Psychological Medicine (2013), **43**, 225–238. © Cambridge University Press 2012
doi:10.1017/S0033291712000785

REVIEW ARTICLE

Childhood adversity in schizophrenia: a systematic meta-analysis

S. L. Matheson[1,2]*, A. M. Shepherd[1,2], R. M. Pinchbeck[1], K. R. Laurens[1,2,3] and V. J. Carr[1,2]

[1] *Schizophrenia Research Institute, Darlinghurst, Sydney, Australia*
[2] *Research Unit for Schizophrenia Epidemiology, School of Psychiatry, University of New South Wales, Sydney, Australia*
[3] *Department of Forensic and Neurodevelopmental Sciences, Institute of Psychiatry, King's College London, UK*

Background. Childhood adversity is a putative risk factor for schizophrenia, although evidence supporting this suggestion is inconsistent and controversial. The aim of this review was to pool and quality assess the current evidence pertaining to childhood adversity in people with schizophrenia compared to other psychiatric disorders and to non-psychiatric controls.

Method. Included were case-control, cohort and cross-sectional studies. Medline, EMBASE and PsycINFO databases were searched. Study reporting was assessed using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist and pooled evidence quality was assessed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Results. Twenty-five studies met inclusion criteria. Moderate to high quality evidence suggests increased rates of childhood adversity in schizophrenia compared to controls [odds ratio (OR) 3.60, $p<0.00001$]. Increased childhood adversity was also reported in schizophrenia compared to anxiety disorders (OR 2.54, $p=0.007$), although the effect was not significant in the subgroup analysis of five studies assessing only sexual abuse. No differences in rates of childhood adversity were found between schizophrenia and affective psychosis, depression and personality disorders whereas decreased rates of childhood adversity were found in schizophrenia relative to dissociative disorders and post-traumatic stress disorder (OR 0.03, $p<0.0001$).

Conclusions. This is the first meta-analysis to report a medium to large effect of childhood adversity in people with schizophrenia and to assess specificity for schizophrenia. Further research is required that incorporates longitudinal design and other potentially causal variables to assess additive and/or interactive effects.

Received 22 December 2011; Revised 15 March 2012; Accepted 19 March 2012; First published online 30 April 2012

Key words: Aetiology, childhood adversity, psychosis, schizophrenia, trauma.

Introduction

Childhood adversity covers a range of potentially harmful experiences, including emotional or psychological abuse, physical abuse, sexual abuse, neglect and other negative life events. It is a putative risk factor not only for clinical psychiatric disorders such as schizophrenia but also for subclinical symptoms, including subclinical, psychotic-like experiences (Rind *et al*. 1998; Molnar *et al*. 2001; Edwards *et al*. 2003; Read *et al*. 2005; Bendall *et al*. 2008; Larkin & Read, 2008; Kessler *et al*. 2010). However, the evidence indicating that childhood adversity constitutes a risk factor for schizophrenia is inconsistent and controversial (Morgan & Fisher, 2007), and specificity for schizophrenia relative to other psychiatric disorders has not been demonstrated (Chen *et al*. 2010).

Two narrative reviews suggested a causal, dose-dependent relationship between childhood sexual or physical abuse and psychosis later in life (Read *et al*. 2005; Larkin & Read, 2008). Other narrative reviews outline methodological issues at the study level that limit the ability to draw such conclusions (Morgan & Fisher, 2007; Bendall *et al*. 2008). Study limitations include a lack of statistical power, a lack of attention to moderating or mediating variables such as sex effects, and a lack of adequate control groups.

A recent meta-analysis assessing childhood sexual abuse in case-control and cohort studies reported significant increases in sexual abuse in patients with anxiety disorders, depression, eating disorders, post-traumatic stress disorder (PTSD), sleep disorders and suicide attempts, but not schizophrenia (Chen *et al*. 2010). Two studies met inclusion criteria for schizophrenia in that review (Pettigrew & Burcham, 1997;

* Address for correspondence: Ms. S. L. Matheson, UNSW Research Unit for Schizophrenia Epidemiology, O'Brien Centre, Level 4, St Vincent's Hospital, 394–404 Victoria Street, Darlinghurst, NSW 2010, Australia.
(Email: s.matheson@schizophreniaresearch.org.au)

https://doi.org/10.1017/S0033291712000785 Published online by Cambridge University Press

Spataro *et al*. 2004); both assessed rates of schizophrenia in people with a sexual abuse history compared to people with no sexual abuse history or population controls. One of these studies (Spataro *et al*. 2004) has recently been updated (Cutajar *et al*. 2010), and now reports that rates of psychosis, and schizophrenia in particular, were significantly higher in the abused group compared to population controls. Earlier meta-analyses have reported significant, small to medium effect size increases associated with sexual abuse in patients with depression, anxiety, eating disorders, dissociation, PTSD, somatization and borderline personality disorder (Neumann, 1994; Jumper, 1995; Rind *et al*. 1998; Fossati *et al*. 1999; Paolucci *et al*. 2001). One narrative review reported increased rates of depression, PTSD and suicide attempts in adulthood in children exposed to a broader range of childhood adversities, including physical and emotional abuse and neglect (Gilbert *et al*. 2009).

The aim of this systematic meta-analysis was to assess the current evidence pertaining to rates of all childhood adversities in people with schizophrenia compared to non-psychiatric controls; and furthermore to assess specificity to schizophrenia relative to other psychiatric disorders. The impact of adversity type and adversity measure on the results was investigated, along with quality assessment of reporting of included studies and the overall strength of the current evidence.

Method

Literature search

Inclusion/exclusion criteria

Included are cohort, Case-control and cross-sectional studies reporting rates of childhood adversity (age <18 years; including sexual abuse, physical abuse and neglect) in people with a diagnosis of schizophrenia (i.e. schizophrenia, schizo-affective disorder or schizophreniform disorder) and non-psychiatric controls or in people with other psychiatric disorders. Other psychiatric disorders were grouped into six categories: (1) affective psychoses (bipolar disorder, mania and psychotic depression), (2) other psychoses [delusional, atypical and psychosis not otherwise specified (NOS)], (3) depressive disorders (depression), (4) anxiety disorders (anxiety, panic and neurotic), (5) dissociative disorder, dissociative identity disorder (DID) and PTSD (which is defined in terms of adversity, although not necessarily in childhood), and (6) personality disorders. Inclusion criteria were not limited to published studies or studies written in English. The decision to include or exclude studies was conducted independently by two of the authors (S.M. and R.P.), with disagreements resolved by discussion.

Search strategy

Medline, EMBASE and PsycINFO were searched. The search was conducted in September 2011 and the strategy was designed to be sensitive while retaining acceptable specificity. The search terms were: exp Schizophrenia, schizophreni$.tw, exp Psychotic Disorders, schizo$.tw, child$ trauma.tw, child$ adversity.tw, exp child abuse, child$ abuse.tw, neglect.tw, incest.tw, child$ victimization.mp. Hand searching of reference lists of included reviews was also conducted.

Quality assessment

All quality assessments were completed independently by two authors (S.M. and A.S. or R.P.), with disagreements settled by discussion. The quality of reporting was assessed using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist, which outlines a preferred way to report observational studies (www.strobe-statement.org). Studies were assigned a low ($>66\%$ items checked), medium (33–66% items checked) or high ($<33\%$ items checked) possibility of reporting bias.

To assess the quality of the pooled evidence (not the quality of the individual studies contributing to the meta-analysis), the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach was adopted (Atkins *et al*. 2004). GRADE was developed primarily to quality assess management strategies, using evidence from both randomized controlled trials and observational studies; however, in the absence of robust quality assessment guidelines for pooled aetiological evidence, we have applied GRADE criteria to derive a broad indication of the strength and quality of the meta-analytic results. GRADE suggests that pooled evidence from observational studies is inherently of low quality because of the effects of possible confounding factors. This evidence can be upgraded if sample sizes and pooled effect sizes are large or dose dependent, or if the evidence is direct, consistent or precise (Higgins & Green, 2008). Indirectness pertains to approximated measures; inconsistency to significant heterogeneity between study results; and imprecision to wide confidence intervals (CIs) around the pooled effect size (CIs >0.25 in either direction) (GRADEpro, 2008).

