescent sample	Female US National (NSA-R and NWS-R)	3.91 (2.77–5.52) 1a 4.24 (2.76–6.53) 1b	aOR
Chou (206)	1 Non-consensual touch or intercourse < 16 years	a PTSD b GAD c Panic DO d Phobia e OCD All past week	Computer-assisted self interview	3493 overlaps with (203)	50-UUA	Middle-age or older England National (APMS)	3.22 (1.62–6.39) 1a 2.06 (1.19–3.55) 1b 2.25 (0.72–7.03) 1c 2.62 (1.02–6.73) 1d 2.01 (0.54–7.55) 1e	OR
Sartor (207)	Hi-risk exposure (eg CSA, physical abuse, severe neglect) v low risk	Lifetime PTSD	National Comorbidity Survey interview	1643	38.6 $\pm$ 4.7	Twins and siblings Australia National	4.36 (3.25-5.85)	aOR
Li (210)	Exposure, peeping, touch, touching or intercourse < 14 years	Anxiety – single scale item past 6 months	Interview and computer-assisted self-interview	4084	15-24	Taipei representative sample	2.00 (1.46–2.73) <i>Pooled across contact and non-contact CSA</i>	aOR
Warner (211)	Sexual assault or rape < 18 years	Any anxiety disorder lifetime	Interview (CID I)	1427	18-UUA	Hispanic Females US National (NLAAS)	2.87 (1.70–4.85)	aOR
<b>Prospective Studies</b>								
Widom (219)	Court substantiated CSA < 12 years	Lifetime PTSD	Interview (DIS)	1196	19-40	US, metropolitan Midwest, 20 yr follow-up	2.34 (1.5–3.7)	OR
Spataro (173)	Confirmed CSA < 16 y by records of the Victorian Institute of Forensic Medicine	Anxiety and acute stress disorders lifetime	Diagnoses from the Victorian Psychiatric Case Registry	3141357	27.1 $\pm$ 13.3	Victoria, Australia 9 year follow-up	3.18 (2.23–4.54)	OR
Fergusson (214)	1 Non-contact sexual activity 2 Contact wo penetration 3 Penetration or attempt. All < 16 years	a Met criteria for one or more anxiety disorders at 21-25 years	Interview (CID I)	1001 extension of (214)	21-25	Christchurch, NZ 3 year follow-up	0.90 (0.31–2.65) 1a 2.20 (1.17–4.12) 2a 4.52 (2.69–7.60) 3a <i>Pooled CSA</i> 2.87 (1.97–4.18) a	OR
Cutajar (175)	1 Confirmed CSA < 16 y by records of the	a Lifetime PTSD b Lifetime Anxiety disorder	Diagnoses from the Victorian	5365 part of (173)	33.8 $\pm$ 11.0	Victoria, Australia 12-43 year	5.56 (3.44–8.99) 1a 2.67 (1.97–3.61) 1b	OR

	Victorian Institute of Forensic Medicine		Psychiatric Case Registry			follow-up		
Scott (2)	Primary client in CPS database plus retrospective assessment of sexual abuse, physical abuse or WDV < 17 y	Lifetime PTSD	Interview (CIDI)	2144	16-27	New Zealand National Survey 10 year follow-up	4.86 (2.26-10.45)	aOR

\*The number indicates which type of maltreatment and the letter indicates which clinical outcome the odds ratio applies to within a given study with multiple types of maltreatment or outcomes (e.g., Fergusson (179) 1a, 1 = Non-contact sexual activity, a = any anxiety disorder).

