

## Childhood adversity

### Introduction

Childhood adversities encompass a range of childhood experiences, including loss of a close relative, parental separation, bullying, physical abuse, sexual abuse, emotional abuse, and neglect. The nature, timing, severity, and duration of exposure are likely to influence mental health, however any evidence that childhood adversity directly causes psychosis or schizophrenia is controversial. Firstly, psychotic disorders may be secondary to comorbid affective, substance use, personality, or post-traumatic stress disorders, all of which have been linked to early adversities and all of which are common in those with a psychotic mental illness. Another difficulty is accurately measuring childhood adversity, as it is dependent on assessment of the experiences via information collected retrospectively. This is particularly problematic if having a psychotic disorder impacts on memory recall. This summary of evidence table contains reviews that have attempted to summarize the evidence pertaining to childhood adversity as a risk factor for schizophrenia, however the limitations outlined above should be taken into consideration when interpreting the evidence. Further, the studies also include patients with other psychotic disorders such as psychotic depression.

### Method

We have included only systematic reviews with detailed literature search, methodology, and inclusion/exclusion criteria that were published in full text, in English, from the year 2000. Reviews were identified by searching the databases MEDLINE, EMBASE, and PsycINFO. Reviews with pooled data are prioritized for inclusion. Reviews reporting fewer than 50% of items on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses ([PRISMA](#)<sup>1</sup>) checklist have been excluded from the library. The evidence was graded guided by the Grading of Recommendations Assessment, Development and Evaluation ([GRADE](#)) Working Group approach<sup>2</sup>. The resulting table represents an

objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

### Results

We found 21 systematic reviews that met our inclusion criteria<sup>3-23</sup>.

- Moderate to high quality evidence found a small to medium-sized increased risk of psychotic disorders following exposure to childhood adversities (abuse, neglect, bullying, parental loss) compared to people without exposure to childhood adversity.
- Rates of childhood sexual abuse in people with psychosis was approximately 26.3%, childhood physical abuse was approximately 38.8%, and childhood emotional abuse was approximately 34%. Rates were highest in older studies, in studies with more females, in studies with older patients, and in studies of patients with comorbid substance abuse.
- Moderate to high quality evidence found exposure to any childhood adversity was associated with more severe symptom severity. For positive symptoms, there were small associations with sexual abuse, physical abuse, emotional abuse, and emotional neglect, and no association with physical neglect. For negative symptoms, there were small associations with sexual abuse, physical abuse, physical neglect, and emotional neglect, and no association with emotional abuse. For depression, there were small to medium-sized associations with sexual abuse, physical abuse, emotional abuse, emotional neglect, and physical neglect. Women showed greatest effects on depression severity. For mania symptoms, there was a small association with sexual abuse only.
- Moderate quality evidence found a large increased rate of emotional abuse, a medium increased rate of physical abuse and a small increased rate of sexual abuse in people at clinical ultra-high risk of psychosis than in people without high-risk of

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psychosis. There were no differences in rates of emotional or physical neglect between these groups.

- Compared to people with anxiety disorders, there was a medium-sized increased risk of childhood adversity in people with schizophrenia. Compared to people with dissociative disorders or post-traumatic stress disorder, there is a large decreased risk of childhood adversity in people with schizophrenia. There were no differences in rates of childhood adversity between schizophrenia and depressive disorders, including affective psychosis.
- Moderate to high quality evidence finds small significant associations between childhood adversity and poorer treatment outcomes and poorer overall cognition.
- Moderate to low quality evidence finds mediation and moderating effects of other life events and stressors, social defeat, loneliness, and social support on the relationship between childhood adversity and psychosis. Mediation, but not moderating effects were found for negative cognitive schemas about the self, the world, and others, attachment style and parental bonding, mood symptoms, emotional dysregulation, PTSD, and dissociation. Mediators are mechanisms through which the relationship may be explained. Moderators were factors that changed the relationship.

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*Alameda L, Christy A, Rodriguez V, Salazar de Pablo G, Thrush M, Shen Y, Alameda B, Spinazzola E, Iacoponi E, Trotta G, Carr E, Ruiz Veguilla M, Aas M, Morgan C, Murray RM*

**Association Between Specific Childhood Adversities and Symptom Dimensions in People With Psychosis: Systematic Review and Meta-Analysis**

Schizophrenia Bulletin 2021; 47(4): 975-985

[View review abstract online](#)

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| <p><b>Comparison</b></p>  | <p>Association between childhood adversities and symptom severity in people with psychotic disorders (schizophrenia, schizophreniform, and schizoaffective disorder, also brief psychotic episode, bipolar disorder with psychotic features, major depression with psychotic features, and psychosis not otherwise specified).</p>  |
| <p><b>Summary of evidence</b></p>   | <p>Moderate to high quality evidence (large samples, some inconsistency, precise, direct) finds childhood adversity in general is associated with more severe symptom severity.</p> <p>For positive symptoms, there were small associations with sexual abuse, physical abuse, emotional abuse, and emotional neglect, and no association with physical neglect.</p> <p>For negative symptoms, there were small associations with sexual abuse, physical abuse, physical neglect, and emotional neglect all increased severity, and no association with emotional abuse.</p> <p>For depression, there were small-medium associations with sexual abuse, physical abuse, emotional abuse, emotional neglect, and physical neglect. Women showed greater effects than men.</p> <p>For mania, there was a small association with sexual abuse, and no associations with physical abuse, emotional abuse, emotional neglect, or physical neglect.</p> <p>For disorganised symptoms, limited data showed no association with sexual abuse.</p> |
| <p><b>Positive symptom severity</b></p>   |   |
| <p><i>Small associations were found between increased positive symptom severity and:</i></p> <p>All adversity: 27 studies, N = 4,762, <math>r = 0.16</math>, 95%CI 0.12 to 0.20, <math>p &lt; 0.001</math>, <math>I^2 = 39%</math>, <math>p = 0.021</math></p> <p>Sexual abuse: 16 studies, N = 2,588, <math>r = 0.14</math>, 95%CI 0.08 to 0.19, <math>p &lt; 0.001</math>, <math>I^2 = 42%</math>, <math>p = 0.035</math></p> |   |

Physical abuse: 13 studies, N = 2,260,  $r = 0.15$ , 95%CI 0.09 to 0.21,  $p < 0.001$ ,  $I^2 = 41%$ ,  $p = 0.064$

Emotional abuse: 11 studies, N = 1,580,  $r = 0.16$ , 95%CI 0.07 to 0.25,  $p < 0.01$ ,  $I^2 = 70%$ ,  $p < 0.0001$

Emotional neglect: 12 studies, N = 1,663,  $r = 0.10$ , 95%CI 0.01 to 0.18,  $p = 0.021$ ,  $I^2 = 66%$ ,  $p < 0.01$

*There was no significant association with;*

Physical neglect: 10 studies, N = 1,151,  $r = 0.06$ , 95%CI -0.01 to 0.14,  $p = 0.124$ ,  $I^2 = 44%$ ,  $p = 0.065$

### **Negative symptom severity**

*Small associations were found between increased negative symptom severity and;*

All adversity: 25 studies, N = 4,562,  $r = 0.09$ , 95%CI 0.05 to 0.13,  $p < 0.001$ ,  $I^2 = 34%$ ,  $p = 0.049$

Sexual abuse: 16 studies, N = 2,097,  $r = 0.04$ , 95%CI 0.00 to 0.09,  $p = 0.037$ ,  $I^2 = 25%$ ,  $p = 0.172$

Physical abuse: 14 studies, N = 2,455,  $r = 0.08$ , 95%CI 0.03 to 0.14,  $p = 0.002$ ,  $I^2 = 44%$ ,  $p = 0.041$