Data extraction and analysis

All data extraction was completed independently by two of the authors (S.M. and A.S. or R.P.). The

https://doi.org/10.1017/S0033291712000785 Published online by Cambridge University Press

following variables were extracted: (1) rates of childhood adversity in schizophrenia patients, non-psychiatric controls and other psychiatric groups, (2) study characteristics including study design, diagnostic tool, adversity measure and adversity type, and (3) sample characteristics including number and diagnoses in each psychiatric group, number and characteristics of controls, and subject age and sex.

Comprehensive Meta-Analysis version 2 (CMA V2; Borenstein *et al*. 2005) was used to conduct the meta-analyses. We report odds ratios (ORs) and 95% CIs. An OR >1.0 indicates greater reporting of childhood adversity in schizophrenia patients compared to controls or other psychiatric groups; an OR <1.0 indicates greater reporting of childhood adversity in controls or other psychiatric groups compared to schizophrenia. An effect size is considered medium to large if OR >2 or <0.5 and large if OR >5 or <0.2 (GRADEpro, 2008). A random effects model was used as heterogeneity across study results was expected. The I^2 statistic is the percentage of the variability in effect estimates that is due to heterogeneity rather than to sampling error. A guideline for interpreting I^2 (heterogeneity) is that 0–40% might not be important, 50–75% 'may' be important, and >75% should be regarded as 'considerable'. Planned subgroup analyses were conducted to explore possible sources of heterogeneity in each comparison. These analyses considered adversity type (e.g. sexual abuse, physical abuse, neglect), adversity measure (e.g. questionnaire, clinical interview, medical chart review), specific diagnoses within other psychiatric groups, and sex. Publication bias was assessed by Egger's test to determine statistically the degree of funnel plot asymmetry, with asymmetry representing publication bias (Egger *et al*. 1997). Forest plots were generated using RevMan 5.1 (Review Manager, 2011).

Where studies included the same individual in multiple adversity types, to prevent sample overlap within each diagnostic analysis we included only data on the most commonly reported adversity, sexual abuse. Where studies report several diagnoses for the one individual, these were able to be included in each analysis because analyses on diagnostic groups were conducted separately and samples therefore did not overlap.

Results

Search results (*Fig. 1*)

The searches yielded 1104 published and unpublished references, of which 805 were excluded following review of the abstract, and a further 274 were excluded following review of the full text. This left 25 studies meeting inclusion criteria (Friedman & Harrison, 1984; Craine *et al*. 1988; Stein *et al*. 1988; Ross *et al*. 1989; Byrne *et al*. 1990; Fink & Golinkoff, 1990; Goff *et al*. 1991; Darves-Bornoz *et al*. 1995; Nettelbladt *et al*. 1996; Nurcombe *et al*. 1996; Wurr & Partridge, 1996; Wexler *et al*. 1997; Honig *et al*. 1998; Friedman *et al*. 2002; Hlastala & McClellan, 2005; Spence *et al*. 2006; Choi *et al*. 2009; Rubino *et al*. 2009; Conus *et al*. 2010; Husted *et al*. 2010; Kingdon *et al*. 2010; McCabe *et al*. 2012; Aas *et al*. 2011; Alvarez *et al*. 2011; Vogel *et al*. 2011).

Study characteristics

Study characteristics and STROBE assessments are presented in Table 1. Overall, inter-rater agreement on the STROBE checklist was 88% (range for individual items: 62–100%). All 25 studies scored ⩾66% on applicable items on the STROBE, indicating that studies adhered to recommended reporting methods. There were insufficient data reported separately for males and females to allow subgroup analyses of sex effects. Assessment of publication bias using Egger's test was not significant for any of the seven analyses ($p>0.05$), so the results are unlikely to be subject to publication bias.

Meta-analyses results

Schizophrenia versus non-psychiatric controls (*Fig. 2a*)

Meta-analysis of seven controlled studies was conducted on a total of 798 patients with schizophrenia and 883 non-psychiatric controls. The random effects estimate yielded a medium to large effect of increased reporting of childhood adversity among schizophrenia patients (OR 3.60, 95% CI 2.08–6.23, $p<0.00001$). Data were imprecise and with moderate heterogeneity ($I^2=65\%$, $p=0.009$). One study was an obvious outlier, being the only study reporting reduced childhood adversity rates in schizophrenia compared to controls (Honig *et al*. 1998). This study used non-patient (psychiatrically healthy) voice hearers as controls, and removing it from the analysis increased the OR to 4.15 and reduced I^2 to 51% ($p=0.07$). Two other studies used unconventional non-psychiatric control groups; one used unaffected relatives (Husted *et al*. 2010); the other used diabetic patients, their partners, and the partners of the schizophrenia patients (Nettelbladt *et al*. 1996). Removing all three studies from the analysis did not change the overall results, and heterogeneity was reduced (four studies, $n=1414$, OR 3.92, 95% CI 2.37–6.50, $p<0.001$, $I^2=55\%$, $p=0.08$). Planned subgroup analyses of the complete set of studies indicated no differences in results due to adversity type (sexual; or combined sexual, physical

https://doi.org/10.1017/S0033291712000785 Published online by Cambridge University Press

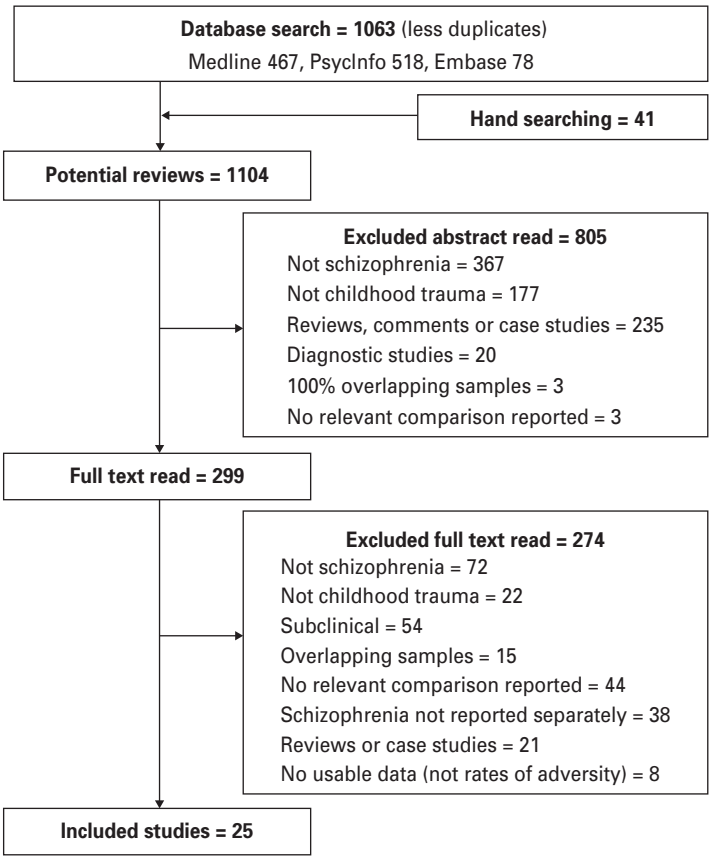


Fig. 1. Flow diagram showing the flow of information through the different phases of this meta-analysis.

and other adversity: $Q_B = 0.01$, $p = 0.92$) or adversity measure (clinical interview or questionnaire: $Q_B = 0.00$, $p = 0.97$). These findings indicate moderate to high quality evidence of increased childhood adversity in schizophrenia patients compared to non-psychiatric controls. This evidence is consistent (without the outlier), of medium to large effect, uses large samples, but has considerable imprecision.

Schizophrenia versus affective psychosis (*Fig. 2b*)

Eight studies compared 751 patients with schizophrenia to 309 patients with an affective psychosis. The random effects estimate showed no differences between groups in childhood adversity rates (OR 1.23, 95% CI 0.77–1.97, $p = 0.39$). Data were imprecise but consistent ($I^2 = 42\%$, $p = 0.10$). Planned subgroup analyses showed no significant differences in results due to diagnoses (bipolar disorder, manic disorder or combined bipolar and psychotic depression: $Q_B = 2.83$, $p = 0.24$), adversity type (sexual; or combined sexual and physical, or other adversity: $Q_B = 3.58$, $p = 0.17$) or adversity measure (clinical interview, questionnaire or chart review: $Q_B = 1.14$, $p = 0.54$). This evidence is of moderate to high quality because of the large samples and consistent data, but it is also imprecise.