Abbreviations: aOR – odds ratio adjusted for covariates, APMS - Adult Psychiatric Morbidity Survey CIDI - World Health Organization Composite International Diagnostic Interview, CIS-R - Clinical Interview Schedule – Revised, CPA - Childhood Physical Abuse, CPS – Child Protective Service or similar agency, CSA - Childhood Sexual Abuse, DIS - Diagnostic Interview Schedule, CWHS –California Women’s Health Survey, DISC - Diagnostic Interview Schedule for Children, DSM - Diagnostic and Statistical Manual of Mental Disorders, F - Female, GAD – Generalized anxiety disorder, HADS – Hospital Anxiety and Depression Scale, M - Male, mo - month, NCS-R – National Comorbidity Survey – Replication, NLAAS - National Latino and Asian American Survey, NSA-R - National Survey of Adolescents–Replication, NCS-R – National Comorbidity Survey – Replication, NWS - National Women’s Study, NWS–R - National Women’s Study–Replication, OR – raw odds ratio, SCID - Structured Clinical Interview for DSM Disorders, SQ – Symptom Questionnaire, SR - Self-Report, SSAGA - Semi-Structured Assessment for the Genetics of Alcoholism, UUA - Unspecified Upper Age, w – with, wo - without, y – year.

**TABLE S3. Odds of developing substance abuse disorders or problems in individuals exposed to childhood sexual abuse or multiple forms of maltreatment including sexual abuse**

First Author (Reference)	Types of Maltreatment	Clinical Outcome	Method	N	Age Range	Restrictions Location	Odds Ratio (95% CI)*	Model
<b>Cross-sectional Studies</b>								
Nagy (220)	Forced intercourse w identified perpetrators v sexually experienced controls < 18 y	Lifetime drug use	SR (In school survey)	3124	13-18	Females Urban, semiurban and rural Southern US	1.50 (1.04-2.50)	OR
Fergusson (179)	1 Non-contact sexual activity 2 Contact w/o penetration 3 Penetration or attempt All < 16 years of age	a Alcohol abuse-dependence b Drug abuse-dependence Between ages 16-18	Interview (CID)	1019	18	Christchurch, NZ Longitudinal evaluation	1.9 (0.7-5.0) 1a 3.2 (1.6-6.5) 2a 2.7 (1.2-6.0) 3a 0.7 (0.1-5.8) 1b 1.8 (0.7-4.8) 2b 6.6 (2.9-15.2) 3b <i>Pooled CSA</i> 3.66 (2.31-5.81) a 3.28 (1.80-5.97) b	aOR
Wilsnack (180)	1 Unwanted familial sexual activity < 18 y or w ≥ 5 y older individual or unwanted extra-familial sexual activity < 18 y or < 13 y w ≥ 5 y older person	a Heavy episodic drinking past y b Intoxication c Alcohol dependence symptoms d Problem Drinking Index ≥ 2 e Lifetime illicit drug use	Interview surveys including Composite Problem Drinking Index	1099	21-UUA	Females US National	1.58 (0.94-2.65) 1a 1.65 (1.04-2.62) 1b 3.04 (1.71-5.39) 1c 2.52 (1.49-4.27) 1d 2.52 (1.58-4.03) 1e	aOR
Harrison (221)	Forced or unwanted touch / touching by extrafamilial adult or older person or older stronger family member ± physical abuse	Lifetime substance use v never used	SR (In school survey)	122824	10-19 Grades 6, 9 & 12	Minnesota public school students	2.86 (2.73-3.00)  <i>Pooled across grades and genders</i>	OR
McCauley (181)	1 Ever sexually abused and/or physically abuse < 18 but not after 18	a Current street drug use b Lifetime street drug use c Current alcohol abuse d Lifetime drinking problems	SCL-22	1931	18-UUA	Females Baltimore primary care sample	12.15 (3.0-49.0) 1a 3.52 (2.37-5.22) 1b 1.27 (0.65-2.47) 1c 2.65 (1.58-4.46) 1d	OR
Garnefski (222)	Sexually abused (e.g., forced to perform sexual acts, assaulted or raped)	Addiction-risk behaviors (past month alcohol or past year drugs)	SR	1490 (50% history of CSA)	12-19	Netherlands subsample of representative 2nd school sample	2.61 (2.06-3.32)	OR
Jantzen (223)	Forced sexual activity < 18 y ± physical abuse	Lifetime cocaine use	SR use semi-structured abuse interview	1059	18-UUA	Pregnant New Haven CT obstetric sample	3.48 (2.49-4.87)	OR