Physical neglect: 10 studies, N = 1,151,  $r = 0.13$ , 95%CI 0.07 to 0.18,  $p < 0.001$ ,  $I^2 = 0%$ ,  $p = 0.78$

Emotional neglect: 11 studies, N = 1,580,  $r = 0.13$ , 95%CI 0.08 to 0.18,  $p < 0.001$ ,  $I^2 = 0%$ ,  $p = 0.972$

*There was no significant association with;*

Emotional abuse: 12 studies, N = 1,680,  $r = 0.03$ , 95%CI -0.08 to 0.15,  $p = 0.568$ ,  $I^2 = 84%$ ,  $p < 0.001$

### **Disorganised symptom severity**

*A small association was found between increased disorganised symptom severity and;*

All adversity: 7 studies, N = 967,  $r = 0.09$ , 95%CI 0.03 to 0.15,  $p = 0.003$ ,  $I^2 = 0%$ ,  $p = 0.679$

*There was no significant association with;*

Sexual abuse: 3 studies, N = 375,  $r = 0.10$ , 95%CI -0.04 to 0.24,  $p = 0.157$ ,  $I^2 = 39%$ ,  $p = 0.197$

### **Depression symptom severity**

*Small to medium associations were found between increased depression symptom severity and;*

All adversity: 13 studies, N = 2,750,  $r = 0.24$ , 95%CI 0.15 to 0.34,  $p < 0.001$ ,  $I^2 = 82%$ ,  $p < 0.001$

Sexual abuse: 12 studies, N = 1,597,  $r = 0.21$ , 95%CI 0.13 to 0.29,  $p < 0.001$ ,  $I^2 = 64%$ ,  $p = 0.001$

Physical abuse: 9 studies, N = 1,296,  $r = 0.16$ , 95%CI 0.06 to 0.25,  $p = 0.001$ ,  $I^2 = 63%$ ,  $p = 0.001$

Emotional abuse: 8 studies, N = 1,060,  $r = 0.31$ , 95%CI 0.20 to 0.41,  $p < 0.001$ ,  $I^2 = 73%$ ,  $p < 0.001$

Physical neglect: 7 studies, N = 832,  $r = 0.16$ , 95%CI 0.00 to 0.31,  $p = 0.047$ ,  $I^2 = 81%$ ,  $p < 0.001$

Emotional neglect: 7 studies, N = 832,  $r = 0.19$ , 95%CI 0.06 to 0.32,  $p = 0.004$ ,  $I^2 = 73%$ ,  $p = 0.001$

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Women exposed to trauma tended to show higher severity of depression than men.

**Mania symptom severity**

*Small associations were found between increased mania symptom severity and;*

All adversity: 11 studies, N = 652,  $r = 0.08$ , 95%CI 0.01 to 0.15,  $p = 0.020$ ,  $I^2 = 44%$ ,  $p = 0.056$

Sexual abuse: 5 studies, N = 763,  $r = 0.13$ , 95%CI 0.00 to 0.24,  $p = 0.039$ ,  $I^2 = 61%$ ,  $p = 0.038$

*There were no significant associations with;*

Physical abuse: 4 studies, N = 743,  $r = 0.07$ , 95%CI -0.05 to 0.20,  $p = 0.277$ ,  $I^2 = 69%$ ,  $p = 0.021$

Emotional abuse: 3 studies, N = 507,  $r = 0.04$ , 95%CI -0.19 to 0.27,  $p = 0.734$ ,  $I^2 = 86%$ ,  $p = 0.001$

Physical neglect: 3 studies, N = 507,  $r = 0.05$ , 95%CI -0.05 to 0.16,  $p = 0.343$ ,  $I^2 = 36%$ ,  $p = 0.211$

Emotional neglect: 3 studies, N = 507,  $r = -0.00$ , 95%CI -0.12 to 0.11,  $p = 0.957$ ,  $I^2 = 44%$ ,  $p = 0.169$

**Consistency in results<sup>‡</sup>**      Some inconsistency

**Precision in results<sup>§</sup>**      Precise

**Directness of results<sup>||</sup>**      Direct

*Alameda L, Rodriguez V, Carr E, Aas M, Trotta G, Marino P, Vorontsova N, Herane-Vives A, Gadelrab R, Spinazzola E, Di Forti M, Morgan C, Murray RM*

**A systematic review on mediators between adversity and psychosis: potential targets for treatment**

Psychological medicine 2020; 50(12): 1966-76

[View review abstract online](#)

**Comparison**      **Factors that mediate the association between adversity and psychosis.**

**Summary of evidence**      **Moderate quality evidence (large sample, unable to assess precision or consistency, direct) finds mediation between childhood adversity and psychosis by negative cognitive schemas about the self, the world, and others, and by dissociation and other post-traumatic stress disorder symptoms.**

**Mediators**

48 studies, N = 85,541

Authors report there is solid evidence of mediation between childhood adversity and psychosis by

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negative cognitive schemas about the self, the world and others, and by dissociation and other post-traumatic stress disorder symptoms.

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| <b>Consistency in results<sup>‡</sup></b> | Unable to assess; no measure of consistency is reported. |
| <b>Precision in results<sup>§</sup></b>   | Unable to assess; no measure of precision is reported.   |
| <b>Directness of results<sup>  </sup></b> | Direct   |

*Ayerbe L, Pérez-Piñar M, Foguet-Boreu Q, Ayis S*

**Psychosis in children of separated parents: A systematic review and meta-analysis**

European Psychiatry 2020; 63: e3

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| <b>Comparison</b>  | <b>Association between parental separation and psychotic disorders.</b>   |
| <b>Summary of evidence</b>   | <b>Moderate to high quality evidence (large sample, inconsistent, precise, direct) finds a small, significant association between parental separation in childhood and the subsequent development of psychotic disorders.</b> |
| <b>Psychotic disorders</b>   |   |
| <p><i>Small, significant association between parental separation in childhood and psychotic disorders; 12 studies, N = 305,652, OR = 1.53, 95%CI 1.29 to 1.76, p &lt; 0.001, I<sup>2</sup> = 44%, p = 0.03</i></p> <p>Subgroup analysis of study design (cohort, case-control, and cross-sectional) showed similar results. The cohort subgroup data was consistent (small effect in all studies).</p> |   |
| <b>Consistency in results</b>  | Inconsistent  |
| <b>Precision in results</b>  | Precise   |
| <b>Directness of results</b>   | Direct  |

*Bailey T, Alvarez-Jimenez M, Garcia-Sanchez AM, Hulbert C, Barlow E, Bendall S*

**Childhood trauma is associated with severity of hallucinations and**

**delusions in psychotic disorders: A systematic review and meta-analysis**

Schizophrenia Bulletin 2018; 44: 1111-22

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| <b>Comparison</b>  | <b>Association between childhood trauma and severity of symptoms in people with psychotic disorders.</b>   |
| <b>Summary of evidence</b>   | <b>Moderate to high quality evidence (large samples, inconsistent, precise, direct) finds a small, significant association between childhood trauma and increased severity of positive symptoms, with no association with negative symptoms, apart from neglect.</b> |
| <b>Psychotic symptoms</b>  |  |
| <p><i>Small, significant associations between childhood trauma and severity of positive symptoms;</i><br/>                 Positive symptoms: 18 studies, N = 3,857, <math>r = 0.14</math>, 95%CI 0.09 to 0.19, <math>p &lt; 0.001</math>, <math>I^2 = 40%</math>, <math>p = 0.04</math></p> <p>Subgroup analyses of abuse type (sexual abuse or neglect) and symptom type (hallucinations or delusions) showed similar results.</p> <p><i>There were no associations with negative symptoms;</i><br/>                 Negative symptoms: 15 studies, N = 3,712, <math>r = 0.05</math>, 95%CI -0.01 to 0.11, <math>p = 0.095</math>, <math>I^2 = 52%</math>, <math>p = 0.01</math></p> <p>Subgroup analysis of abuse type found neglect showed a small, significant association.</p> |  |
| <b>Consistency in results</b>  | Inconsistent   |
| <b>Precision in results</b>  | Precise  |
| <b>Directness of results</b>   | Direct   |