Schizophrenia versus anxiety disorders (*Fig. 2c*)

Seven studies compared 199 patients with schizophrenia to 580 patients with a diagnosis of an anxiety disorder. The random effects overall estimate showed a medium increased risk of childhood adversity in schizophrenia (OR 2.54, 95% CI 1.29–5.01, $p = 0.007$). Data were imprecise but consistent ($I^2 = 37\%$, $p = 0.15$). Planned subgroup analyses indicated significant differences between adversity type (sexual; or combined sexual, physical and other adversity: $Q_B = 5.43$, $p = 0.02$), with five studies of sexual abuse reporting no significant differences between groups ($n = 649$, OR 1.66, 95% CI 0.90–3.08, $p = 0.10$, $I^2 = 12\%$, $p = 0.27$) and two studies with mixed sexual and physical abuse and neglect (Spence *et al*. 2006; Vogel *et al*. 2011) reporting increased childhood adversity in schizophrenia ($n = 130$, OR 6.95, 95% CI 2.48–19.51, $p < 0.001$, $I^2 = 12\%$, $p < 0.27$). Other subgroup analyses showed no differences in adversity measure (clinical interview, questionnaire or chart review: $Q_B = 0.33$, $p = 0.57$) or diagnoses (anxiety disorder, panic disorder, neurotic

https://doi.org/10.1017/S0033291712000785 Published online by Cambridge University Press

disorder or combined anxiety and depression: $Q_B = 5.21$, $p = 0.27$). The evidence for the overall effect is of moderate quality; data are consistent, with a medium effect size and large sample size; however, there is considerable imprecision, and the subgroup analysis of the majority of the studies reporting only sexual abuse revealed no significant differences between groups.

Schizophrenia versus depressive disorder (*Fig. 2d*)

Seven studies compared 526 patients with schizophrenia to 885 patients with a diagnosis of a depressive disorder. The random effects estimate showed no differences between these patient groups (OR 1.37, 95% CI 0.53–3.49, $p = 0.51$). Data were imprecise and with considerable heterogeneity ($I^2 = 88\%$, $p < 0.00001$). Planned subgroup analyses revealed no differences in adversity type (sexual; or combined sexual, physical and other adversity: $Q_B = 2.30$, $p = 0.13$) but significant differences in adversity measure ($Q_B = 8.98$, $p < 0.01$). The pooled estimate from six studies using questionnaires reported no differences between groups ($n = 982$, OR 1.77, 95% CI 0.73–4.25, $p = 0.20$, $I^2 = 76\%$, $p < 0.01$) whereas the one study using chart review (Wexler *et al*. 1997) reported significantly reduced childhood adversity in schizophrenia, with data imprecise ($n = 429$, OR 0.39, 95% CI 0.25–0.61, $p < 0.001$). There were also significant differences between diagnoses ($Q_B = 8.69$, $p < 0.01$), with five studies including patients with depression reporting similar adversity rates to schizophrenia patients ($n = 1281$, OR 0.83, 95% CI 0.32–2.18, $p = 0.71$, $I^2 = 88.0\%$, $p < 0.001$) whereas two studies with mixed samples of depression and anxiety patients (Spence *et al*. 2006; Vogel *et al*. 2011) reported increased childhood adversity in schizophrenia ($n = 130$, OR 6.95, 95% CI 2.48–19.51, $p < 0.001$, $I^2 = 12\%$, $p < 0.27$). The evidence of no differences between patients with depressive disorder relative to schizophrenia is of moderate to low quality because of substantial heterogeneity and considerable imprecision, although the overall sample size is large.

Schizophrenia versus dissociative disorders and PTSD (*Fig. 2e*)

Four studies compared 59 patients with schizophrenia to 76 patients with a diagnosis of a dissociative disorder or PTSD. The random effects overall estimate showed a large effect such that patients with schizophrenia were less likely to report childhood adversity (OR 0.03, 95% CI 0.01–0.15, $p < 0.0001$). Data were precise and consistent ($I^2 = 51\%$, $p = 0.11$). Planned subgroup analyses showed no significant differences between diagnoses (DID or combined dissociative disorder and PTSD: $Q_B = 0.92$, $p = 0.34$) or adversity measure (clinical interview or chart review: $Q_B = 0.92$, $p = 0.34$). All studies assessed only sexual abuse. This evidence is of moderate quality, with consistent, precise data, and a large effect size, although the sample size was small.

Schizophrenia versus other psychoses (*Fig. 2f*)

Three studies compared 103 patients with schizophrenia to 36 patients with other psychoses. The random effects estimate showed no significant differences between groups (OR 0.69, 95% CI 0.28–1.68, $p = 0.41$). Data were imprecise but consistent ($I^2 = 2\%$, $p = 0.36$). Planned subgroup analyses showed no significant differences in results due to diagnosis (psychosis NOS or atypical psychosis: $Q_B = 1.98$, $p = 0.15$), adversity type (sexual; or combined sexual, physical and other adversity: $Q_B = 2.03$, $p = 0.36$) or adversity measure (clinical interview or questionnaire: $Q_B = 0.24$, $p = 0.63$). This evidence is of moderate to low quality, with consistent but imprecise data, and uses small samples.

Schizophrenia versus personality disorders (*Fig. 2g*)

Three studies compared 116 patients with schizophrenia to 71 patients with a personality disorder. The random effects overall estimate showed no differences between these patient groups (OR 0.65, 95% CI 0.09–4.71, $p = 0.67$). Data were imprecise and with substantial heterogeneity ($I^2 = 80\%$, $p = 0.006$). Subgroup analyses showed no significant differences according to diagnoses (borderline personality disorder or all personality disorders combined: $Q_B = 0.83$, $p = 0.36$) or adversity measures (clinical interview or questionnaire: $Q_B = 0.83$, $p = 0.36$). All studies assessed only sexual abuse. This evidence is of low quality due to substantial heterogeneity and considerable imprecision.

Discussion

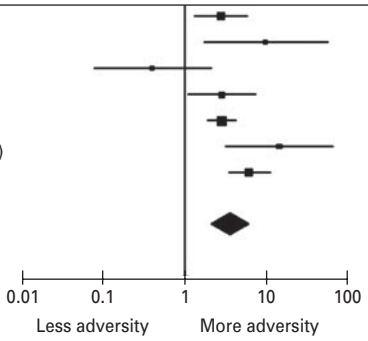
The aim of this meta-analysis was to investigate the evidence for childhood adversity as a risk factor for schizophrenia, taking into consideration the effects of adversity type, adversity measure and psychiatric diagnosis. The effects of sex were not investigated because of lack of reporting in primary studies. We found a medium to large effect of childhood adversity in people with schizophrenia compared to non-psychiatric controls, with the evidence rated as moderate to high quality according to GRADE guidelines. These results are consistent with the, often tentative, conclusions of previous reviews of childhood trauma and psychosis (Rind *et al*. 1998; Read *et al*. 2005;

https://doi.org/10.1017/S0033291712000785 Published online by Cambridge University Press

(*a*)

Study or subgroup	Schizophrenia Events	Schizophrenia Total	Controls Events	Controls Total	Weight	Odds ratio M-H, Random, 95% CI
Aas 2011	21	83	15	138	17.9%	2.78 (1.34–5.76)
Friedman 1984	12	20	2	15	7.2%	9.75 (1.72–55.37)
Honig 1998	3	18	5	15	7.8%	0.40 (0.08–2.06)
Husted 2010	16	79	7	86	14.7%	2.87 (1.11–7.40)
McCabe 2012	354	408	186	267	23.2%	2.85 (1.94–4.21)
Nettlebladt 1996	8	17	3	52	8.8%	14.52 (3.22–65.41)
Rubino 2009	50	173	19	310	20.4%	6.23 (3.53–11.00)
Total (95% CI)		798		883	100.0%	3.60 (2.08–6.23)
Total events	464		237			

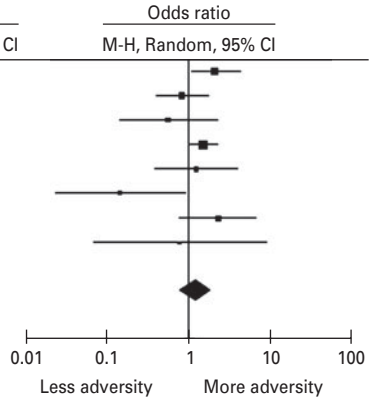
Heterogeneity: $\tau^2 = 0.30$; $\chi^2 = 17.05$, df = 6 ($p = 0.009$); $I^2 = 65\%$
Test for overall effect: $Z = 4.58$ ($p < 0.00001$)



