



Colledge, S., Larney, S., Peacock, A., Leung, J., Hickman, M., Grebely, J., Farrell, M., & Degenhardt, L. (2020). Depression, post-traumatic stress disorder, suicidality and self-harm among people who inject drugs: A systematic review and meta-analysis. *Drug and Alcohol Dependence*, 207, [107793].
<https://doi.org/10.1016/j.drugalcdep.2019.107793>

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[10.1016/j.drugalcdep.2019.107793](https://doi.org/10.1016/j.drugalcdep.2019.107793)

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1 **Depression, post-traumatic stress disorder, suicidality and self-harm among**
2 **people who inject drugs: a systematic review and meta-analysis¹**

3

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13 Word count: 2250

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¹ Supplementary material can be found by accessing the online version of this paper at <http://dx.doi.org> and by entering doi:

17 **Abstract**

18 *Background:* A range of negative experiences and circumstances that are common among people who
19 inject drugs (PWID) are risk factors for developing mental disorders. Despite this, there has been no
20 systematic review of the prevalence of mental health indicators among PWID. Thus, we aimed to
21 estimate the prevalence of depression, post-traumatic stress disorder (PTSD), suicidality and self-
22 harm among PWID.

23 *Methods:* We searched the peer-reviewed and grey literature for data on depression, PTSD, suicidality
24 and non-suicidal self-harm among PWID from sources published from 2008-2018. We pooled
25 estimates of depression and suicidality using random-effects meta-analysis and provided a narrative
26 summary of estimates of PTSD and self-harm.

27 *Findings:* We found 23 studies that reported on these mental health indicators among PWID. The
28 pooled estimate for current severe depressive symptomology was 42.0% (95% confidence interval
29 [CI] = 21.3, 62.8%), and for a depression diagnosis was 28.7% (95% CI = 20.8, 36.6%). With much
30 variation, the pooled lifetime prevalence of a suicide attempt was 22.1% (95% CI = 19.3, 24.9%).
31 There were only two studies each that reported on PTSD and non-suicidal self-harm among PWID.

32 *Interpretation:* Recent data investigating these mental health indicators among PWID was limited,
33 particularly from low- and middle-income countries. Even so, estimates were high and call for further
34 research into the epidemiology of such mental health disorders and self-harming behaviours, as well
35 as the promotion of integrated mental health and substance dependence treatment. Finally,
36 incorporating suicide prevention strategies into services accessed by PWID must be considered as a
37 harm reduction priority.

38 *Keywords:* Mental health, depression, suicide, people who inject drugs, injecting drug use, PTSD,
39 self-harm.

40

41 **1. Introduction**

42 Mental disorders, including depression and self-harm, are a major source of morbidity and mortality
43 worldwide (Vigo et al., 2016; WHO, 2013, 2017). It is common for people who inject drugs (PWID)
44 to be exposed to distressing circumstances, such as unstable housing, unemployment, legal problems,
45 physical injury or disease (Degenhardt et al., 2017; Havens et al., 2006; Larney et al., 2017; Milloy et
46 al., 2008; Richardson et al., 2014; Richardson et al., 2010), as well as having experienced traumatic
47 events such as childhood maltreatment and stigma (Darke and Torok, 2013; Wilson et al., 2014). Such
48 events, particularly in combination, may increase the risk of mental disorders among this population.

49 Although injecting drug use is not necessarily indicative of substance use disorders, their comorbidity
50 with mental health problems can elevate the risk of poor mental, physical and behavioural outcomes
51 in PWID (Bartoli et al., 2014; Darke and Torok, 2013; Lemstra et al., 2011; Mills et al., 2006;
52 Plotzker et al., 2007; Teesson et al., 2015). For example, depression is consistently associated with a
53 higher prevalence of overdose, injecting-related injuries and diseases, and sharing injecting equipment
54 among PWID (Lemstra et al., 2011; Teesson et al., 2015). Considering this, better evidence is needed
55 to inform integrated treatment services and address the mental health needs of PWID.