*Bloomfield MAP, Chang T, Woodl MJ, Lyons LM, Cheng Z, Bauer-Staeb C, Hobbs C, Bracke S, Kennerley H, Isham L, Brewin C, Billings J, Greene T, Lewis G*

**Psychological processes mediating the association between developmental trauma and specific psychotic symptoms in adults: a systematic review and meta-analysis**

World Psychiatry 2021; 20(1): 107-23

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| <b>Comparison</b>  | <b>Psychological factors that mediate the association between adversity and psychosis.</b>  |
| <b>Summary of evidence</b>   | <b>Moderate quality evidence (unclear sample size, inconsistent, precise, direct) suggests dissociation and emotional dysregulation mediates the relationship between childhood adversity and hallucinations.</b> |
| <b>Mediators</b>   |   |
| <p><i>A medium-sized effect of dissociation mediating the relationship between childhood adversity and hallucinations;</i></p> <p>Dissociation and hallucinations: 4 studies, N not reported, <math>d = 0.35</math>, 95%CI 0.25 to 0.45, <math>p &lt; 0.05</math>, <math>I^2 = 72\%</math></p> <p><i>A small effect of emotional dysregulation mediating the relationship between childhood adversity and hallucinations;</i></p> <p>Emotional dysregulation and hallucinations: 3 studies, N = not reported, <math>d = 0.06</math>, 95%CI 0.02 to 0.10, <math>p &lt; 0.05</math>, <math>I^2 = 86\%</math></p> <p><i>No significant effect of negative beliefs;</i></p> <p>Negative beliefs and paranoia: 3 studies, N = not reported, <math>d = 0.02</math>, 95%CI -0.04 to 0.09, <math>p &gt; 0.05</math>, <math>I^2 = 48\%</math></p> |   |
| <b>Consistency in results</b>  | Inconsistent  |
| <b>Precision in results</b>  | Precise   |
| <b>Directness of results</b>   | Direct  |

Bonoldi I, Simeone E, Rocchetti M, Codjoe L, Rossi G, Gambi F, Balottin U, Caverzasi E, Politi P, Fusar-Poli P

**Prevalence of self-reported childhood abuse in psychosis: A meta-analysis of retrospective studies**

Psychiatry Research 2013; 210: 8-15

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| <b>Comparison</b>          | <b>Prevalence of childhood trauma in people with a psychotic disorder.</b>   |
| <b>Summary of evidence</b> | <b>Moderate to high quality evidence (large samples, some inconsistency, appears precise, direct) suggests the prevalence of</b> |



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|   | <p><b>childhood sexual abuse in people with psychosis is approximately 26.3%, physical abuse is approximately 38.8%, and emotional abuse is approximately 34%.</b></p> <p><b>Rates may be highest in older studies, in studies with more females, in studies with older patients, and in studies of patients with substance abuse.</b></p> |
| <b>Sexual abuse</b>   |  |
| <p>20 studies, N = 1,889, prevalence = 26.3%, 95%CI 21.2% to 32.2%, <math>I^2 = 82.54%</math>, <math>p &lt; 0.001</math></p> <p>Higher rates of sexual abuse were reported in older studies vs. more recent studies (<math>\beta = -0.038</math>, <math>p &lt; 0.001</math>), in studies with older vs. younger patients (<math>\beta = 0.038</math>, <math>p &lt; 0.001</math>), in studies with a higher proportion of females vs. males (<math>\beta = 0.009</math>, <math>p &lt; 0.001</math>), and in studies of patients with substance abuse vs. no substance abuse (41.4% vs. 21%, <math>p &lt; 0.001</math>).</p> <p>Authors state that overall, these moderators were able to explain approximately 60% of the observed heterogeneity.</p>                      |  |
| <b>Physical abuse</b>   |  |
| <p>15 studies, N = 1,704, prevalence = 38.8%, 95%CI 36.2% to 42.4%, <math>I^2 = 92.71%</math>, <math>p &lt; 0.001</math></p> <p>Higher rates of physical abuse were reported in older studies vs. more recent studies (<math>\beta = -0.027</math>, <math>p = 0.047</math>), in studies with older vs. younger patients (<math>\beta = 0.0817</math>, <math>p &lt; 0.001</math>), in studies of outpatients vs. inpatients (32.7% vs. 14.5%, <math>p &lt; 0.001</math>), and in studies of patients with substance abuse vs. no substance abuse (53.8% vs. 25.5%, <math>p = 0.002</math>).</p> <p>Authors state that overall, these moderators were able to explain approximately 60% of the observed heterogeneity, with age alone accounting for approximately 40%.</p> |  |
| <b>Emotional abuse</b>  |  |
| <p>8 studies, N = 520, prevalence = 34%, 95%CI 29.7% to 38.5%, <math>I^2 = 87.14%</math>, <math>p &lt; 0.001</math></p> <p>Higher rates of sexual abuse were reported in older studies vs. more recent studies (<math>\beta = -0.075</math>, <math>p = 0.05</math>), and in studies with a higher proportion of females vs. males (<math>\beta = 0.017</math>, <math>p = 0.003</math>).</p> <p>Authors state that overall, these moderators were able to explain approximately 23% of the observed heterogeneity.</p>   |  |
| <b>Consistency in results</b>   | Consistent for sexual and physical abuse (most heterogeneity is explained by moderators).  |
| <b>Precision in results</b>   | Unable to formally assess; appears precise   |
| <b>Directness of results</b>  | Direct   |

*Brew B, Doris M, Shannon C, Mulholland C*

**What impact does trauma have on the at-risk mental state? A systematic literature review**

Early intervention in psychiatry 2017 May 30; 10.1111/eip.12453

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| <b>Comparison</b>  | <b>Association between childhood trauma and symptoms, functioning and transition to psychosis in people at high-risk of psychosis.</b>  |
| <b>Summary of evidence</b>   | <b>Moderate quality evidence (small to medium sample sizes, appears consistent, some imprecision, direct) suggests small to medium-sized relationships between exposure to childhood sexual abuse and transition to psychosis in those at risk, and between exposure to any childhood trauma and more severe symptoms and poor functioning.</b> |
| <b>Transition to psychosis</b>   |   |
| <p><i>Significant, small associations between childhood sexual abuse and transition to psychosis;</i><br/>           1 prospective study, N = 92, OR = 2.96, 95%CI 1.16 to 7.57, <math>p &lt; 0.05</math><br/>           1 prospective study, N = 233, HR = 1.08, 95%CI 1.03 to 1.13, <math>p &lt; 0.01</math></p>   |   |
| <b>Functioning</b>   |   |
| <p><i>Childhood maltreatment was an independent predictor of poor functional outcome (medium-sized effect);</i><br/>           1 prospective study, N = 268, <math>\beta = -0.44</math>, <math>p &lt; 0.001</math><br/> <i>A significant association between childhood trauma and poor functioning (small effect);</i><br/>           1 prospective study, N = 245, <math>r = -0.16</math>, <math>p &lt; 0.05</math></p>   |   |
| <b>Psychotic symptoms</b>  |   |
| <p><i>A significant association between childhood sexual abuse and more paranoid symptoms (small effect);</i><br/>           1 prospective study, N = 245, <math>r = 0.12</math>, 95%CI 0.03 to 0.20, <math>p &lt; 0.01</math><br/> <i>A significant association between childhood trauma and more positive symptoms (medium-sized effect);</i><br/>           1 cross-sectional study, N = 30, <math>r = 0.44</math>, <math>p &lt; 0.05</math><br/> <i>Significant associations between childhood trauma and more social anxiety and depression (small effect);</i></p> |   |