(*b*)

Study or subgroup	Schizophrenia Events	Schizophrenia Total	Affective psychosis Events	Affective psychosis Total	Weight	Odds ratio M-H, Random, 95% CI
Aas 2011	63	83	32	55	18.7%	2.26 (1.09–4.72)
Alveraz 2011	28	62	20	40	17.3%	0.82 (0.37–51.83)
Choi 2009	11	20	9	13	7.9%	0.54 (0.12–2.36)
Conus 2010	174	469	37	136	26.8%	1.58 (1.04–2.41)
Darves-Bornoz 1995	12	64	4	26	10.2%	1.27 (0.37–4.37)
Fink 1990	2	11	7	11	4.9%	0.13 (0.02–0.90)
Hlastala 2005	17	27	9	22	11.2%	2.46 (0.77–7.79)
Stein 1988	2	15	1	6	3.0%	0.77 (0.06–10.49)
Total (95% CI)		751		309	100.0%	1.23 (0.77–1.97)
Total events	309		119			

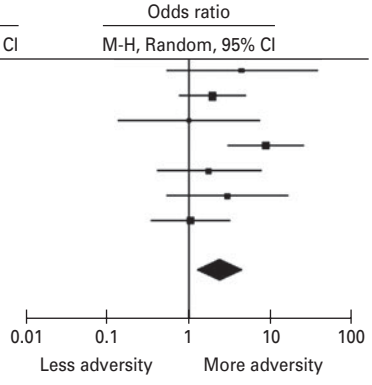
Heterogeneity: $\tau^2 = 0.17$; $\chi^2 = 12.13$, df = 7 ($p = 0.10$); $I^2 = 42\%$
Test for overall effect: $Z = 0.87$ ($p = 0.39$)



(*c*)

Study or subgroup	Schizophrenia Events	Schizophrenia Total	Anxiety disorders Events	Anxiety disorders Total	Weight	Odds ratio M-H, Random, 95% CI
Craine 1988	21	43	1	6	7.6%	4.77 (0.51–44.33)
Friedman 2002	7	22	30	160	22.0%	2.02 (0.76–5.39)
Ross 1989	2	20	2	20	8.5%	1.00 (0.13–7.89)
Spence 2006	30	40	7	30	19.5%	9.86 (3.25–29.85)
Stein 1988	2	15	24	310	13.1%	1.83 (0.39–8.60)
Vogel 2011	4	25	2	35	107%	3.14 (0.53–18.70)
Wurr 1996	13	34	7	19	18.6%	1.06 (0.33–3.39)
Total (95% CI)		199		580	100.0%	2.54 (1.29–5.01)
Total events	79		73			

Heterogeneity: $\tau^2 = 0.30$; $\chi^2 = 9.46$, df = 6 ($p = 0.15$); $I^2 = 37\%$
Test for overall effect: $Z = 2.69$ ($p = 0.007$)



(*d*)

Study or subgroup	Schizophrenia Events	Schizophrenia Total	Depressive disorders Events	Depressive disorders Total	Weight	Odds ratio M-H, Random, 95% CI
Friedman 2022	7	22	8	19	13.4%	0.64 (0.18–2.30)
Rubino 2009	50	173	44	305	17.1%	2.41 (1.52–3.81)
Spence 2006	30	40	7	30	14.3%	9.86 (3.25–29.85)
Stein 1988	2	15	24	241	12.0%	1.39 (0.30–6.54)
Vogel 2011	4	25	2	35	10.8%	3.14 (0.53–18.70)
Wexler 1997	39	217	76	212	17.1%	0.39 (0.25–0.61)
Wurr 1996	13	34	24	43	15.2%	0.49 (0.20–1.23)
Total (95% CI)		526		885	100.0%	1.37 (0.53–3.49)
Total events	145		185			

Heterogeneity: $\tau^2 = 1.29$; $\chi^2 = 51.87$, df = 6 ($p < 0.00001$); $I^2 = 88\%$
Test for overall effect: $Z = 0.65$ ($p = 0.51$)

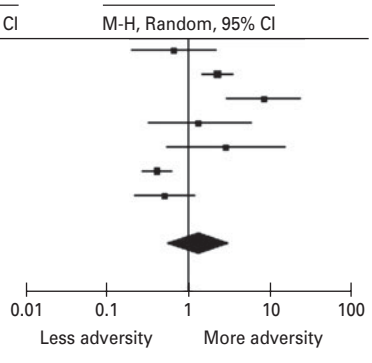


Fig. 2. For legend see opposite page.

https://doi.org/10.1017/S0033291712000785 Published online by Cambridge University Press

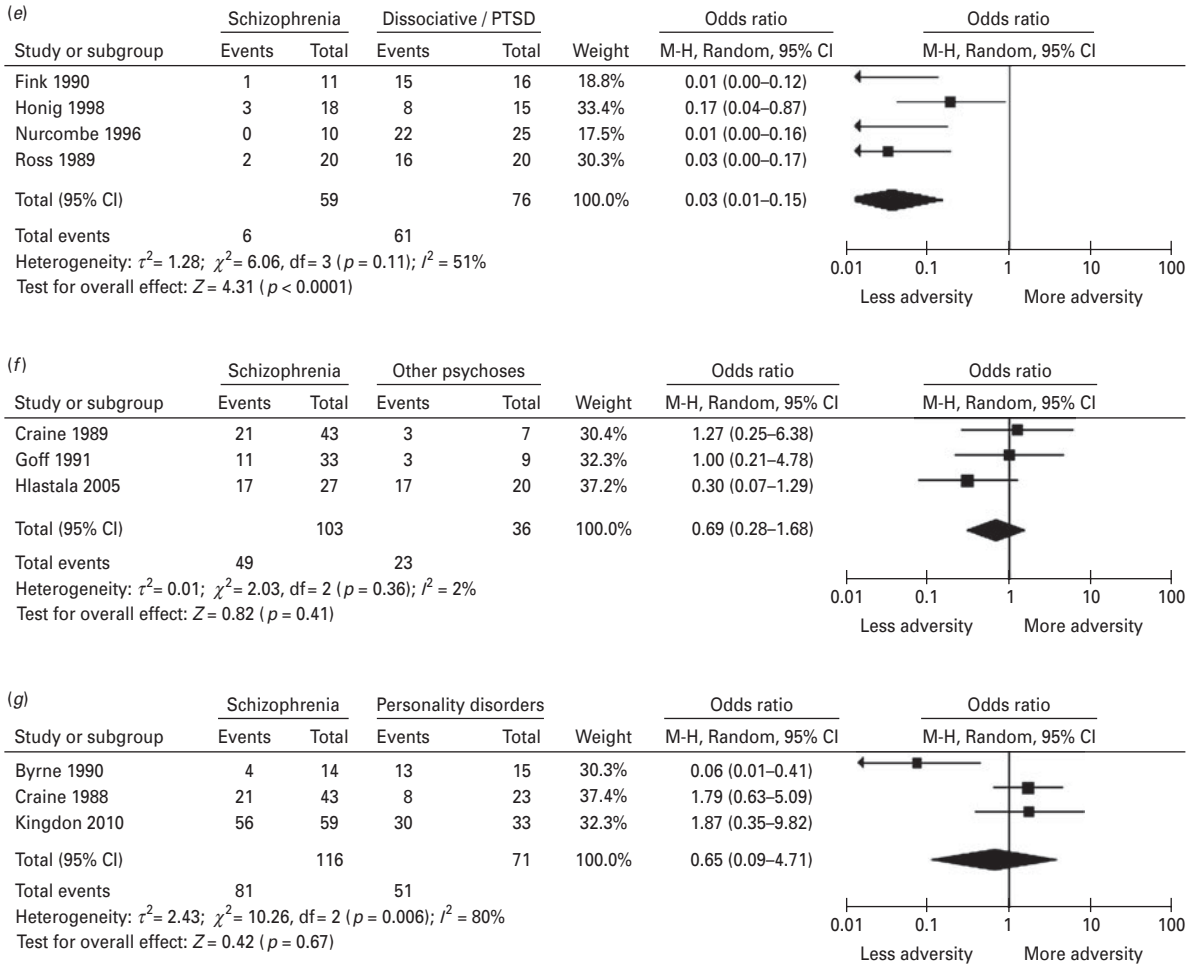


Fig. 2. Forest plots for comparisons between schizophrenia and (*a*) non-psychiatric controls, (*b*) affective psychosis, (*c*) anxiety disorders, (*d*) depressive disorder, (*e*) dissociative disorders and post-traumatic stress disorder (PTSD), (*f*) other psychoses and (*g*) personality disorders.