56 There has been no systematic review of the evidence of mental health indicators among PWID. This
57 paper aimed to synthesise the existing literature on the prevalence of mental health problems among
58 PWID, specifically: depression, post-traumatic stress disorder (PTSD), suicidal thoughts, plans and
59 attempts, and non-suicidal self-harm.

60

61 **2. Methods**

62 This systematic review uses data gathered for a previous review (PROSPERO registration numbers
63 CRD42016052858 and CRD42016052853) investigating sociodemographic and risk characteristics of
64 PWID. Details of the methodology have been described elsewhere (Degenhardt et al., 2017).
65 Adhering PRISMA and GATHER guidelines (Appendix 1-2²) we searched peer-reviewed (Medline,
66 Embase, and PsycINFO) and grey literature, and online databases for data published from January
67 2008-June 2018 (see Appendix 3-4²). We then circulated data requests to international experts and
68 agencies.

69 Two researchers provided independent screening, and conflicts were resolved by a third reviewer. We
70 included all studies providing sociodemographic or risk characteristics, or reporting on blood borne
71 viruses, overdose, mental health, or injecting related injuries and diseases among PWID, and did not
72 limit the search results by language. Studies were excluded if they:

- 73 a) had fewer than 40 participants;
- 74 b) limited participants on key outcomes except for treatment status (e.g. gender, age, HIV status,
75 prison status etc.); or
- 76 c) were a follow-up study of a previously recruited sample (e.g. cohort studies).

77 Suicide, self-harm, depression and PTSD data were included in this review. Where two studies
78 provided data on the same sample, the study with the most complete reporting on the variables of
79 interest was retained. Study quality was assessed using previously developed grading systems of
80 methodology and literature type (Mathers et al., 2008) (see Appendix 5²).

81 The studies that met inclusion criteria for this paper were those that reported on experience of suicide
82 attempt, suicide plan, suicidal thoughts, and non-suicidal self-harm (past month/current, 6 months, 12
83 months and lifetime). Self-report measures were used as there were no studies that reported using a
84 validated scale. Also, studies that assessed current depression, or depressive symptomology, and

² Supplementary material can be found by accessing the online version of this paper at <http://dx.doi.org> and by entering doi:

85 PTSD using validated screening scales or diagnostic interviews (i.e. any peer-reviewed
86 scales/inventories with publications supporting their validity and reliability) were included. We did
87 not limit the validated screening scales in the extraction phase, although studies that reported self-
88 report depression or PTSD (i.e. answering yes to “have you been diagnosed with depression/PTSD”)
89 were excluded due to low validity. Although definitions of current or active PWID differ between
90 studies, we define PWID as those who have injected drugs within the previous 12 months for this
91 review.

92 To generate a pooled estimate of the prevalence of depression, and the proportion who had attempted
93 suicide, we ran a random-effects meta-analysis in STATA 15 using the ‘metan’ command. For studies
94 that reported depressive symptomology by severity, we categorised estimates to reflect mild to severe,
95 moderate to severe, and severe symptomology. Estimates from studies that used measures to diagnose
96 participants with major depressive disorder (MDD) were pooled separately. Studies providing
97 estimates of suicide attempts among PWID were pooled by timeframe (12 months and lifetime).

98

99 3. Results

100 Of 61,077 studies and reports, screened for eligibility for the original review, information on
101 characteristics and harms among PWID was extracted from 1,381 sources. Among those, there were
102 22 eligible studies of depression, PTSD, suicidality or non-suicidal self-harm (see flowchart in
103 Appendix 6³). Nearly all (n=20) included studies were peer-reviewed journal articles (Table 1). There
104 were 39 estimates, and most were from samples recruited in one city (n=20), while six were recruited
105 from multiple geographical sites across a country.

106 3.1. Depression

107 From 12 studies, there were five different inventories used to measure depression or depressive
108 symptomology: the Center for Epidemiologic Studies Depression Scale (CES-D; n=4), the Patient
109 Health Questionnaire (PHQ-9; n=3), the Mini International Neuropsychiatric Interview (MINI; n=2),
110 the John Hopkins symptoms checklist for anxiety and depression (n=2), and the Depression Anxiety
111 Stress Scale 21 (DASS-21; n=1).