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| <p><i>effects);</i></p> <p>Anxiety: 1 cross-sectional study, N = 360, <math>r = 0.34</math>, <math>p &lt; 0.001</math></p> <p>Depression: 1 cross-sectional study, N = 360, <math>r = 0.26</math>, <math>p &lt; 0.001</math></p> <p><i>A significant association between childhood sexual or emotional abuse and more suspiciousness (small effect);</i></p> <p>1 prospective study, N = 245, <math>r = 0.15</math>, <math>p &lt; 0.01</math></p> |  |
| <b>Consistency in results</b>   | Appears consistent   |
| <b>Precision in results</b>   | Precise for HR and paranoid symptoms, imprecise for OR, unable to assess correlations where no CIs are reported. |
| <b>Directness of results</b>  | Direct   |

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| <p><i>Chen L, Murad MH, Paras M, Colbenson K, Sattler A, Goranson E, Elamin M, Seime R, Shinozaki G, Prokop L, Zirakzadeh A</i></p> <p><b>Sexual abuse and lifetime diagnosis of psychiatric disorders: systematic review and meta-analysis</b></p> <p><b>Mayo Clinic Proceedings 2010; 85(7): 618-629</b></p> <p><a href="#">View review abstract online</a></p> |   |
| <b>Comparison</b>   | <b>Prevalence of schizophrenia among those exposed to childhood sexual abuse vs. those not exposed.</b>   |
| <b>Summary of evidence</b>  | <b>Moderate to high quality evidence (large sample, consistent, imprecise, direct) finds no association between childhood sexual abuse and schizophrenia.</b> |
| <b>Schizophrenia</b>  |   |
| <p><i>No significant difference between groups;</i></p> <p>3 longitudinal studies, N = 3,131,503, OR = 1.36, 95%CI 0.81 to 2.30, <math>I^2 = 0\%</math>, <math>p = 0.45</math></p> <p>The subgroup analysis found no moderating effects of gender or study design</p>   |   |
| <b>Consistency in results</b>   | Consistent  |
| <b>Precision in results</b>   | Imprecise   |
| <b>Directness of results</b>  | Direct  |

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*Cunningham T, Hoy K, Shannon C*

**Does childhood bullying lead to the development of psychotic symptoms?  
A meta-analysis and review of prospective studies**

**Psychosis 2016; 8(1): 48-59**

[View review abstract online](#)

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| <b>Comparison</b>   | <b>Psychotic symptoms in people exposed to childhood bullying vs. people not exposed to childhood bullying.</b>   |
| <b>Summary of evidence</b>  | <b>Moderate quality evidence (large sample, direct, inconsistent, imprecise) suggests a medium-sized increased risk of psychotic symptoms after exposure to childhood bullying.</b> |
| <b>Psychotic symptoms</b>   |   |
| <i>A medium-sized effect of increased psychotic symptoms in people who have experienced bullying;<br/>7 studies, N = 23,668, OR = 2.15, 95%CI 1.14 to 4.04, p &lt; 0.05, Q = 5.590, p = 0.018</i> |   |
| <b>Consistency in results</b>   | Inconsistent  |
| <b>Precision in results</b>   | Imprecise   |
| <b>Directness of results</b>  | Direct  |

*Fusar-Poli P, Tantardini M, De Simone S, Ramella-Cravaro V, Oliver D, Kingdon J, Kotlicka-Antczak M, Valmaggia L, Lee J, Millan MJ, Galderisi S, Balottin U, Ricca V, McGuire P*

**Deconstructing vulnerability for psychosis: Meta-analysis of environmental risk factors for psychosis in subjects at ultra high-risk**

**European Psychiatry 2017; 40: 65-75**

[View review abstract online](#)

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| <b>Comparison</b> | <b>Childhood trauma in people with ultra high-risk (UHR) mental states; attenuated psychotic symptoms, brief and limited intermittent psychotic symptoms, and genetic risk and functional deterioration.</b> |
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| <b>Summary of evidence</b>  | <b>Moderate to high quality evidence (large sample, consistent, imprecise, direct) suggests a large effect of increased childhood trauma in people with ultra high-risk mental states, in particular emotional abuse, and physical neglect.</b> |
| <b>Childhood trauma</b>   |   |
| <p><i>A significant, large effect of increased childhood trauma in people with UHR mental states;</i><br/>3 studies, N = 1,333, OR = 5.94, 95%CI 2.90 to 12.20, <math>p &lt; 0.001</math>, <math>I^2 = 42%</math>, <math>p = 0.181</math></p> <p><i>A significant, large effect of increased childhood emotional abuse in people with UHR mental states;</i><br/>2 studies, N = 160, OR = 5.84, 95%CI 1.79 to 19.03, <math>p = 0.003</math>, <math>I^2 = 8%</math>, <math>p = 0.298</math></p> <p><i>A significant, medium-sized effect of increased childhood physical neglect in people with UHR mental states;</i><br/>2 studies, N = 160, OR = 3.07, 95%CI 1.04 to 9.01, <math>p = 0.042</math>, <math>I^2 = 0%</math>, <math>p = 0.411</math></p> <p>No associations were found between UHR and sexual abuse, physical abuse, emotional neglect, or childhood bullying.</p> <p style="text-align: center;">There was no evidence of publication bias</p> |   |
| <b>Consistency in results</b>   | Consistent  |
| <b>Precision in results</b>   | Imprecise   |
| <b>Directness of results</b>  | Direct  |

*Linscott R J, van Os J*

**An updated and conservative systematic review and meta-analysis of epidemiological evidence on psychotic experiences in children and adults: on the pathway from proneness to persistence to dimensional expression across mental disorders**

**Psychological Medicine 2013; 43: 1133-1149**

[View review abstract online](#)

|                            |   |
|----------------------------|---|
| <b>Comparison</b>          | <b>Rates of subclinical psychotic symptoms in people exposed to stress and trauma compared to people not exposed to stress and trauma.</b>  |
| <b>Summary of evidence</b> | <b>Moderate to low quality evidence (unclear sample size, some inconsistency, imprecise, direct) suggests a small increase in prevalence and a medium increase in incidence of subclinical psychotic symptoms in people exposed to stress and trauma.</b> |

**Childhood adversity**

| <b>Subclinical psychotic symptoms</b>   |                               |
|---|-------------------------------|
| <p><i>Significant, small increase in the prevalence and a medium increase in the incidence of subclinical psychotic symptoms in people previously exposed to stress or trauma;</i></p> <p>Prevalence: 11 studies, N not reported, OR = 2.57, 95%CI 1.89 to 3.51, <math>p &lt; 0.05</math>, <math>I^2 = 80%</math>, <math>p &lt; 0.01</math></p> <p>Incidence: 2 studies, N not reported, OR = 4.77, 95%CI 2.15 to 19.2, <math>p &lt; 0.05</math>, <math>I^2 = 0%</math>, <math>p &gt; 0.05</math></p> |                               |
| <b>Consistency in results</b>   | Consistent for incidence only |
| <b>Precision in results</b>   | Imprecise                     |
| <b>Directness of results</b>  | Direct                        |