Morgan & Fisher, 2007; Bendall *et al*. 2008; Larkin & Read, 2008) and extend those previous conclusions by quantifying the effect size for schizophrenia. However, the findings are not consistent with the most recent meta-analysis (Chen *et al*. 2010), which reported no significant association between childhood sexual abuse and schizophrenia. This is because of differing inclusion criteria: Chen *et al*. (2010) included case-control and cohort studies that assessed rates of schizophrenia in people with a sexual abuse history compared to people with no sexual abuse history or population controls only, whereas our review assessed rates of all childhood adversities in schizophrenia patients compared to controls, with no cohort study meeting inclusion criteria.

Moderate quality evidence supported a medium effect of increased risk of childhood adversity in schizophrenia patients relative to anxiety disorders, and a large effect of increased risk of childhood adversity in dissociative disorders or PTSD patients compared to schizophrenia patients. No differences were reported in moderate to high quality evidence comparing patients with schizophrenia and affective psychosis, or in moderate to low quality evidence comparing schizophrenia with depression, other psychoses and personality disorders. Compared to controls, Chen *et al*. (2010) reported significant medium-sized increases in sexual abuse in people with PTSD, anxiety disorders and depression. A small to medium size effect was also observed in one meta-analysis of childhood sexual abuse in borderline personality disorder patients compared to controls (Fossati *et al*. 1999). No meta-analysis has yet been conducted that assesses rates of childhood adversity in affective psychosis.

In each comparison we conducted planned subgroup analyses for adversity type, adversity measure and, where applicable, specific diagnoses within the

https://doi.org/10.1017/S0033291712000785 Published online by Cambridge University Press

https://doi.org/10.1017/S0033291712000785 Published online by Cambridge University Press

Table 1. *Characteristics of included studies*

Study (first-named author)	Design	Samples	Diagnostic tool	No. of males	Age (years), mean (S.D.)	Adversity type	Adversity measure	STROBE (%)
Aas, 2011	Case-control	Schizophrenia, $n=83$ Bipolar disorder, $n=29$ Affective psychosis (depressive), $n=26$ Controls (randomly selected, screened psychosis), $n=138$	ICD-10	73 patients 64 controls	30.6 (10.9) patients 32.2 (9.3) controls	Sexual abuse	CECAQ	79
Alvarez, 2011	Cross-sectional	Schizophrenia/schizo-affective disorder, $n=62$ Bipolar disorder, $n=40$	DSM-IV	40 schizophrenia 14 bipolar	39.4 (10.4) total sample	Sexual abuse Physical abuse Witness domestic violence	TLEQ, DEQ	79
Byrne, 1990	Cross-sectional	Schizophrenia, $n=14$ Borderline personality disorder, $n=15$	DSM-III	4 schizophrenia 2 borderline	25.9 (3.3) schizophrenia 24.6 (N.R.) borderline	Sexual abuse	Childhood Life Events and Family Characteristics Questionnaire	74
Choi, 2009	Cross-sectional	Schizophrenia/schizo-affective disorder, $n=20$ Bipolar disorder, $n=13$	DSM-IV	17 total sample	30.8 (8.5) CA 37.7 (10.8) no CA	Sexual abuse	Medical chart review	74
Conus, 2010	Cross-sectional	Schizophrenia/schizo-affective disorder, $n=469$ Bipolar disorder, $n=118$ Affective psychosis (depressive), $n=18$	DSM-IV	432 total sample	22.0 (3.4) total sample	Sexual abuse Physical abuse	Clinical interview	85
Craine, 1988	Cross-sectional	Schizophrenia, $n=43$ Other psychosis, $n=7$ Neurotic disorder, $n=6$ Personality disorders, $n=23$	DSM-III	0	34.7 (N.R.) total sample	Sexual abuse	Clinical interview	76
Darves-Bornoz, 1995	Cross-sectional	Schizophrenia, $n=64$ Bipolar disorder, $n=26$	DSM-III-R	0	34.4 (N.R.) schizophrenia 32.7 (N.R.) bipolar	Sexual abuse	Clinical interview	76
Fink, 1990	Cross-sectional	Schizophrenia, $n=11$ Bipolar disorder, $n=11$ Multiple personality disorder, $n=16$	DSM-III-R DDIS	N.R.	N.R.	Sexual abuse	DDIS	66
Friedman, 1984	Case-control	Schizophrenia, $n=20$ Controls (matched, screened psychiatric), $n=15$	DSM-III	0	30.8 (6.8) schizophrenia 31.9 (7.0) controls	Sexual abuse	Clinical interview	76

https://doi.org/10.1017/S0033291712000785 Published online by Cambridge University Press

Friedman, 2002	Cross-sectional Random recruitment	Schizophrenia, $n=22$ Depressive disorder, $n=19$ Anxiety/panic disorder, $n=160$	SCID ADIS-R	60 total sample	39 (13) total sample	Sexual abuse	LHQ	85
Goff, 1991	Cross-sectional	Schizophrenia, $n=33$ Delusional psychosis/ psychosis NOS, $n=9$	DSM-III-R SCID-D	40 total sample	40.5 (13.5) CA 43.1 (9.6) no CA	Sexual abuse Physical abuse	LEQ	76
Hlastala, 2005	Cross-sectional	Schizophrenia, $n=27$ Bipolar disorder, $n=22$ Psychosis NOS, $n=20$	DSM-IV DICA-R	19 schizophrenia 14 bipolar 13 psychosis	14.7 (2.2) schizophrenia 15.2 (1.7) bipolar 14.6 (2.7) psychosis	Sexual abuse Physical abuse Neglect	The PTSD modules of the structured diagnostic interviews	82
Honig, 1998	Case-control	Schizophrenia, $n=18$ Dissociative identity disorder, $n=15$ Controls (voice hearers, screened psychiatric), $n=15$	CIDI (DSM-IV criteria) DES	7 schizophrenia 1 dissociative 4 controls	37 (11) schizophrenia 40 (8) dissociative 56 (11) controls	Sexual abuse	Clinical interview	71
Husted, 2010	Case-control	Schizophrenia/schizo-affective disorder, $n=79$ Controls (relatives, screened schizophrenia), $n=86$	DSM-III-R	42 schizophrenia 35 controls	51.8 (14.1) schizophrenia 49.6 (11.8) controls	Sexual abuse Physical abuse Negative life events	Clinical interview	82
Kingdon, 2010	Cross-sectional	Schizophrenia, $n=59$ Borderline personality disorder, $n=33$	DSM-IV	40 schizophrenia 3 borderline	40.2 (10.7) schizophrenia 32.9 (10.0) borderline	Sexual abuse	CTQ	76
McCabe, 2012	Case-control	Schizophrenia, $n=408$ Controls (screened psychiatric), $n=267$	ICD-10	268 schizophrenia 116 controls	40.7 (11.1) schizophrenia 39.3 (13.7) controls	Sexual abuse Physical abuse Emotional abuse Loss Neglect	CTQ	76
Nettelbladt, 1996	Case-control	Schizo-affective disorder, $n=17$ Controls (diabetics, partners screened psychiatric), $n=52$	DSM-III	4 schizophrenia 21 controls	40.5 (6.2) schizophrenia Controls – age matched	Sexual abuse	Clinical interview	91
Nurcombe, 1996	Cross-sectional	Schizophrenia, $n=10$ Dissociative disorder/ PTSD, $n=25$	DSM-III-R	6 schizophrenia 5 dissociative/ PTSD	16.2 (2.5) schizophrenia 14.5 (2.16) dissociative/ PTSD	Sexual abuse	Medical chart review	72
Ross, 1989	Cross-sectional	Schizophrenia, $n=20$ Panic disorder, $n=20$ Multiple personality disorder, $n=20$	DSM-III DDIS	14 schizophrenia 3 panic 1 personality	38.4 (10.0) schizophrenia 34.6 (9.1) panic disorder 32.0 (7.7) multiple personality	Sexual abuse	Clinical interview	68

https://doi.org/10.1017/S0033291712000785 Published online by Cambridge University Press

Table 1 (*cont.*)