Bensley (224)	Unwanted touch or touching < 18 years ± physical abuse	Heavy drinking (5 or more drinks per occasion ≥ 4 times in past mo)	Telephone Interview	3473	18-UUA	Washington state population sample (BRFSS)	2.18 (1.32–3.61) <i>Pooled M &amp; F</i>	aOR
Dinwiddie (182)	Forced into sexual activity, including intercourse < 18 y	Alcoholism	Telephone Interview (SSAGA)	3868	27-90	Female twins Australia National	1.78 (1.31-2.42)	OR
Kendler (8)	1 Non-genital 2 Genital touch or view 3 Intercourse or attempt All < 16 years	a Lifetime alcohol dependence b Lifetime drug dependence	Interview (SCID DSMIIIIR)	1411	17-55	Female twins Virginia population	1.89 (0.79-4.55) 1a 2.55 (1.39–4.69) 2a 4.75 (2.34–9.62) 3a 2.37 (0.93–6.03) 1b 1.23 (0.58–2.60) 2b 5.68 (2.55–12.6) 3b <i>Pooled any CSA</i> 2.90 (1.79–4.69) a 2.50 (1.39–4.50) b	aOR
Molnar (183)	1 Raped or molested < 18 years	a Lifetime alcohol dependence b Lifetime drug dependence	Interview (CID)	5866	15-54	US National Comorbidity Study	1.57 (1.14–2.15) 1a 2.00 (1.38–2.90) 1b <i>Pooled M and F</i>	aOR
MacMillan (34)	1 Unwanted exposure, threats, touching attempted sex or attack w adult while “growing up”	a Lifetime alcohol abuse or dependence b Lifetime drug abuse or dependence	Interview (CID)	7016	15-64	Ontario Canada probability sample (OHS)	2.5 (1.7–3.7) 1a 3.8 (2.2–6.7) 1b	aOR
Thompson (225)	1 Penetration force or attempt < 18 y controlling for physical abuse	a Drug use past month b Daily alcohol use past year	Telephone interview	8000	18-UUA	Females US National (NVAWS)	1.55 (1.29–1.87) 1a 0.95 (0.59–1.54) 1b	aOR
Anda (1)	Touch, attempt or penetration < 18 y with person ≥ 5 yrs older from ACE	Lifetime or current alcoholism	SR (Postal survey)	9346	19-94	San Diego HMO sample	1.9 (1.6–2.4)	aOR
Dube (226)	1 Touch attempt or penetration < 18 with person ≥ 5 yrs older from ACE scale	a Heavy drinking b Alcohol problem c Self-reported alcoholic	SR (Postal survey)	17337 overlaps with (1)	19-94	San Diego HMO sample	1.29 (1.17–1.43) 1a 1.94 (1.73–2.16) 1b 1.80 (1.58–2.06) 1c	OR
Turner (227)	1 rape or attempt, sexual assault or fear of, forced unwanted sex, unwanted advances	a Cannabis use only b Multidrug use	SR (Postal survey)	9512	22-27	Females Australia National (ALSWH)	1.2 (1.0–1.4) 1a 1.7 (1.4–2.0) 1b	aOR
Dube (9)	1 Touch attempt or penetration < 18 with person ≥ 5 yrs older from ACE scale	a Drug use ≤ 14 years b Lifetime drug use	SR (Postal survey)	8613 overlaps with (1)	19-94	San Diego HMO sample	2.8 (2.1–3.7) 1a 2.0 (1.8–2.3) 1b	aOR
Coid (215)	Unwanted sex ± intercourse < 16 y controlling for other abuse and sexual assault >	Alcohol misuse	SR Survey (CAGE ≥ 2)	718	16-85	Females community medical sample UK	1.11 (0.63–1.97)	aOR