| <p><i>Matheson SL, Shepherd AM, Pinchbeck RM, Laurens KR, Carr VJ</i></p> <p><b>Childhood adversity in schizophrenia: a systematic meta-analysis</b></p> <p><b>Psychological Medicine 2012; 43(2): 225-238</b></p> <p><a href="#">View review abstract online</a></p>   |   |
|---|---|
| <b>Comparison 1</b>   | <b>Rates of childhood adversity in people with schizophrenia vs. controls.</b>  |
| <b>Summary of evidence</b>  | <b>Moderate to high quality evidence (large samples, consistent [without outliers], imprecise, direct) suggests a medium-sized effect of increased rates of childhood adversity in people with schizophrenia.</b> |
| <b>Childhood adversity</b>  |   |
| <p><i>A significant, medium-sized effect of increased childhood adversity in people with schizophrenia;</i></p> <p>7 studies, N = 1,681, OR = 3.60, 95%CI 2.08 to 6.23, <math>p &lt; 0.00001</math>, <math>I^2 = 65%</math>, <math>p = 0.009</math></p> <p><i>A similar effect was found in the analysis without outliers or atypical controls;</i></p> <p>4 studies, N = 1,414, OR = 3.92, 95%CI 2.37 to 6.50, <math>p &lt; 0.001</math>, <math>I^2 = 55%</math>, <math>p = 0.08</math></p> <p>There were no moderating effects of adversity type (sexual or combined sexual, physical and other adversity), or adversity measure (clinical interview or questionnaire).</p> |   |
| <b>Consistency in results</b>   | Consistent in analysis without outliers or atypical controls.   |
| <b>Precision in results</b>   | Imprecise   |
| <b>Directness of results</b>  | Direct  |

|  |   |
|--|---|
| <b>Comparison 2</b>  | <b>Rates of childhood adversity in people with schizophrenia vs. affective psychosis.</b>   |
| <b>Summary of evidence</b>   | <b>Moderate to high quality evidence (large sample, consistent, imprecise, direct) suggests no differences between groups.</b>  |
| <b>Childhood adversity</b>   |   |
| <p><i>No significant differences between groups;</i><br/>             8 studies, N = 1,060, OR = 1.23, 95%CI 0.77 to 1.97, <math>p = 0.39</math>, <math>I^2 = 42%</math>, <math>p = 0.10</math><br/>             There were no moderating effects of diagnoses (bipolar disorder, manic disorder or combined bipolar and psychotic depression), adversity type or adversity measure.</p>   |   |
| <b>Consistency in results</b>  | Consistent  |
| <b>Precision in results</b>  | Imprecise   |
| <b>Directness of results</b>   | Direct  |
| <b>Comparison 3</b>  | <b>Rates of childhood adversity in people with schizophrenia vs. anxiety disorders.</b>   |
| <b>Summary of evidence</b>   | <b>Moderate to high quality evidence (large sample, consistent, imprecise, direct) suggests a medium-sized effect of increased rates of childhood adversity in people with schizophrenia.</b> |
| <b>Childhood adversity</b>   |   |
| <p><i>A significant, medium-sized increased risk of childhood adversity in people with schizophrenia;</i><br/>             7 studies, N = 779, OR = 2.54, 95%CI 1.29 to 5.01, <math>p = 0.007</math>, <math>I^2 = 37%</math>, <math>p = 0.15</math><br/> <i>A significant difference in effect sizes was found between adversity types (<math>Q_B = 5.43</math>, <math>p = 0.02</math>);</i><br/>             5 studies of sexual abuse report no significant differences between groups: N = 649, OR = 1.66,<br/>             95%CI 0.90 to 3.08, <math>p = 0.10</math>, <math>I^2 = 12%</math>, <math>p = 0.27</math><br/>             2 studies with mixed sexual and physical abuse and neglect report increased childhood adversity in<br/>             schizophrenia: N = 130, OR = 6.95, 95% CI 2.48 to 19.51, <math>p &lt; 0.001</math>, <math>I^2 = 12%</math>, <math>p &lt; 0.27</math><br/>             There were no moderating effects of adversity measure or diagnoses.</p> |   |
| <b>Consistency in results</b>  | Consistent  |
| <b>Precision in results</b>  | Imprecise   |
| <b>Directness of results</b>   | Direct  |
| <b>Comparison 4</b>  | <b>Rates of childhood adversity in people with schizophrenia vs. depressive disorders.</b>  |

**Childhood adversity**

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| <b>Summary of evidence</b>  | <b>Moderate quality evidence (large sample, inconsistent, imprecise, direct) suggests no differences between groups.</b>   |
| <b>Childhood adversity</b>  |  |
| <p><i>No significant differences between groups;</i><br/>           7 studies, N = 1,411, OR = 1.37, 95%CI 0.53 to 3.49, <math>p = 0.51</math>, <math>I^2 = 88\%</math>, <math>p &lt; 0.00001</math><br/> <i>A significant difference in effect sizes was reported between adversity measures (<math>Q_B = 8.98</math>, <math>p &lt; 0.01</math>);</i><br/>           6 studies using questionnaires reported no differences between groups: N = 982, OR = 1.77, 95%CI 0.73 to 4.25, <math>p = 0.20</math>, <math>I^2 = 76\%</math>, <math>p &lt; 0.01</math><br/>           1 study using chart review reported significantly reduced childhood adversity in schizophrenia: N = 429, OR = 0.39, 95%CI 0.25 to 0.61, <math>p &lt; 0.001</math><br/> <i>A significant difference in effect sizes was reported between diagnoses (<math>Q_B = 8.69</math>, <math>p &lt; 0.01</math>);</i><br/>           5 studies included patients with depression reported no differences to schizophrenia: N = 1,281, OR = 0.83, 95%CI 0.32 to 2.18, <math>p = 0.71</math>, <math>I^2 = 88.0\%</math>, <math>p &lt; 0.001</math><br/>           2 studies with mixed samples of depression and anxiety patients reported increased childhood adversity in schizophrenia: N = 130, OR = 6.95, 95%CI 2.48 to 19.51, <math>p &lt; 0.001</math>, <math>I^2 = 12\%</math>, <math>p &lt; 0.27</math><br/>           There were no moderating effects of adversity type.</p> |  |
| <b>Consistency in results</b>   | Inconsistent   |
| <b>Precision in results</b>   | Imprecise  |
| <b>Directness of results</b>  | Direct   |
| <b>Comparison 5</b>   | <b>Rates of childhood adversity in people with schizophrenia vs. dissociative disorders or post-traumatic stress disorder (PTSD).</b>  |
| <b>Summary of evidence</b>  | <b>Moderate to high quality evidence (small sample, consistent, precise, direct) suggests a large effect of fewer rates of childhood adversity in people with schizophrenia.</b> |
| <b>Sexual abuse</b>   |  |
| <p><i>A significant, large effect of decreased reporting of childhood adversity in people with schizophrenia compared to dissociative disorders and PTSD;</i><br/>           4 studies, N = 135, OR = 0.03, 95%CI 0.01 to 0.15, <math>p &lt; 0.0001</math>, <math>I^2 = 51\%</math>, <math>p = 0.11</math><br/>           There were no moderating effects of diagnosis or adversity measure.</p>   |  |
| <b>Consistency in results</b>   | Consistent   |
| <b>Precision in results</b>   | Precise  |