Study (first-named author)	Design	Samples	Diagnostic tool	No. of males	Age (years), mean (S.D.)	Adversity type	Adversity measure	STROBE (%)
Rubino, 2009	Case-control	Schizophrenia, $n=173$ Depressive disorder, $n=305$ Controls (not screened psychiatric), $n=310$	DSM-IV	111 schizophrenia 92 depressive 135 controls	36.2 (11.2) schizophrenia 43.1 (14.8) depressive 37.4 (12.3) controls	Sexual abuse Physical abuse Emotional abuse Loss	The Abuse Questionnaire	68
Spence, 2006	Cross-sectional	Schizophrenia, $n=40$ Depressive/anxiety disorder, $n=30$	DSM-IV	25 schizophrenia 13 depressive/anxiety	42.6 (12.6) schizophrenia 45.5 (12.2) depressive/anxiety	Sexual abuse Physical abuse Negative life events	THQ	85
Stein, 1988	Cross-sectional	Schizophrenia, $n=15$ Manic disorder, $n=6$ Depressive disorder, $n=241$ Anxiety disorder, $n=310$	DIS DSM-III	5 schizophrenia 5 manic 96 depressive 109 anxiety	N.R.	Sexual abuse	Survey – Los Angeles Epidemiologic Catchment Area Study	82
Vogel, 2011	Cross-sectional	Schizophrenia, $n=25$ Depressive/anxiety disorders, $n=35$	DSM-IV	18 schizophrenia 10 depression/anxiety	36.0 (12.4) schizophrenia 37.4 (10.3) depressive/anxiety	Sexual abuse Physical abuse Emotional abuse Neglect	CTQ	76
Wexler, 1997	Cross-sectional	Schizophrenia, $n=217$ Depressive disorder, $n=212$	DSM-III-R	N.R.	N.R.	Sexual abuse Physical abuse Loss	Medical chart review	76
Wurr, 1996	Cross-sectional	Schizophrenia, $n=34$ Depressive disorder, $n=43$ Neurotic disorder, $n=19$	ICD-9	16 schizophrenia 14 depressive 1 neurotic	N.R.	Sexual abuse	Self-administered questionnaire	76

ADIS-R, Anxiety Disorders Interview Schedule – Revised; CA, childhood adversity; CECAQ, Childhood Experiences of Care Abuse Questionnaire; CIDI, Composite International Diagnostic Interview; CTQ, Childhood Trauma Questionnaire; DDIS, Dissociative Disorder Interview Schedule; DEQ, Distressing Event Questionnaire; DES, Dissociative Experiences Scale; DICA-R, Diagnostic Interview for Children and Adolescents – Revised; DIS, Diagnostic Interview Schedule; DSM, Diagnostic and Statistical Manual of Mental Disorders; ICD, International Classification of Disease; LEQ, Life Experiences Questionnaire; LHQ, Life History Questionnaire; NOS, not otherwise specified; N.R., not reported; PTSD, post-traumatic stress disorder; SCID, Structured Clinical Interview; SCID-D, Structured Clinical Interview Dissociative Disorders; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology; THQ, Trauma History Questionnaire; TLEQ, Traumatic Life Events Questionnaire.

other psychiatric groups. As most of the primary studies were not designed to specifically address these questions, these analyses are not hypothesis driven, but hypothesis generating. Subgroup analyses indicated a lack of differences in adversity types, adversity measures or diagnoses (where applicable) when schizophrenia was compared to non-psychiatric controls, affective psychosis, other psychoses, and dissociative disorders and PTSD. The comparison of schizophrenia with depressive disorders revealed that the six studies using questionnaires reported no differences between groups whereas one study using chart review reported significantly reduced childhood adversity in schizophrenia. The result indicating lack of differences between schizophrenia and depressive disorder is more robust because of the larger samples and the use of standardized questionnaires, as chart review methods may not be as reliable as these methods (Read *et al*. 2005; Larkin & Read, 2008). In the anxiety comparison, the overall analysis was significant, showing increased childhood adversity in schizophrenia. However, five out of seven studies that included only patients with anxiety disorders and reported only on sexual abuse (*versus* combining patients with anxiety or depression and reporting combined sexual, physical and other forms of abuse) indicated a lack of differences between groups. Therefore, the larger subgroup analysis reporting no significant differences between groups is more robust, with larger samples using anxiety disorders only. The finding of increased childhood adversity in dissociative disorders and PTSD is not surprising given that PTSD requires the existence of prior trauma for a diagnosis, and flashbacks of abuse or trauma are a common symptom in people with dissociative disorders (Nurcombe *et al*. 1996).

These findings highlight a lack of specificity of childhood adversity as a possible risk factor for schizophrenia. A pathological stress response that adversely impacts on psychological development, involving the hypothalamic–pituitary–adrenal (HPA) axis, is likely to be an important effect of childhood adversity and a component cause of a variety of different adult psychiatric disorders. Childhood adversity has been found to be associated with persistent sensitization and increased activation of the HPA axis, and hyperactivity of the HPA axis has been observed in people with first-episode psychosis (Mondelli *et al*. 2010), and depression or anxiety (Heim *et al*. 2000). The finding that exposure to seemingly similar childhood adversities contributes to a variety of psychiatric disorder outcomes may reflect genetic influences, which may further interact with environmental factors such as obstetric complications (Cannon *et al*. 2002) to create a unique causal pathway.

Limitations

A limitation of this meta-analysis is the reliance on retrospective measures of childhood abuse experiences, such that results may be prone to recall bias, particularly as memory deficits are reported consistently in both schizophrenia and affective disorders (Stefanopoulou *et al*. 2009). However, if under-reporting of abuse in psychiatric disorders has occurred, then the effect reported in this review is lower than what would be indicated in the absence of under-reporting. Conversely, if over-reporting in psychiatric patients has occurred, then the effect reported here is higher than would be expected. This is unlikely to be the case. One study reported that incorrect allegations of sexual assaults were no different for patients with schizophrenia than the general population (Darves-Bornoz *et al*. 1995). Another study reported that childhood histories of physical and sexual abuse can be reliably assessed in women with severe mental illness using a standardized instrument (Meyer *et al*. 1996; Goodman *et al*. 1999) and most studies used standardized instruments. Moreover, there were no differences in the subgroup analyses of adversity measure in most comparisons. One record linkage study using prospectively recorded data did not meet inclusion criteria because it assessed psychiatric outcome in a large cohort of individuals selected for having been sexually abused, rather than assessing rates of childhood adversity in psychiatric groups (Cutajar *et al*. 2010). Therefore, we were unable to pool their data for this meta-analysis. Compared with a community-based control group, this study reported an OR of 3.3, which is similar to what is reported here for increased risk of schizophrenia in people with histories of childhood sexual abuse with penetration.

Other limitations of this review are that causation and specificity for schizophrenia have not been established. Without sufficient data that could be pooled or categorized regarding the severity of trauma and the severity of symptoms experienced, we were unable to investigate dose dependence. One large study conducted in England (the Adult Psychiatric Morbidity Survey, 2007) did not meet our inclusion criteria because rates for schizophrenia were not reported separately from other psychosis outcomes (Bebbington *et al*. 2011). The authors report a higher risk of psychosis after exposure to non-consensual sexual intercourse compared to non-consensual sexual talk or touching in children aged <16 years, a result that was not mediated by cannabis use. These findings suggest the effects may be dose dependent for psychosis; however, this has not yet been demonstrated in schizophrenia.

https://doi.org/10.1017/S0033291712000785 Published online by Cambridge University Press

No included studies presented data on other potentially causal variables, such as family history of schizophrenia, cannabis use, paternal age and obstetric complications (Matheson *et al*. 2011), which would have permitted analyses of possible effects of these variables on the relationship between childhood adversity and schizophrenia. Causality is also compromised by the assumption that the trauma precedes the psychopathology; however, there is evidence of developmental anomalies, such as antisocial and withdrawn behaviour in young children who later develop schizophrenia (Tarbox & Pogue-Geile, 2008), that may indicate early psychopathological processes operating prior to the experience of abuse. Children with developmental anomalies of these kinds may be more vulnerable to victimization (Bendall *et al*. 2008). Alternatively, it is possible that developmental anomalies result from abuse and may mediate the link between sexual abuse and later schizophrenia.

There is evidence that childhood adversities tend to cluster (Kessler *et al*. 2010). Where multiple adversities were reported for the same individual, our review reported on sexual abuse, being the most commonly reported adversity, and thus our results may have overestimated the relative importance of this adversity (Green *et al*. 2010). Similarly, many individuals with schizophrenia have co-morbid psychiatric diagnoses (Kessler *et al*. 2011). When co-morbid conditions were apparent, studies included in the meta-analysis allocated participants according to their 'primary' diagnoses, so any observed effects might be attributable to the co-morbid condition.