	16 years							
Nichols (228)	CSA assault, frequent exposure or fear ± physical abuse < 12 years	Smoking (> 100 cigarettes lifetime)	SR (Postal survey)	722	36-45	Females Massachusetts population sample	2.55 (1.46–4.48)	aOR
Bergen (229)	1 'Have you ever been sexually abused'? Single item	a Frequent alcohol use (≥ weekly) b Frequent marijuana use c Ever use inhalants, hallucinogens, stimulants, injected drugs	SR (In school survey)	2596	13-15	South Australia community sample	3.63 (2.75–4.78) 1a 4.61 (3.45–6.16) 1b 11.7 (8.91–15.4) 1c  <i>Pooled M &amp; F and across 3 time points</i>	OR
Libby (230)	1 CSA rape, unwanted sex, forced touch < 13 years	a Lifetime alcohol dependence b Lifetime drug dependence	Interview (CIDI)	3056	15-54	American Indians, 2 tribes	2.30 (1.08-4.89) 1a 4.18 (1.20-14.6) 1b <i>Pooled across tribes</i>	aOR
Bebbington (231)	1 Uncomfortable talk, non-consensual touch, touching, intercourse (232)	a Alcohol dependence past 6 month b Drug dependence past week	SR (SADQ)	8580	16–74	England National (APMS)	2.36 (1.5-3.6) 1a 1.84 (1.1-3.2) 1c	OR
Kaukinen (233)	1 CSA forced threatened intercourse, penetration or attempt < 14 or 14-19 y	a Current heavy episodic drinking b Current illicit drug use	Interview	7689	18-UUA	Females US National (NVAWS)	1.29 (0.96–1.73) 1a 2.55 (1.80–3.63) 1b <i>Pooled across child and adolescent CSA</i>	aOR
Young (234)	Touch attempt or penetration < 18 y with person ≥ 5 years older from ACE scale	Risky drinking past year	RAP survey	41482	18–20	US Marine Corps Recruits	1.55 (1.31–1.84)	OR
Hussey (188)	1 Touched forced to touch or forced sex by parents or other adult-care givers < 6 <sup>th</sup> grade	a Binge Drinking b Marijuana past month c Lifetime use of Inhalants	SR	10828	18-26	US National (Add Health)	1.6 p<0.05 1a 2.0 p<0.05 1b 1.7 p<0.05 1c	aOR
Nelson (235)	1 Forced sexual activity or intercourse < 18 y or sexual contact < 16 y w ≥ 5 y older extra-familial or adult familial or raped /molested	a Cannabis b Alcohol c Opioids d Sedatives e Stimulants f Cocaine Lifetime abuse or dependence	Interview (SSAGA)	6050	25-36	Australia National Twins	2.52 (1.97–3.21) 1a 2.19 (1.95–2.46) 1b 7.11 (3.68–13.8) 1c 9.80 (4.30–22.3) 1d 2.83 (1.85–4.34) 1e 2.03 (0.43–9.63) 1f <i>Pooled across all drugs</i> 3.04 (2.50–3.69)	aOR
Trent (236)	1 Familial touch or penetration or w someone older before 18 years	a Ever drank b Current drinker c Binge drinking d Alcohol arrest e Alcoholic MAST f Alcohol abuser	SR (CSEC, MAST)	5697	Mean 19.9	US Navy recruits (53% male)	2.07 (1.73–2.48) 1a 1.28 (1.10–1.49) 1b 1.54 (1.35–1.77) 1c 1.57 (1.25–1.98) 1d 1.80 (1.56–2.08) 1e 1.57 (1.35–1.83) 1f	aOR
Al Mamun (237)	1 Non-penetration (exposure, touch, touching) 2 Penetration (oral sex intercourse) < 16 y	a Lifetime nicotine dependence	SR (CIDI-Auto)	2150	21	South Brisbane Australia Hospital sample	2.08 (1.54-2.80) 1a 2.88 (1.99-4.16) 2a <i>Pooled across criteria</i> 2.37 (1.88–2.99) a	aOR