**Childhood adversity**

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|--|---|
| <b>Directness of results</b>   | Direct  |
| <b>Comparison 6</b>  | <b>Rates of self-reported childhood adversities in schizophrenia spectrum patients vs. other psychoses.</b>                     |
| <b>Summary of evidence</b>   | <b>Moderate quality evidence (small sample, consistent, imprecise, direct) suggests no differences between groups.</b>          |
| <b>Childhood adversity</b>   |   |
| <p><i>No significant differences between groups;</i><br/>                     3 studies, N = 139, OR = 0.69, 95%CI 0.28 to 1.68, <math>p = 0.41</math>, <math>I^2 = 2\%</math>, <math>p = 0.36</math><br/>                     There were no moderating effects of diagnosis, adversity type or adversity measure.</p> |   |
| <b>Consistency in results</b>  | Consistent  |
| <b>Precision in results</b>  | Imprecise   |
| <b>Directness of results</b>   | Direct  |
| <b>Comparison 7</b>  | <b>Rates of childhood adversity in people with schizophrenia vs. personality disorders.</b>                                     |
| <b>Summary of evidence</b>   | <b>Moderate to low quality evidence (small sample, inconsistent, imprecise, direct) suggests no differences between groups.</b> |
| <b>Sexual abuse</b>  |   |
| <p><i>No significant differences between groups;</i><br/>                     3 studies, N = 187, OR = 0.65, 95%CI 0.09 to 4.71, <math>p = 0.67</math>, <math>I^2 = 80\%</math>, <math>p = 0.006</math><br/>                     There were no moderating effects of diagnosis or adversity measure.</p>               |   |
| <b>Consistency in results</b>  | Inconsistent  |
| <b>Precision in results</b>  | Imprecise   |
| <b>Directness of results</b>   | Direct  |

*Pastore A, de Girolamo G, Tafuri S, Tomasicchio A, Margari F*

**Traumatic experiences in childhood and adolescence: a meta-analysis of prospective studies assessing risk for psychosis**

**European Child and Adolescent Psychiatry 2020; 31(2): 215-228**

**Childhood adversity**

|   |  |
|---|--|
| <a href="#">View review abstract online</a>   |  |
| <b>Comparison</b>   | <b>Parental death, bullying by peers, and maltreatment by an adult and psychotic disorders in adulthood.</b>   |
| <b>Summary of evidence</b>  | <b>Moderate quality evidence (unclear sample size, some inconsistency and imprecision, direct) found medium-sized effects of increased risk of psychotic disorders in adulthood following maltreatment by an adult or bullying by peers. A small effect was found for parental death in childhood.</b> |
| <b>Maltreatment by an adult, bullying by peers, and parental death</b>  |  |
| <p><i>Medium-sized effects of increased risk of psychotic disorders with;</i></p> <p>Maltreatment by an adult: 15 studies, N not reported, OR = 2.20, 95%CI 1.72 to 2.81, <math>p &lt; 0.05</math>, <math>I^2 = 81\%</math></p> <p>Bullying by peers: 8 studies, N not reported, OR = 2.28, 95%CI 1.64 to 4.34, <math>p &lt; 0.05</math>, <math>I^2 = 92\%</math></p> <p>Exposure to multiple trauma types + bullying was associated with greater risk of psychosis</p> <p><i>Small effect of increased risk of psychotic disorders with;</i></p> <p>Parental death: 4 studies, N not reported, OR = 1.24, 95%CI 1.06 to 1.44, <math>p &lt; 0.05</math>, <math>I^2 = 0\%</math></p> <p>Studies with more females showed lower effect sizes for parental death</p> |  |
| <b>Consistency in results</b>   | Inconsistent for maltreatment and bullying, consistent for parental death  |
| <b>Precision in results</b>   | Imprecise for maltreatment and bullying, precise for parental death  |
| <b>Directness of results</b>  | Direct   |

|   |   |
|---|---|
| <p><i>Peh OH, Rapisarda A, Lee J</i></p> <p><b>Childhood adversities in people at ultra-high risk (UHR) for psychosis: A systematic review and meta-analysis</b></p> <p><b>Psychological Medicine 2019; 49: 1089-101</b></p> <p><a href="#">View review abstract online</a></p> |   |
| <b>Comparison 1</b>   | <b>Rates of childhood adversity in people at ultra-high risk of psychosis compared to people not at ultra-high risk of psychosis.</b> |

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| <b>Summary of evidence</b>   | <b>Moderate quality evidence (large samples, mostly inconsistent, imprecise, direct) suggests a large increased rate of emotional abuse, a medium increased rate of physical abuse and a small increased rate of sexual abuse in people at ultra-high risk of psychosis than controls. There were no differences in rates of emotional or physical neglect.</b> |
| <b>Emotional abuse</b>   |   |
| <i>A significant large increase in rates of emotional abuse in people at ultra-high risk for psychosis;</i><br>5 studies, N = 1108, OR = 5.06, 95%CI 1.55 to 16.58, $p = 0.007$ , $I^2 = 94\%$<br>No significant differences in rates of emo |   |
| <b>Physical abuse</b>  |   |
| <i>A significant medium increase in rates of physical abuse in people at ultra-high risk for psychosis;</i><br>5 studies, N = 1108, OR = 3.19, 95%CI 1.05 to 9.75, $p = 0.04$ , $I^2 = 89\%$   |   |
| <b>Sexual abuse</b>  |   |
| <i>A significant small increase in rates of sexual abuse in people at ultra-high risk for psychosis;</i><br>5 studies, N = 1108, OR = 1.95, 95%CI 0.99 to 3.83, $p = 0.05$ , $I^2 = 69\%$  |   |
| <b>Emotional neglect</b>   |   |
| <i>No significant difference in rates of emotional neglect;</i><br>4 studies, N = 1012, OR = 2.62, 95%CI 0.80 to 8.58, $p = 0.11$ , $I^2 = 94\%$   |   |
| <b>Physical neglect</b>  |   |
| <i>No significant difference in rates of physical neglect;</i><br>2 studies, N = 422, OR = 0.90, 95%CI 0.68 to 1.19, $p = 0.45$ , $I^2 = 0\%$  |   |
| <b>Consistency in results</b>  | Consistent for physical neglect only.   |
| <b>Precision in results</b>  | Imprecise   |
| <b>Directness of results</b>   | Direct  |
| <b>Comparison 2</b>  | <b>Association between childhood adversity and time to transition to psychosis in people at ultra-high risk for psychosis.</b>  |
| <b>Summary of evidence</b>   | <b>High quality evidence (large samples, consistent, precise, direct) suggests no association between time to transition to psychosis and exposure to childhood adversity.</b>  |

|  |            |
|--|------------|
| <b>Time to transition to psychosis after emotional abuse</b>   |            |
| <i>No significant association between emotional abuse and transition to psychosis;</i><br>5 studies, N = 1730, HR = 1.00, 95%CI 0.96 to 1.05, $p = 0.91$ , $I^2 = 0\%$   |            |
| <b>Time to transition to psychosis after physical abuse</b>  |            |
| <i>No significant association between physical abuse and transition to psychosis;</i><br>5 studies, N = 1730, HR = 1.04, 95%CI 0.99 to 1.09, $p = 0.11$ , $I^2 = 0\%$  |            |
| <b>Time to transition to psychosis after sexual abuse</b>  |            |
| <i>A significant shorter time to transition to psychosis in people at ultra-high risk for psychosis with a history of childhood sexual abuse;</i><br>5 studies, N = 1730, HR = 1.05, 95%CI 1.05 to 1.09, $p = 0.009$ , $I^2 = 0\%$<br>Authors report this effect became non-significant with the removal of one large study. |            |
| <b>Time to transition to psychosis after emotional neglect</b>   |            |
| <i>No significant association between physical abuse and transition to psychosis;</i><br>5 studies, N = 1730, HR = 1.02, 95%CI 0.98 to 1.07, $p = 0.31$ , $I^2 = 0\%$  |            |
| <b>Time to transition to psychosis after physical neglect</b>  |            |
| <i>No significant association between physical abuse and transition to psychosis;</i><br>4 studies, N = 966, HR = 1.01, 95%CI 0.93 to 1.08, $p = 0.89$ , $I^2 = 0\%$   |            |
| <b>Consistency in results</b>  | Consistent |
| <b>Precision in results</b>  | Precise    |
| <b>Directness of results</b>   | Direct     |