112 Among PWID, 28.7% (95% confidence intervals [CI] = 20.8, 36.6%; $I^2 = 91.5%$) met diagnostic
113 criteria for MDD (Figure 1). Four estimates representing PWID sampled from Tanzania, the United
114 States, and Australia were pooled to generate this estimate (see study details in Table 1). An estimated
115 42.0% (95%CI = 21.3, 62.8%; $I^2 = 99.1%$) of PWID screened as having 'severe' depressive
116 symptomology. Estimates ranged from 17.3% (95%CI = 13.9, 21.2%) (Armstrong et al., 2013b) to
117 75.1% (95%CI = 69.3, 80.3%) (Li et al., 2015) from five different studies in India, the United States,
118 New Zealand, Canada and China.

119 The prevalence of moderate to severe depressive symptomology among PWID was estimated to be
120 59.7% (95%CI = 42.7, 76.8%; $I^2 = 99.6%$), derived from seven estimates from six countries. Finally,
121 the pooled mild to severe depression estimate was 78.0% (95%CI = 66.1, 89.8%; $I^2 = 97.4%$), which
122 included samples of PWID from the United States, New Zealand, Canada and China. Although the
123 range in the estimates was notably smaller when pooling mild to severe depression, with the lowest

³ Supplementary material can be found by accessing the online version of this paper at <http://dx.doi.org> and by entering doi:

124 and highest point estimates being 25.3 percentage points apart ($I^2=97.4\%$), there was less
125 heterogeneity when pooling the MDD estimates ($I^2=91.5\%$).

126 3.2. *Suicidality*

127 There were 11 studies that included data on self-reported suicide attempts among PWID across four
128 different time frames, comprising past month ($n=1$), past 6 months ($n=2$), past 12 months ($n=5$) and
129 lifetime ($n=4$) (Figure 1). Estimates of past year attempted suicide among PWID ranging from 3.0%
130 (95%CI = 1.4, 5.6%) from an Australian sample (Darke and Torok, 2013) to 36.2% (95%CI = 31.8,
131 40.9%) among an Indian sample (Armstrong et al., 2013b). Estimates of lifetime suicide attempts
132 were less heterogenous ($I^2=34.2\%$), resulting in a pooled estimate of 22.1% (95%CI = 19.3, 24.9%)
133 and a range of 20.0% (95%CI = 17.6, 22.6%; (Backmund et al., 2011)) to 25.7% (95%CI = 20.8,
134 31.0%; (Darke and Torok, 2013)).

135 Only five studies reported on suicidal thoughts ($n=5$) or planning ($n=2$) (Appendix 7⁴). Estimates of
136 suicidal thoughts were high, with three studies reporting estimates of over 40% within the previous
137 year (Slovenia, past 12 months: 41.0% (Reitox National Focal Point, 2010); Puerto Rico, past 6
138 months: 43.8% (Zerden et al., 2010); and India, past 12 months 53.1% (Armstrong et al., 2013b)).

139 3.3. *Non-suicidal self-harm*

140 Due to the small numbers of studies we were unable to pool the PTSD or non-suicidal self-harm data.
141 There were two Australian studies that investigated non-suicidal self-harm among PWID. Among
142 those recruited from a supervised injecting facility in Sydney, Australia, the most recent estimate of
143 lifetime engagement in non-suicidal self-harm was 13.0% (KPMG, 2010). In the second study, Darke
144 and Torok (2013) found nearly one in four PWID recruited from needle syringe programs in Sydney,
145 Australia had ever engaged in non-suicidal self-harm (23.7%) and nearly one in ten had done so in the
146 previous year (8.0%).

⁴ Supplementary material can be found by accessing the online version of this paper at <http://dx.doi.org> and by entering doi:

147 3.4. PTSD

148 Two studies that met inclusion criteria reported clinically assessed PTSD among PWID. Using the

149 MINI inventory, a study in the United States reported a prevalence of 14.8% (Havens et al., 2013).

150 The second study from an Australian sample found that 42.0% scored >3 on the Primary Care PTSD

151 (PC-PTSD) screening tool, indicating “possible presence” of PTSD (Larance et al., 2015).