Timko (238)	Forced into unwanted sexual activity < 18 y	Binge drinking ( $\geq$ 5 drinks occasion) past month	Telephone Interview	6942	18-UUA	Females California (CWHS)	1.53 (1.21–1.92)	aOR
Roberts (239)	1 Forced sex w adult care-taker < 6 <sup>th</sup> grade	a Regular smoking past year b Lifetime ever regular smoking	Home Interview	15197 overlaps w (188)	18-26	US National (Add Health) Wave 3)	1.06 (0.68–1.66) 1a 1.43 (1.07–1.92) 1b	aOR
Hamburger (240)	1 Forced or unwanted sexual activity < 10 years	a Ever drink b Early alcohol use (< 13 years) c Heavy episodic drinking past year	SR (Youth Violence Survey)	3559	15-19	Hi Risk US school district in small city	1.87 (1.39-2.52) 1a 1.57 (1.16-2.14) 1b 1.70 (1.26-2.30) 1c	aOR
Duncan (241)	Raped, molested or forced sex < 16 years	Lifetime cannabis abuse or dependence	Interview (SSAGA)	819	15-29	US off-spring of twins (VETR)	2.81 (1.69–4.65)	OR
Afifi (190)	Intercourse or penetration w force or threat or unwanted touch < 16 y	Any substance abuse disorder lifetime	Interview (CIDI)	5142 F 4149 M	18-UUA	US National (NCS-R)	1.48 (1.07-2.03) F 1.45 (NS) M	aOR
Zlotnick (191)	1 Potentially traumatic childhood event including rape < 15 y v none	a Lifetime drug / alcohol disorder b Lifetime nicotine dependence	Interview (DIS) (CIDI)	2390	15-UUA	Chile National	3.0 (1.8-5.0) 1a 1.3 (0.5-3.2) 1b	aOR
Draper (194)	1 Victim of any sexual abuse $\pm$ physical abuse < 15	a Ever smoker b Current smoker c Harmful alcohol use > 4 drinks/day	Postal survey	21822	60-UUA	Australia, general medical practice	1.36 (1.23–1.51) 1a 1.95 (1.62–2.34) 1b 1.14 (0.91–1.42) 1c	aOR
Pederson (242)	1 Childhood sexual abuse (undefined)	a Nicotine Use b Marijuana Use c Cocaine Use <i>All Lifetime</i>	SR (Tel Quest)	811	18-59	Females Ohio convenience sample	1.91 (1.38-2.66) 1a 2.20 (1.53-3.17) 1b 1.63 (1.04-2.53) 1c	OR
Jun (243)	CSA forced touch or activity < 17	Smoking by age 14	Mailed survey	68107	37-54	Females US National (NHS)	1.6 (1.4–1.8)	aOR
Chartier (244)	1 Unwanted exposure, threats, touching attempted sex or attack w adult while “growing up”	a Current smoking b Alcohol abuse or dependence	SR (CIDI)	8116 overlaps w (34)	15-64	Ontario CA population sample (OHS)	1.52 (1.16–1.99) 1a 2.44 (1.74–3.44) 1b	aOR
Hayatbakhsh (245)	1 Pressured or forced to have unwanted sexual contact < 16	a Amphetamine use (ever) b Lifetime amphetamine use disorder	SR (CIDI-Auto)	2042 overlaps w (237)	21	South Brisbane Australia Hospital sample	1.82 (1.30–2.55) 1a 1.75 (1.18–2.58) 1b <i>Pooled ‘once-twice and 3 or more times’</i>	aOR
Ramiro (201)	1 Touch attempt or penetration < 18 with person $\geq$ 5 yrs older from ACE scale	a Current smoker b Early smoking c Driving drunk d Illicit drug use <i>Lifetime c &amp; d</i>	SR (ACE survey)	1068	35-92	Metro Manila, Philippines	1.9 (1.0–3.4) 1a 2.1 (1.0–4.7) 1b 1.7 (0.6–4.8) 1c 2.9 (1.4–5.9) 1d	aOR
Hughes (246)	1 Sexually assaulted, molested, raped or experienced unwanted sexual	a Alcohol abuse b Drug abuse <i>All past year</i>	Interview (AUDADIS-IV)	33487	20-UUA	US National (NESARC)	1.06 (0.81–1.38) 1a 1.73 (1.12–2.68) 1b <i>Pooled M &amp; F</i>	aOR