A potential source of bias in any review is a failure to retrieve a comprehensive sample of studies. This problem applies to the present meta-analysis, where our search strategy, although very sensitive, may have missed studies, particularly unpublished studies, although the results of our Egger's tests suggest that this review is unlikely to be subject to publication bias. Furthermore, our definition of childhood adversity was restricted to include studies of childhood sexual and physical abuse and neglect but not the loss of, or separation from, a parent. Nevertheless, three studies within the meta-analysis (Wexler *et al*. 1997; Rubino *et al*. 2009; McCabe *et al*. 2012) incorporated rates of loss and separation among their adversity data, potentially contributing to imprecision in our estimation of the effect of childhood adversity. Finally, in the absence of published quality assessment methods developed specifically for rating aetiological evidence, we applied GRADE guidelines. GRADE criteria were developed primarily for quality assessment of management strategies and provide only a broad indication of the strength of these findings.

Conclusions

This is the first meta-analysis to report moderate to high quality evidence of a medium to large effect of childhood adversity in people with schizophrenia relative to non-psychiatric controls. We also report no consistent differences in risk compared to other psychiatric diagnoses. These findings may give clinicians greater confidence to investigate the possibility of childhood adversity in patients with schizophrenia, and to enquire concerning possible symptoms of schizophrenia in patients reporting a history of childhood adversity. More research is required that incorporates longitudinal design and other environmental risk factors to assess possible additive and/or interactive causal effects.

Acknowledgements

This study was funded by the Schizophrenia Research Institute using an infrastructure grant from the NSW Department of Health. K. R. Laurens is affiliated with the National Institute for Health Research (NIHR) Specialist Biomedical Research Centre for Mental Health at the South London and Maudsley National Health Trust (NHS) Foundation Trust and the Institute of Psychiatry, King's College London, UK; she also gratefully acknowledges funding support from an NIHR Career Development Fellowship (CDF/08/01/015). This manuscript is part of an ongoing PhD with the University of New South Wales, Sydney, Australia.

Declaration of Interest

None.

References

Aas M, Dazzan P, Fisher HL, Morgan C, Morgan K, Reichenberg A, Zanelli J, Fearon P, Jones PB, Murray RM, Pariante CM (2011). Childhood trauma and cognitive function in first-episode affective and non-affective psychosis. *Schizophrenia Research* **129**, 12–19.

Alvarez M, Roura P, Osés A, Foguet Q, Solà J, Arrufat F (2011). Prevalence and clinical impact of childhood trauma in patients with severe mental disorders. *Journal of Nervous and Mental Disease* **199**, 156–161.

Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, Guyatt GH, Harbour RT, Haugh MC, Henry D, Hill S, Jaeschke R, Leng G, Liberati A, Magrini N, Mason J, Middleton P, Mrukowicz J, O'Connell D, Oxman AD, Phillips B, Schünemann HJ, Edejer TT, Varonen H, Vist GE, Williams Jr. JW, Zaza S; GRADE Working Group (2004). Grading quality of evidence and strength of recommendations. *British Medical Journal* **328**, 1490.

https://doi.org/10.1017/S0033291712000785 Published online by Cambridge University Press

Bebbington P, Jonas S, Kuipers E, King M, Cooper C, Brugha T, Meltzer H, McManus S, Jenkins R (2011). Childhood sexual abuse and psychosis: data from a cross-sectional national psychiatric survey in England. *British Journal of Psychiatry* **199**, 29–37.

Bendall S, Jackson HJ, Hulbert CA, McGorry PD (2008). Childhood trauma and psychotic disorders: a systematic, critical review of the evidence. *Schizophrenia Bulletin* **34**, 568–579.

Borenstein M, Hedges L, Higgins J, Rothstein H (2005). *Comprehensive Meta-Analysis, Version 2*. Biostat: Englewood, NJ.

Byrne CP, Velamoor VR, Cernovsky ZZ, Cortese L (1990). A comparison of borderline and schizophrenic patients for childhood life events and parent-child relationships. *Canadian Journal of Psychiatry* **35**, 590–595.

Chen LP, Murad MH, Paras ML, Colbenson KM, Sattler AL, Goranson EN, Elamin MB, Seime RJ, Shinozaki G, Prokop LJ, Zirakzadeh A (2010). Sexual abuse and lifetime diagnosis of psychiatric disorders: systematic review and meta-analysis. *Mayo Clinic Proceedings* **85**, 618–629.

Choi KH, Reddy LF, Liu NH, Spaulding WD (2009). Memory as a moderator in the relationship between child sexual abuse and maladaptive functioning in people with severe mental illness. *Journal of Nervous and Mental Disease* **197**, 282–286.

Conus P, Cotton S, Schimmelmann B, McGorry P, Lambert M (2010). Pretreatment and outcome correlates of sexual and physical trauma in an epidemiological cohort of first-episode psychosis patients. *Schizophrenia Bulletin* **36**, 1105–1114.

Craine L, Henson C, Colliver J, MacLean D (1988). Prevalence of a history of sexual abuse among female psychiatric patients in a state hospital system. *Hospital and Community Psychiatry* **39**, 300–304.

Cutajar MC, Mullen PE, Ogloff JRP, Thomas SD, Wells DL, Spataro J (2010). Schizophrenia and other psychotic disorders in a cohort of sexually abused children. *Archives of General Psychiatry* **67**, 1114–1119.

Darves-Bornoz JM, Lemperiere T, Degiovanni A, Gaillard P (1995). Sexual victimization in women with schizophrenia and bipolar disorder. *Social Psychiatry and Psychiatric Epidemiology* **30**, 78–84.

Edwards VJ, Holden GW, Felitti VJ, Anda RF (2003). Relationship between multiple forms of childhood maltreatment and adult mental health in community respondents: results from the Adverse Childhood Experiences Study. *American Journal of Psychiatry* **160**, 1453–1460.

Egger M, Davey Smith G, Schneider M, Minder C (1997). Bias in meta-analysis detected by a simple, graphical test. *British Medical Journal* **315**, 629–634.

Fink DL, Golinkoff M (1990). MPD, borderline personality disorder and schizophrenia: a comparative study of clinical features. *Dissociation: Progress in the Dissociative Disorders* **3**, 127–134.

Fossati A, Madeddu F, Maffei C (1999). Borderline personality disorder and childhood sexual abuse: a meta-analytic study. *Journal of Personality Disorders* **13**, 268–280.

Friedman S, Harrison G (1984). Sexual histories, attitudes, and behavior of schizophrenic and 'normal' women. *Archives of Sexual Behavior* **13**, 555–567.

Friedman S, Smith L, Fogel D, Paradis C, Viswanathan R, Ackerman R, Trappler B (2002). The incidence and influence of early traumatic life events in patients with panic disorder: a comparison with other psychiatric outpatients. *Journal of Anxiety Disorders* **16**, 259–272.

Gilbert R, Widom CS, Browne K, Fergusson D, Webb E, Janson S (2009). Burden and consequences of child maltreatment in high-income countries. *Lancet* **373**, 68–81.

Goff DC, Brotman AW, Kindlon D, Waites M, Amico E (1991). Self-reports of childhood abuse in chronically psychotic patients. *Psychiatry Research* **37**, 73–80.

Goodman L, Thompson K, Weinfurt K (1999). Reliability of violent victimization and PTSD among men and women with serious mental illness *Journal of Trauma Stress* **12**, 587–599.

GRADEpro (2008). [Computer program]. Version 3.2 for Windows. Jan Brozek, Andrew Oxman, Holger Schünemann.

Green JG, McLaughlin KA, Berglund PA, Gruber MJ, Sampson NA, Zaslavsky AM, Kessler RC (2010). Childhood adversities and adult psychiatric disorders in the National Comorbidity Survey Replication I. Associations with first onset of DSM-IV disorders. *Archives of General Psychiatry* **67**, 113–123.

Heim C, Newport DJ, Heit S, Graham YP, Wilcox M, Bonsall R, Miller AH, Nemeroff CB (2000). Pituitary-adrenal and autonomic responses to stress in women after sexual and physical abuse in childhood. *Journal of the American Medical Association* **284**, 592–597.

Higgins JPT, Green S (eds) (2008). Cochrane Handbook for Systematic Reviews of Interventions. Wiley: Chichester.