152

153

154 **4. Discussion**

155 *4.1 Main findings*

156 To our knowledge, this is the first systematic review synthesising the recent evidence of depression,
157 PTSD, suicidality and non-suicidal self-harm among PWID. We estimated that over half of PWID had
158 moderate to severe depressive symptomology, and one in six had attempted suicide in the previous
159 year. Our results call for further investigation to expand our global understanding of the prevalence of
160 mental health disorders and self-harming behaviours among PWID.

161 *4.2. Implications*

162 Studies among the general population have found that less than 1% had attempted suicide in the
163 previous year and less than 3% had ever attempted suicide (Borges et al., 2010; Bromet et al., 2017).

164 Our review found that estimates of recent attempts were as high as one third in samples of PWID
165 from Taiwan and India (Armstrong et al., 2013b; Lee et al., 2011). Considering previous suicide
166 attempts are associated with future fatal and non-fatal attempts (Borges et al., 2000), as well as
167 morbidity relating to the method used (Dunn and Lopez, Updated 2019 Jul 3; Warner-Smith et al.,
168 2002), there is substantial opportunity for intervention within this group. The scale up of suicide
169 prevention strategies targeting PWID must be considered in order to reduce the risk of suicide
170 fatalities.

171 Around 5% and 0.3% of the population are estimated to have current MDD and PTSD, respectively
172 (Baxter et al., 2014a; Baxter et al., 2014b). We found that among PWID these estimates are many
173 magnitudes higher. There is ample evidence that mental health and substance use comorbidities
174 contribute to poorer prognosis on health outcomes and extensive morbidity and mortality (Allsop,
175 2008). Integrating mental health and substance dependence treatment with a multifaceted approach
176 has been widely considered best practice (Roberts et al., 2015; Torrens et al., 2012). Although there
177 are several models that have been developed, a review found that including a harm reduction
178 approach (e.g. discouraging abstinence only conditions and providing access to sterile needles and
179 syringes) was an important element to be considered in integrated mental health and substance
180 dependence treatment (Mueser and Gingerich, 2013).

181 *4.3. Limitations*

182 We noted several limitations. Firstly, there were few studies, particularly for non-suicidal self-harm
183 and PTSD, that met our inclusion criteria. We know that data on mental health indicators has been
184 researched extensively in conjunction with substance use disorders; however, compared to people
185 with substance dependence that do not inject, PWID have been found to have an elevated risk of
186 depression and suicidality (Cepeda et al., 2012; Darke and Kaye, 2004). Depression, PTSD and
187 suicidality are also associated with engaging in injecting risk behaviours, increasing the likelihood of
188 contracting blood borne viruses (Armstrong et al., 2013a; Mackesy-Amiti et al., 2014; Plotzker et al.,
189 2007). Future research monitoring the prevalence of psychiatric comorbidities among PWID is
190 important for informing harm reduction and treatment strategies that respond to major mental and
191 physical health issues.

192 Much of the available data was from high-income countries. The lack of data investigating self-
193 harming behaviours among people who use drugs in low- and middle-income countries, where 75% of
194 suicides occur (World Health Organization (WHO), 2014), has been highlighted in a recent review
195 (Breet et al., 2018). Updated epidemiological research investigating these harms, globally, remain
196 important for measuring our progress in improving outreach of intervention strategies and reducing
197 self-harming behaviour.

198 Several screening scales and inventories were used to measure depression, and cut-off scores of
199 severities were not always consistent. Therefore, variability in our results might be explained by the
200 differences in these inventories or the cut-off scores used. We found that most inventories were
201 measuring current depressive symptomology, compared to diagnosing MDD. There were too few
202 studies to undertake meta-regressions exploring associations between inventories and depression
203 prevalence; however, we found that among the few MDD estimates there was less heterogeneity than
204 the scales measuring severe depressive symptomology.