	activity < 18 y							
Derringer (247)	1 Sexual contact < 13 w anyone ≥ 5 y older or unwanted forced or threatened sexual contact < 16 years	a Alcohol abuse b Tobacco abuse c Cannabis abuse All lifetime history	Interview (CIDI substance abuse module)	841	25	Same sex twins Minnesota	0.98 (0.71-1.35) 1a 1.27 (0.87-1.85) 1b 1.15 (0.76-1.74) 1c	aOR
King (202)	Exposure, touch ± force, penetration or intercourse < 18 years	Any substance use disorder past 6 months	Interview (DISC)	1735	10-18	Cook County IL. Juvenile Detention Center stratified	2.64 (1.68-4.14) <i>Pooled sexual abuse ± severe physical abuse</i>	OR
Chu (248)	1 Sexual act perpetrated by adult or coercive sexual act by a peer < 14 years 2 unwanted contact, verbal coercion, rape or attempt high school	a Marijuana use in high school b Marijuana use in college (yr 2)	Interviews	1569	18-22	Females South-eastern US university sample	1.68 (1.12-2.52) 1a 2.03 (1.37-3.02) 2a 1.09 (0.74-1.61) 1b 1.13 (0.78-1.64) 2b  <i>Pooled &lt; 14 and high school CSA</i> 1.85 (1.39-2.46) a 1.11 (0.85-1.45) b	aOR
Vander Weg (249)	1 Touched 2 Forced to touch 3 Forced sex < 18 y from ACE scale	a Lifetime smoking b Current smoking	Telephone survey	10277	18-UUA	Arkansas Louisiana representative sample (BRFSS)	2.23 (1.96-2.52) a 2.02 (1.71-2.38) b  <i>Pooled across CSA exposure levels</i>	aOR
Huang (73)	1 CSA touch or forced sex < 6 <sup>th</sup> grade	a Use drugs past year b Use drugs past 30 days c Drug use problems	SR (In-Home Survey.)	4882 overlaps w (188, 239)	18-26	US National (Add Health)	1.01 (0.67-1.50) 1a 1.24 (0.81-1.90) 1b 1.78 (1.09-2.90) 1c	OR
Jonas (203)	1 Non-consensual touch 2 Non-consensual intercourse < 16 years	a Alcohol dependence past 6 months b Drug dependence past year	SR (AUDIT & SADQ-C)	7403	16-UUA	England National (APMS)	1.41 (0.94-2.1) 1a 3.71 (2.2-6.4) 2a 1.26 (0.7-2.3) 1b 5.49 (3.0-10.) 2b <i>Pooled exposure</i> 2.00 (1.45-2.76) a 2.61 (1.71-3.98) b	OR
Chou (206)	1 Non-consensual touch or intercourse < 16 years	a Alcohol dependence b Drug dependence. All past 6 months	Computer-assisted self interview	3493 overlaps with (203)	50-UUA	Middle-age or older England National (APMS)	1.50 (0.69-3.29) 1a 1.39 (0.38-5.10) 1b	OR
Fuller-Thomson (250)	Forced sex < 18 y by someone ≥ 5 years older from ACE scale	Lifetime smoking history	Telephone survey	19356	18-99	US 5 States (BRFSS)	1.54 (1.32-1.79)	aOR
<b>Prospective Studies</b>								
Widom (174)	Court substantiated abuse or neglect < 12 y	Current Alcoholism	SR (DIS)	1066	18-40	US, metropolitan Midwest, 22 yr follow-up	0.93 (0.69-1.25)	OR
Thornberry (213)	1 Substantiated maltreatment CPS (including	a Drug use b Alcohol-related problems	Interviews SR drug and	881 Early Adol	~13	Rochester NY stratified high-	2.12 (1.47-3.08) 1a Early adolescence 1.44 (0.99-2.10) 1a	aOR