Read J, van Os J, Morrison AP, Ross CA

**Childhood trauma, psychosis and schizophrenia: a literature review with theoretical and clinical implications**

Acta Psychiatrica Scandinavica 2005; 112(5): 330-350

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|   |  |
|---|--|
| <b>Comparison</b>   | <b>Prevalence of childhood trauma in people with a psychotic disorder.</b>   |
| <b>Summary of evidence</b>  | <b>Moderate to low quality evidence (medium-sized samples, inconsistent, unable to assess precision, direct) suggests rates of childhood trauma may range from 14 to 100% across studies of females with schizophrenia and from 0 to 47% across studies of males with schizophrenia.</b> |
| <b>Prevalence of retrospective self-reported childhood trauma</b>   |  |
| <p>11 observational studies of female patients diagnosed with schizophrenia or schizophrenia spectrum disorder, N = 197; overall prevalence of childhood trauma: range 14% to 100%.</p> <p>11 observational studies of male patients with schizophrenia or schizophrenia spectrum disorder, N = 330; Overall prevalence of childhood trauma: range 0% to 47%.</p> <p><i>Relationships between child abuse and symptoms of schizophrenia or related schizotypal traits</i></p> <p>Physical or sexual abuse; 7 out of 9 observational studies found that patients with a history of childhood trauma reported significantly more hallucinations than patients with no history of childhood trauma. 5 studies out of 8 also reported significantly more delusions. No differences for thought disorder or negative symptoms.</p> <p>Incest; 1 out of 5 observational studies found that patients with a history of childhood trauma reported significantly more hallucinations than patients with no history of childhood trauma. No differences for delusions, thought disorder or negative symptoms.</p> |  |
| <b>Consistency in results</b>   | Inconsistent   |
| <b>Precision in results</b>   | CI's not reported  |
| <b>Directness of results</b>  | Direct   |

Sideli L, Murray RM, Schimmenti A, Corso M, La Barbera D, Trotta A, Fisher HL

**Childhood adversity and psychosis: a systematic review of bio-psycho-social mediators and moderators**

Psychological Medicine 2020; 1-22

[View review abstract online](#)

|                   |  |
|-------------------|--|
| <b>Comparison</b> | <p><b>Mediators and moderators affecting the relationship between childhood adversity and psychotic disorders.</b></p> <p><b>Mediators are mechanisms through which the relationship may be explained. Moderators were factors that changed the relationship</b></p> |
|-------------------|--|

|  |  |
|--|--|
|  | (interactions).  |
| <b>Summary of evidence</b>   | <b>Moderate to low quality evidence (unclear sample size, unable to assess consistency or precision, direct) finds mediation and moderating effects of life events and stressors, social defeat, loneliness, and social support. Mediation effects were also found for attachment style and parental bonding, mood symptoms, PTSD, and dissociation.</b> |
| <b>Psychotic disorders or symptoms</b>   |  |
| <p>Of 121 studies, 32 satisfied the criteria for robustness</p> <p><i>Robust mediation effects were found for;</i></p> <p style="padding-left: 40px;">Life events and stressors</p> <p style="padding-left: 40px;">Social defeat, loneliness, and social support</p> <p style="padding-left: 40px;">Attachment and parental bonding</p> <p style="padding-left: 40px;">Mood symptoms</p> <p style="padding-left: 40px;">PTSD and dissociation</p> <p><i>Robust moderation/interaction effects were found for;</i></p> <p style="padding-left: 40px;">Life events and stressors</p> <p style="padding-left: 40px;">Social defeat, loneliness, and social support</p> <p>There were no mediating, and mixed moderating, effects of genetic vulnerabilities</p> |  |
| <b>Consistency in results</b>  | Unable to assess; no measure of consistency is reported.   |
| <b>Precision in results</b>  | Unable to assess; no measure of precision is reported.   |
| <b>Directness of results</b>   | Direct   |

*Thomas S, Hofler M, Schafer I, Trautmann S*

**Childhood maltreatment and treatment outcome in psychotic disorders: a systematic review and meta-analysis**

**Acta Psychiatrica Scandinavica: 2019; doi: 10.1111/acps.13077**

[View review abstract online](#)

|                   |   |
|-------------------|---|
| <b>Comparison</b> | <b>Association between childhood trauma and treatment outcomes in people with a psychotic disorder, mostly schizophrenia spectrum (mean treatment duration 59.2 weeks).</b> |
|-------------------|---|

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| <b>Summary of evidence</b>   | <b>Moderate to high quality evidence (large sample, consistent, imprecise, direct) finds a small effect of poorer treatment outcomes in people with a psychotic disorder and exposure to childhood maltreatment. The effect was largest in schizophrenia samples, in samples with an established illness and in older samples.</b> |
| <b>Symptom severity</b>  |  |
| <p><i>A significant, small effect of poorer treatment outcomes in people with psychotic disorders and exposure to childhood maltreatment;</i></p> <p>7 studies, N = 636 patients, OR = 1.55, 95%CI 1.03 to 2.34, <math>p = 0.036</math>, <math>I^2 = 29%</math>, <math>p = 0.159</math><br/>                 Meta-regression found larger effect sizes in samples with an established illness (OR = 6.59) and increasing age (regression coefficient not reported).<br/>                 Subgroup analysis of diagnosis found a larger effect size in schizophrenia samples (OR = 3.09).</p> |  |
| <b>Consistency in results</b>  | Consistent   |
| <b>Precision in results</b>  | Imprecise  |
| <b>Directness of results</b>   | Direct   |

|   |   |
|---|---|
| <p><i>Trotta A, Murray RM, Fisher HL</i></p> <p><b>The impact of childhood adversity on the persistence of psychotic symptoms: a systematic review and meta-analysis</b></p> <p>Psychological Medicine 2015; 45: 2481-2498<br/> <a href="#">View review abstract online</a></p>             |   |
| <b>Comparison</b>   | <b>Persistence of psychotic symptoms in people with a history of childhood adversity vs. people without a history of childhood adversity.</b>   |
| <b>Summary of evidence</b>  | <b>Moderate to high quality evidence (large sample, consistent, imprecise, direct) suggests greater persistence of psychotic experiences in people with a history of childhood adversity.</b> |
| <b>Persistence of psychotic experiences</b>   |   |
| <p><i>A significant, small effect of greater persistence of psychotic experiences in people with a history of childhood adversity;</i></p> <p>Overall: 9 studies, N = 13,887, OR = 1.73, 95%CI 1.26 to 2.20, <math>p &lt; 0.05</math>, <math>I^2 = 36.4%</math>, <math>p = 0.127</math></p> |   |

**Childhood adversity**

General population: 5 studies, N = 13,699, OR = 1.76, 95%CI 1.19 to 2.32,  $p < 0.001$ ,  $I^2 = 58%$ ,  $p = 0.049$

Clinical populations: 4 studies, N = 188, OR = 1.55, 95%CI 0.32 to 2.77,  $p = 0.007$ ,  $I^2 = 0%$ ,  $p = 0.407$

|                               |   |
|-------------------------------|---|
| <b>Consistency in results</b> | Consistent for overall effect and clinical populations, inconsistent for general population studies |
| <b>Precision in results</b>   | Imprecise   |
| <b>Directness of results</b>  | Direct  |

*van Dam DS, van der Ven E, Velthorst E, Selten JP, Morgan C, de Haan L*

**Childhood bullying and the association with psychosis in non-clinical and clinical samples: a review and meta-analysis**