205 Finally, there is a lack of data that is representative of diverse geographical regions. Notably, two
206 studies set in India using the same scale to measure (moderate to severe) depression found a 51-
207 percentage point difference in estimates (Armstrong et al., 2013b; Sabri et al., 2017). The higher

208 estimate sampled male PWID from one city (Delhi), while the lower estimate was a sample of both
209 men and women recruited from 15 cities. The latter is an example of incorporating mental health
210 screening in large-scale, routine surveillance data collection and could be employed by more national-
211 level research to better inform our global understanding of mental health in PWID (WHO, 2016).

212 *4.4. Conclusion*

213 We estimate that perhaps one in three PWID has been diagnosed with depression and one in four had
214 ever attempted suicide. There were few studies identified and were primarily from high-income
215 countries. Results call for further research examining the prevalence of mental health indicators
216 among PWID and for the availability of integrated mental health and substance dependence treatment
217 and interventions.

218

219

Table 1: Study-level information for estimates of depression, post-traumatic stress disorder (PTSD), suicide attempts, and non-suicidal self-harm among people who inject drugs (PWID)

Country	Geographical region	Study year	Literature grade	Method grade	Sample description	Measure	Sample size (N)	Case/Score	Estimate (%)	Reference
Depression										
Australia	Sub-national	2014	A1	A	Recruited people who tampered with pharmaceutical opioids	PHQ-9	606	Moderate to severe (score ≥ 10)	61.0	(Larance et al., 2015)
Australia	City	2004	A1	A	People who inject drugs (PWID) recruited from needle-syringe programs (NSPs) and a primary health center	MINI	103	Mood disorder diagnosis	49.5	(Gibbie et al., 2011)
Canada	City	2010	A2	B1	Set in Saskatoon, a region with a high prevalence of indigenous/First Nations people. Nearly 90% of the sample were Aboriginal (First Nations, Metis or Inuit)	CES-D	603	Mild to severe (score ≥ 16) Severe (score ≥ 23)	81.4 57.7	(Lemstra et al., 2011)
China	City	2013	A1	B1	People who primarily inject heroin recruited from three different NSPs	CES-D	257	Mild to severe (score ≥ 16)	93.4	(Li et al., 2015)
								Moderate to severe (score ≥ 21)	86.4	
								Severe (score ≥ 25)	75.1	
India	National	2013	A1	B1	PWID recruited from 15 cities around India	PHQ-9	6449	Moderate to severe (score ≥ 10)	33.5	(Sabri et al., 2017)
India	City	2012	A1	B1	Men who inject drugs who are not enrolled in treatment	PHQ-9	450	Moderate to severe (score ≥ 15)	84.4	(Armstrong et al., 2013b)
								Severe (score ≥ 20)	17.4	
New Zealand	National	2015	A1	A	PWID recruited from NSPs and pharmacies	DASS-21	225	Mild to severe (score ≥ 10)	68.4	(Hay et al., 2017)
								Moderate to severe (score $\geq \text{NR}^*$)	54.2	
								Severe (score $\geq \text{NR}$)	32.0	
Tanzania	City	2012	A1	C	People who were enrolled in a methadone program recruited from Muhimbili National Hospital	John Hopkins Symptoms Checklist for Depression -25	400	Depression diagnosis	22.0	(Lambdin et al., 2013)
Tanzania	City	2013	A1	C	People who were enrolled in a methadone program recruited	John Hopkins Symptoms Checklist for Depression -25	629	Depression diagnosis	23.0	(Lambdin et al., 2014)