	physical and sexual abuse; neglect; lack of supervision; moral, legal, and educational neglect; and emotional abuse)	during early or late adolescence	alcohol problems	818 Late Adol	18	risk study Early Adol Late Adol 3 yr follow-up	Late adolescence 2.02 (1.27–3.26) 1b Early adolescence 1.46 (0.90–2.29) 1b Late adolescence <i>Pooled outcome</i> 1.75 (1.35–2.28) 1a 1.71 (1.23–2.39) 1b	
Smith (251)	CSA from CPS 12-17 y subjects w early abuse only excluded	Drug use in late adolescents or early adulthood	SR (Survey)	884	16-18 20-22	Rochester NY, 9 year follow-up	1.99 (0.91–4.36)	aOR
Widom (252)	Court substantiated abuse or neglect < 12 years	a Marijuana b Cocaine c Heroin d Psychedelics <i>Past year use</i>	Interview (structured module for illicit drug use)	892 overlaps with (174)	30-47	US, metropolitan Midwest, ~ 30 yr follow-up	1.49 (1.10–2.02) 1a 1.21 (0.76–1.92) 1b 1.60 (0.14–17.7) 1c 2.42 (0.49–12.1) 1d <i>Pooled drug use</i> 1.42 (1.11–1.82)	OR
Lo (74)	1 Reported being victim of sexual attack during Waves 1-5.	a Current alcohol abuse b Current drug abuse	Interview	765	21-24	US National (NYS) Waves 1-5 & 7. 11 y follow-up	0.99 NS 1.93 NS	aOR
Fergusson (214)	1 Non-contact sexual activity 2 Contact w/o penetration 3 Penetration or attempt All < 16 years	a Substance dependence between 21-25 years	Interview (CIDI)	1001 overlaps with (179)	21-25	Christchurch, NZ 3 year follow-up	0.95 (0.28–3.20) 1a 0.66 (0.23–1.87) 2a 1.94 (1.02–3.69) 3a <i>Pooled CSA</i> 1.35 (0.82–2.22) a	OR
Cutajar (175)	1 Confirmed CSA < 16 y by records of the Victorian Inst of Forensic Medicine	a Lifetime alcohol abuse b Lifetime drug abuse	Diagnoses from the Victorian Psychiatric Case Registry	5365	33.82 ± 11.03	Victoria, Australia 12-43 year follow-up	5.88 (3.26–10.6) 1a 5.94 (3.68–9.58) 1b	OR

\*The number indicates which type of maltreatment and the letter indicates which clinical outcome the odds ratio applies to within a given study with multiple types of maltreatment or outcomes (e.g., Fergusson (179) 1a, 1 = Non-contact sexual activity, a = alcohol abuse or dependence).

ACE – Adverse Childhood Experience survey, Adol – adolescence, ALSWH - Australian Longitudinal Study on Women’s Health, aOR – adjusted odds ratio, APMS – Adult Psychiatric Morbidity Survey, AUDADIS-IV - Alcohol Use Disorders and Associated Disabilities Interview Schedule DSM-IV, AUDIT - Alcohol Use Disorders Identification Test, BRFSS - Behavioral Risk Factor Surveillance System, CIDI - World Health Organization Composite International Diagnostic Interview, CSA – childhood sexual abuse, CSEC - Childhood Sexual Experiences Checklist, CWHs - California Women's Health Survey, DIS - Diagnostic Interview Schedule, DISC – Diagnostic Interview Schedule for Children, MAST – Michigan Alcoholism Screening Test, NCS-R – National Comorbidity Survey – Replication, NESARC – National Epidemiologic Survey on Alcohol and Related Conditions, NLSAH - National Longitudinal Study of Adolescent Health, NHS - Nurses Health Survey, NVAWS - Violence and Threats of Violence against Women and Men in the United States Survey, OHS – Ontario Health Survey, OR - raw odds ratio, RAP - Recruit Assessment Program, SADQ - Severity of Alcohol Dependence Questionnaire, SR – self report, SSAGA - Semi-Structured Assessment for the Genetics of Alcoholism, US – United States of America, UJA – unspecified upper age, VETR – Vietnam Era Twin Registry, w – with, wo – without, y - years

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