Psychological Medicine 2012; 42: 2463-2474

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|   |  |
|---|--|
| <b>Comparison</b>   | Subclinical psychotic symptoms in adolescents and adults who were exposed to childhood bullying vs. those not exposed to childhood bullying.   |
| <b>Summary of evidence</b>  | Moderate to high quality evidence (consistent, imprecise, direct, large sample) suggests a medium-sized increased risk of subclinical psychotic symptoms in adolescents and adults who were exposed to childhood bullying. |
| <b>Subclinical psychotic symptoms</b>   |  |
| <p><i>Significant, medium-sized increased risk of subclinical psychotic symptoms in adolescents and adults who were exposed to childhood bullying;</i></p> <p>7 studies, N = 22,014, OR = 2.67, 95%CI 2.01 to 3.56, <math>p &lt; 0.05</math>, <math>Qp = 0.28</math></p> <p>Adjusted for gender, age, and other negative life events: OR = 2.25, 95%CI 1.49 to 3.40, <math>p &lt; 0.05</math></p> |  |
| <b>Consistency in results</b>   | Consistent   |
| <b>Precision in results</b>   | Imprecise  |
| <b>Directness of results</b>  | Direct   |

*Varese F, Smeets F, Drukker M, Lieveerse R, Lataster T, Viechtbauer W, Read J,*



**Childhood adversity**

*van Os J, Bentall, R*

**Childhood Adversities Increase the Risk of Psychosis: A Meta-analysis of Patient-Control, Prospective- and Cross-sectional Cohort Studies**

Schizophrenia Bulletin 2012; 38(4): 661-671

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|   |  |
|---|--|
| <b>Comparison</b>   | <b>Childhood adversities in people with a psychotic disorder or psychotic symptoms vs. controls.</b>   |
| <b>Summary of evidence</b>  | <b>Moderate quality evidence (large sample, inconsistent, imprecise, direct) suggests a medium to large effect of increased rates of childhood adversity in people with psychosis.</b> |
| <b>Childhood adversity</b>  |  |
| <p><i>A significant medium to large effect of increased childhood adversity in people with psychosis;</i><br/>           36 studies, N = 81,253, OR = 2.78, 95%CI 2.34 to 3.31, <math>p &lt; 0.05</math>, <math>Qp &lt; 0.01</math></p> <p>There were no moderating effects of study design (case-control, population, cross-sectional), sample type (diagnosis of psychosis or psychotic symptoms), gender, age, SES, or any other confounder.</p> <p style="text-align: center;"><i>All types of adversity showed similar effects;</i></p> <p>Sexual abuse: 20 studies, OR = 2.38, 95%CI 1.98 to 2.87, <math>p &lt; 0.001</math>, <math>I^2 = 44.9</math>, <math>p &lt; 0.05</math><br/>           Physical abuse: 13 studies, OR = 2.95, 95%CI 2.25 to 3.88, <math>p &lt; 0.001</math>, <math>I^2 = 74.9</math>, <math>p &lt; 0.001</math><br/>           Emotional abuse: 6 studies, OR = 3.40, 95%CI 2.06 to 5.62, <math>p &lt; 0.001</math>, <math>I^2 = 78.3</math>, <math>p &lt; 0.001</math><br/>           Bullying: 6 studies, OR = 2.39, 95%CI 1.83 to 3.11, <math>p &lt; 0.001</math>, <math>I^2 = 73.9</math>, <math>p &lt; 0.01</math><br/>           Neglect: 7 studies, OR = 2.90, 95%CI 1.71 to 4.92, <math>p &lt; 0.001</math>, <math>I^2 = 81.8</math>, <math>p &lt; 0.001</math><br/>           Parental death: 8 studies, OR = 1.70, 95%CI 0.82 to 3.53, <math>p = 0.154</math>, <math>I^2 = 80</math>, <math>p &lt; 0.001</math><br/>           Parental death (less outlier): 7 studies, OR = 2.30, 95% CI 1.63 to 3.24, <math>p &lt; .001</math></p> |  |
| <b>Consistency in results</b>   | Inconsistent   |
| <b>Precision in results</b>   | Imprecise  |
| <b>Directness of results</b>  | Direct   |

*Vargas T, Lam PH, Azis M, Osborne KJ, Lieberman A, Mittal VA*

**Childhood Trauma and Neurocognition in Adults With Psychotic**

**Disorders: A Systematic Review and Meta-analysis**

Schizophrenia Bulletin 45: 1195-208

[View review abstract online](#)

|   |  |
|---|--|
| <b>Comparison</b>   | Relationship between childhood trauma and cognition in people with a psychotic disorder.   |
| <b>Summary of evidence</b>  | <b>Moderate to high quality evidence (large sample, unable to assess consistency, precise, direct) suggests small, significant associations between poorer overall cognition and working memory in patients with childhood trauma.</b> |
| <b>Cognition</b>  |  |
| N = 3,315   |  |
| <i>There were small, significant associations between poorer overall cognition and working memory in patients with childhood trauma;</i>                |  |
| Overall cognition: $r = -0.055$ , 95%CI -0.09 to -0.02, $p = 0.002$   |  |
| Working memory: $r = -0.091$ , 95%CI -0.15 to -0.03, $p = 0.002$  |  |
| There were no associations with executive functioning, verbal/visual memory, or attention/processing speed.   |  |
| Authors report that the association between childhood trauma and cognition was stronger in healthy controls than in patients with a psychotic disorder. |  |
| <b>Consistency in results</b>   | Unable to assess; no measure of consistency is reported.   |
| <b>Precision in results</b>   | Precise  |
| <b>Directness of results</b>  | Direct   |

**Explanation of acronyms**

$\beta$  = beta coefficient, CI = confidence interval,  $g$  = Hedges  $g$  standardised mean difference, HR = hazard ratio,  $I^2$  = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), N = number of participants, OR = odds ratio,  $p$  = statistical probability of obtaining that result ( $p < 0.05$  generally regarded as significant), Q = test for differences between individual study results,  $Q_B$  = test for differences between results of groups of studies,  $r$  = correlation coefficient, vs. = versus

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### Explanation of technical terms

\* Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; reporting bias – selective reporting of results, publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small<sup>24</sup>.

† Different effect measures are reported by different reviews.

Prevalence refers to how many existing cases there are at a particular point in time. Incidence refers to how many new cases there are per population in a specified time period. Incidence is usually reported as the number of new cases per 100,000 people per year. Alternatively, some studies present the number of new cases that have accumulated over several years against a person-years denominator. This denominator is the sum of individual units of time that the persons in the population are at risk of becoming a case. It takes into account the size of the underlying population sample and its age structure over the duration of observation.

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified

(100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) that allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. 0.2 represents a small effect, 0.5 a medium effect, and 0.8 and over represents a large treatment effect<sup>24</sup>.

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction ( $< 1$ ) or an increase ( $> 1$ ) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, an RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. An RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if  $RR > 2$  or  $< 0.5$  and a large effect if  $RR > 5$  or  $< 0.2$ <sup>25</sup>. InOR stands for logarithmic OR where a InOR of 0 shows no difference between groups. Hazard ratios measure the effect of an explanatory variable on the hazard or risk of an event.

Correlation coefficients (eg,  $r$ ) indicate the strength of association or relationship between variables. They are an indication of

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prediction, but do not confirm causality due to possible and often unforeseen confounding variables. An  $r$  of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents a strong association. Unstandardised ( $b$ ) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the independent variable, statistically controlling for the other independent variables. Standardised regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.

recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, this criteria should be relaxed<sup>26</sup>.

‡ Inconsistency refers to differing estimates of treatment effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate.  $I^2$  is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent substantial heterogeneity and 75% to 100%: considerable heterogeneity.  $I^2$  can be calculated from  $Q$  (chi-square) for the test of heterogeneity with the following formula;

$$I^2 = \left( \frac{Q - df}{Q} \right) \times 100\%$$

|| Indirectness of comparison occurs when a comparison of intervention A versus B is not available but A was compared with C and B was compared with C that allows indirect comparisons of the magnitude of effect of A versus B. Indirectness of population, comparator and or outcome can also occur when the available evidence regarding a particular population, intervention, comparator, or outcome is not available so is inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-to-head comparisons of A and B.

§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also

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