Country	Geographical region	Study year	Literature grade	Method grade	Sample description	Measure	Sample size (N)	Case/Score	Estimate (%)	Reference
					from Muhimbili National Hospital					
Ukraine	Sub-national	2015	A1	A	People who were diagnosed with ICD-10 opioid use disorder	CES-D	1613	Moderate to severe (score ≥ 10)	53.2	(Marcus et al., 2017)
United States	Sub-national	2012	A1	A	PWID recruited through respondent driven sampling (RDS)	CES-D	454	Mild to severe (score \geq NR) Moderate to severe (score \geq NR) Severe (score \geq NR)	68.1 45.4 28.2	(Grau et al., 2016)
United States	Sub-national	2010	A1	B1	PWID recruited from Appalachian, Kentucky	MINI version 5.0	392	Severe: Major depressive disorder diagnosis	28.1	(Havens et al., 2013)
PTSD										
Australia	Sub-national	2014	A1	A	People who tampered with pharmaceutical opioids	PC-PTSD	606	Possible presence of PTSD: Score >3	42.0	(Larance et al., 2015)
United States	Sub-national	2010	A1	B1	PWID recruited from Appalachian, Kentucky	MINI version 5.0	392	DSM-IV PTSD diagnosis	14.8	(Havens et al., 2013)
Suicide						Timeframe		Definition		
Taiwan	Sub-national	2008	A1	B1	People who had recently used heroin and were on methadone maintenance therapy, recruited from four different clinics	Month	523	Attempted suicide	32.7	(Lee et al., 2011)
Canada	City	2011	A1	B1	Street-recruited PWID	6 months	1240	Attempted suicide	5.7	(Artenie et al., 2015)
India	Sub-national	2006	A1	C	Male PWID who were mostly unstably housed (89.0%)	6 months	449	Attempted to take your own life	4.2	(Sarin et al., 2013)
Australia	City	2012	A1	B1	PWID recruited through NSPs who were injecting weekly or more frequently	12 months Lifetime	300	Deliberate self-harm with the intention of causing death	3.0 25.7	(Darke and Torok, 2013)
Canada	City	2013	A1	B1	PWID recruited using RDS	12 months	272	Attempted suicide	7.7	(Shaw et al., 2015)
India	City	2012	A1	B1	Men who inject drugs who are not enrolled in treatment	12 months	450	Attempted suicide	36.3	(Armstrong et al., 2013b)
Puerto Rico	National	2007	A1	B1	PWID recruited using RDS	12 months	124	Attempted suicide	27.4	(Zerden et al., 2010)
Slovenia	National	2008	B2	B1	Data collected from PWID through 10 low-threshold programs	12 months	107	Tried to commit suicide	11.2	(Reitox National Focal Point, 2010)
Germany	City	1997	A1	C	PWID requiring heroin detoxification recruited from a tertiary hospital	Lifetime	1049	Deliberate self-harm with the intention of causing death	20.0	(Backmund et al., 2011)
Nepal	Sub-national	2013	A1	A	PWID recruited from treatment settings	Lifetime	300	Attempted suicide	23.0	(Ojha et al., 2014)

Country	Geographical region	Study year	Literature grade	Method grade	Sample description	Measure	Sample size (N)	Case/Score	Estimate (%)	Reference
Sweden	City	2009	A1	C	PWID recruited using RDS	Lifetime	68	Suicide attempt	22.1	(Hakansson et al., 2012)
Self-harm										
Australia	City	2012	A1	B1	PWID recruited through NSPs who were injecting weekly or more frequently	12 months	300	Non-suicidal self-harm was defined as the deliberate destruction of body tissue without conscious suicidal intent	8.0	(Darke and Torok, 2013)
						Lifetime			23.7	
Australia	City	2010	B3	C	New entrants to the Medically Supervised Injecting Centre in Kings Cross, Sydney	Lifetime	687	Deliberate self-harm	12.9	(KPMG, 2010)
		2009					813		13.9	
		2008					784		9.8	

Note: CES-D: Center for Epidemiologic Studies Depression Scale; DASS-21: Depression Anxiety Stress Scale 21; DSM: Diagnostic and Statistical Manual of Mental Disorders; ICD-10: 10th revision of the International Statistical Classification of Diseases and Related Health Problems; MINI: Mini International Neuropsychiatric Interview; NR: Not reported; NSP: Needle-syringe exchange programs; PHQ-9: Patient Health Questionnaire; PC-PTSD: Primary Care PTSD screen; RDS: Respondent-driven sampling. Literature and method grading systems are in Appendix 3⁵.

⁵ Supplementary material can be found by accessing the online version of this paper at <http://dx.doi.org> and by entering doi:

Figure 1.