Hlastala SA, McClellan J (2005). Phenomenology and diagnostic stability of youths with atypical psychotic symptoms. *Journal of Child and Adolescent Psychopharmacology* **15**, 497–509.

Honig A, Romme MA, Ensink BJ, Escher SD, Pennings MH, deVries MW (1998). Auditory hallucinations: a comparison between patients and nonpatients. *Journal of Nervous and Mental Disease* **186**, 646–651.

Husted JA, Ahmed R, Chow EWC, Brzustowicz LM, Bassett AS (2010). Childhood trauma and genetic factors in familial schizophrenia associated with the NOS1AP gene. *Schizophrenia Research* **121**, 187–192.

Jumper SA (1995). A meta-analysis of the relationship of child sexual abuse to adult psychological adjustment. *Child Abuse and Neglect* **19**, 715–728.

Kessler RC, McLaughlin KA, Green JG, Gruber MJ, Sampson NA, Zaslavsky AM, Aguilar-Gaxiola S, Alhamzawi AO, Alonso J, Angermeyer M, Benjet C, Bromet E, Chatterji S, de Girolamo G, Demyttenaere K, Fayyad J, Florescu S, Gal G, Gureje O, Haro JM, Hu C-Y, Karam EG, Kawakami N, Lee S, Lepine J-P, Ormel J, Posada-Villa J, Sagar R, Tsang A, Ustun TB, Vassilev S, Viana MC, Williams DR (2010). Childhood adversities

https://doi.org/10.1017/S0033291712000785 Published online by Cambridge University Press

and adult psychopathology in the WHO World Mental Health Surveys. *British Journal of Psychiatry* **197**, 378–385.

Kessler RC, Ormel J, Petukhova M, McLaughlin KA, Green JG, Russo LJ, Stein DJ, Zaslavsky AM, Aguilar-Gaxiola S, Alonso J, Andrade L, Benjet C, de Girolamo G, de Graaf R, Demyttenaere K, Fayyad J, Haro JM, Hu C, Karam A, Lee S, Lepine J-P, Matchsinger H, Mihaescu-Pintia C, Posada-Villa J, Sagar R, Ustun TB (2011). Development of lifetime comorbidity in the World Health Organization World Mental Health Surveys. *Archives of General Psychiatry* **68**, 90–100.

Kingdon DG, Ashcroft K, Bhandari B, Gleeson S, Warikoo N, Symons M, Taylor L, Lucas E, Mahendra R, Ghosh S, Mason A, Badrakalimuthu R, Hepworth C, Read J, Mehta R (2010). Schizophrenia and borderline personality disorder: similarities and differences in the experience of auditory hallucinations, paranoia, and childhood trauma. *Journal of Nervous and Mental Disease* **198**, 399–403.

Larkin W, Read J (2008). Childhood trauma and psychosis: evidence, pathways and implications. *Journal of Postgraduate Medicine* **54**, 287–293.

Matheson SL, Shepherd AM, Laurens KR, Carr VJ (2011). A systematic meta-review grading the evidence for non-genetic risk factors and putative antecedents of schizophrenia. *Schizophrenia Research* **133**, 133–142.

McCabe KL, Maloney EA, Stein HJ, Laughland CM, Carr VJ (2012). Relationship between childhood adversity and clinical and cognitive features in schizophrenia. *Journal of Psychiatric Research*. Published online: 11 February 2012. doi:10.1016/j.jpsychires.2012.01.023.

Meyer I, Muenzenmaier K, Cancienne J, Struening E (1996). Reliability and validity of a measure of sexual and physical abuse histories among women with serious mental illness. *Child Abuse and Neglect* **2**, 213–219.

Molnar BE, Buka SL, Kessler RC (2001). Childhood sexual abuse and subsequent psychopathology: results from the National Comorbidity Survey. *American Journal of Public Health* **91**, 753–760.

Mondelli V, Pariante CM, Navari S, Aas M, D'Albenzio A, Di Forti M, Handley R, Hepgul N, Marques TR, Taylor H, Papadopoulos AS, Aitchison KJ, Murray RM, Dazzan P (2010). Higher cortisol levels are associated with smaller left hippocampal volume in first-episode psychosis. *Schizophrenia Research* **119**, 75–78.

Morgan C, Fisher H (2007). Environment and schizophrenia: environmental factors in schizophrenia: childhood trauma – a critical review. *Schizophrenia Bulletin* **33**, 3–10.

Nettelbladt P, Svensson C, Serin U (1996). Background factors in patients with schizoaffective disorder as compared with patients with diabetes and healthy individuals. *European Archives of Psychiatry and Clinical Neuroscience* **246**, 213–218.

Neumann DA (1994). Long-term correlates of childhood sexual abuse in adult survivors. *New Directions for Mental Health Services* **64**, 29–38.

Nurcombe B, Mitchell W, Begtrup R, Ramontana M, Lababera J, Pruitt J (1996). Dissociative hallucinosis and allied conditions. In *Psychoses and Pervasive Developmental Disorders in Childhood and Adolescence* (ed. F. Volkmar), pp. 107–128. American Psychiatric Press: Washington, DC.

Paolucci EO, Genuis ML, Violato C (2001). A meta-analysis of the published research on the effects of child sexual abuse. *Journal of Psychology* **135**, 17–36.

Pettigrew J, Burcham J (1997). Effects of childhood sexual abuse in adult female psychiatric patients. *Australian and New Zealand Journal of Psychiatry* **31**, 208–213.

Read J, van Os J, Morrison AP, Ross CA (2005). Childhood trauma, psychosis and schizophrenia: a literature review with theoretical and clinical implications. *Acta Psychiatrica Scandinavica* **112**, 330–350.

Review Manager (2011). RevMan [Computer program]. Version 5.1. The Nordic Cochrane Centre, The Cochrane Collaboration: Copenhagen.

Rind B, Tromovitch P, Bauserman R (1998). A meta-analytic examination of assumed properties of child sexual abuse using college samples. *Psychological Bulletin* **124**, 22–53.

Ross CA, Heber S, Norton GR, Anderson G (1989). Differences between multiple personality disorder and other diagnostic groups on structured interview. *Journal of Nervous and Mental Disease* **177**, 487–491.

Rubino IA, Nanni RC, Pozzi DM, Siracusano A (2009). Early adverse experiences in schizophrenia and unipolar depression. *Journal of Nervous and Mental Disease* **197**, 65–68.

Spataro J, Mullen PE, Burgess PM, Wells DL, Moss SA (2004). Impact of child sexual abuse on mental health: prospective study in males and females. *British Journal of Psychiatry* **184**, 416–421.

Spence W, Mulholland C, Lynch G, McHugh S, Dempster M, Shannon C (2006). Rates of childhood trauma in a sample of patients with schizophrenia as compared with a sample of patients with non-psychotic psychiatric diagnoses. *Journal of Trauma and Dissociation* **7**, 7–22.

Stefanopoulou E, Manoharan A, Landau S, Geddes JR, Goodwin G, Frangou S (2009). Cognitive functioning in patients with affective disorders and schizophrenia: a meta-analysis. *International Review of Psychiatry* **21**, 336–356.

Stein JA, Goldring JM, Siegal JM, Burnam MA, Sorrenson SB (1988). Long-term psychological sequelae of child sexual abuse. The Los Angeles Epidemiologic Catchment Area study. In *Lasting Effects of Child Sexual Abuse* (ed. G. E. Wyatt and G. J. Powell), pp. 135–154. Sage Publications: Newbury Park, CA.

Tarbox SI, Pogue-Geile MF (2008). Development of social functioning in preschizophrenia children and adolescents: a systematic review. *Psychological Bulletin* **134**, 561–583.

Vogel M, Meier J, Gronke S, Waage M, Schneider W, Freyberger HJ, Klauer T (2011). Differential effects of childhood abuse and neglect: mediation by posttraumatic distress in neurotic disorder and negative symptoms in schizophrenia? *Psychiatry Research* **189**, 121–127.

Wexler BE, Lyons L, Lyons H, Mazure CM (1997). Physical and sexual abuse during childhood and development of psychiatric illnesses during adulthood. *Journal of Nervous and Mental Disease* **185**, 522–524.

Wurr CJ, Partridge IM (1996). The prevalence of a history of childhood sexual abuse in an acute adult inpatient population. *Child Abuse and Neglect* **20**, 867–872.

https://doi.org/10.1017/S0033291712000785 Published online by Cambridge University Press