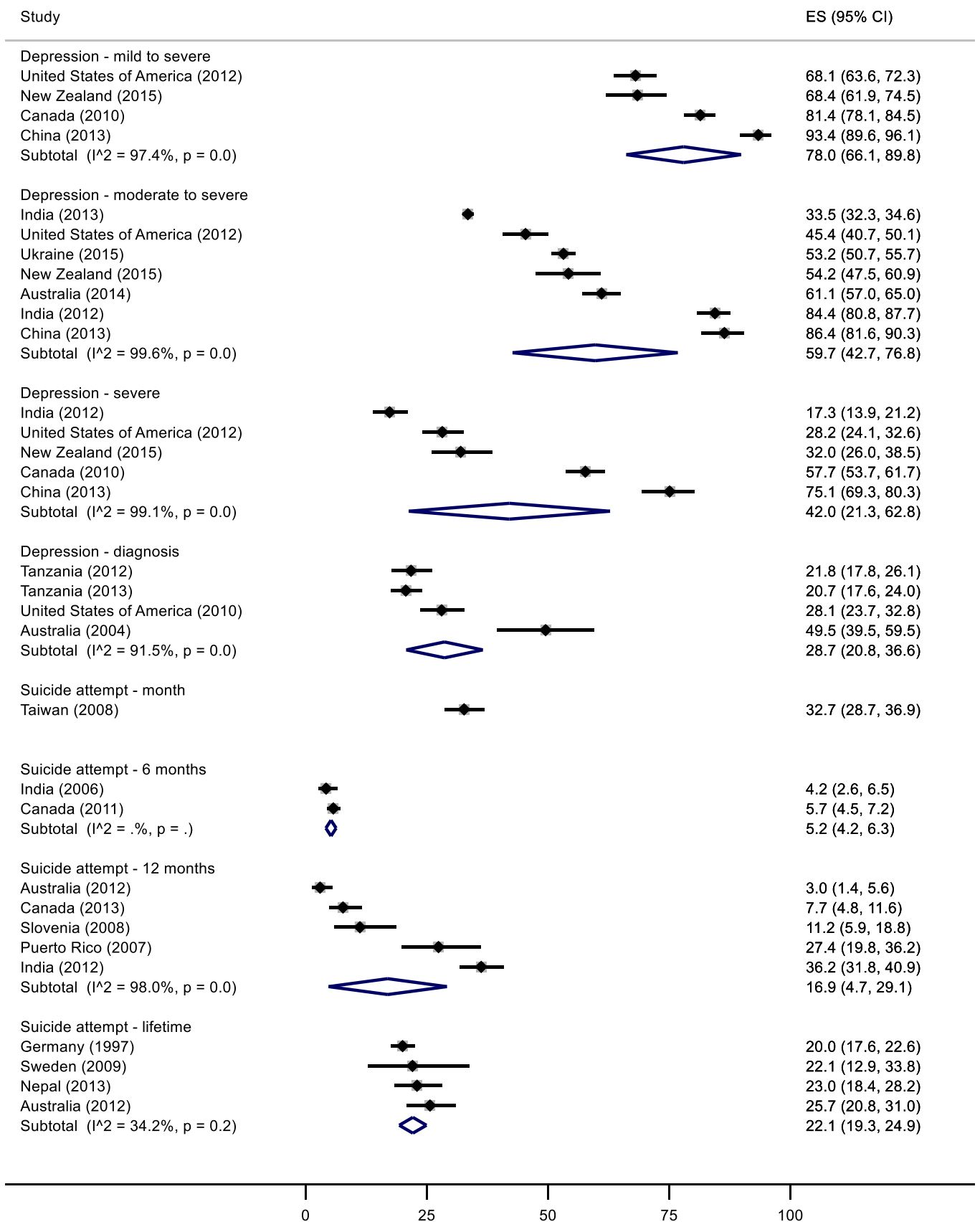


Figure Legend

Figure 1. Prevalence of depression and depressive symptomology, and estimates of suicide attempts among people who inject drugs (PWID) by severity and timeframe

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