

Title:

The relationship between childhood adversity and violence to others among individuals with psychosis: a review and meta-analysis

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Acknowledgements: We are grateful for Dr E Baldwin (PhD, CPsychol, AFBPsS) for her work as an independent second assessor.

Declaration of interest: none of the authors has conflict of interest.

The relationship between childhood maltreatment and violence to others in individuals with psychosis: a systematic review and meta-analysis

Abstract

Background: There is a growing body of literature identifying a relationship between experiences of child abuse and symptoms of psychosis in adults. However, the impact of this relationship on risk of violence has not been systematically explored.

Aims: This meta-analysis aimed to consider the influence of childhood abuse on the risk of violence amongst individuals with psychosis

Method: Five bibliographic databases and two grey literature resources were systematically searched to identify quantitative research which measured risk of violence and experiences of childhood maltreatment in individuals with psychosis. Risk of bias for each study was assessed under pre-defined criteria. Logged odds ratios were synthesised quantitatively in a meta-analysis.

Results: A total of 6298 studies were identified, 11 of which were included in the final analysis (N = 2215), all studies were of a cross-sectional or case-control design. Individuals with psychotic illnesses who reported historical child maltreatment were at approximately twice the risk of perpetrating violence than patients who reported no early abuse (OR = 2.46 (95% CI = 1.91 – 3.16). There was no statistical heterogeneity between main effects ($\tau = 0.00$; $X^2 = 8.87$, $df = 10$, $p = 0.54$, $I^2 = 0\%$).

Discussion: Risk assessments and interventions may benefit from considering the unique contribution of trauma to violence in this population. Future research considering the interaction between childhood experiences and other risk factors for violence in this population, including specific symptoms of psychosis, would inform the current findings. Findings are limited by the lack of longitudinal research in this area, and there was some evidence of publication bias.

Key words: Child abuse and neglect; violent offenders; mental health and violence

Rationale

An increasing body of evidence has demonstrated a relationship between adverse experiences in childhood and poorer adult mental health. Both retrospective (Young, Abelson, Curtis, & Nesse, 1997) and prospective studies (Weich, Patterson, Shaw, & Stewart-Brown, 2009) have established a link between child maltreatment and mood or anxiety disorders. A large scale cohort study has identified poorer health outcomes (including multiple sexual partners, sexually transmitted diseases, ever smoking cigarettes, alcoholism and suicide attempts), increasing in a graded manner with severity of reported childhood emotional, physical or sexual abuse (Dube, Felitti, Dong, Giles, & Anda, 2003). **Adversity during key developmental periods has been associated with various poor outcomes, including: adult criminality (e.g. Jung, Herrenkohl, Klika, Lee, & Brown, 2015); mental health problems (Patterson, Moniruzzaman, & Somers, 2014) and all-cause mortality (Kelly-Irving et al., 2013).** In investigating the behavioural sequelae of experiencing violence in childhood, numerous studies have identified an increased risk of being a victim of or perpetrating violence in later life (Whitfield, Anda, Dube, & Felitti, 2003). For example, an increased risk of perpetrating reactive violence in adulthood has been identified in males who report experiences of physical abuse in childhood (Kolla et al., 2013). Similar studies have suggested that children who witness or experience domestic violence are more likely to perpetrate violence against intimate partners in adulthood (Gil-González, Vives-Cases, Ruiz, Carrasco-Portiño, & Álvarez-Dardet, 2008; Murrell, Christoff, & Henning, 2007).

Given the association between experiencing childhood abuse and negative behavioural, physical and mental health outcomes, more recent research has investigated whether or not childhood **maltreatment** is associated with an increased risk of psychotic disorders. A national co-morbidity survey of England and Wales identified a positive association between reports of physical, sexual and emotional abuse in childhood and the experience of visual, auditory and tactile hallucinations in later life (Shevlin, Dorahy, & Adamson, 2007). A longitudinal cohort study in the UK found that children who experienced maltreatment by an adult were more likely to report psychotic symptoms at age 12, and that this risk remained significant when controlling for genetic vulnerability to psychosis (Arseneault et al., 2011). A recent meta-analysis reported increased rates **of childhood abuse** (including physical abuse, sexual

abuse and neglect) in people with schizophrenia compared to both controls and those suffering from anxious disorders (Matheson, Shepherd, Pinchbeck, Laurens, & Carr, 2013). An earlier review suggested that there was a particular relationship between childhood sexual abuse and hallucinations in adulthood (Read, Os, Morrison, & Ross, 2005).

Another branch of research has **considered** the relationship between psychosis and violence. A meta-analysis of 204 studies found an overall association between psychosis and violence, but cautioned that the strength of this relationship varied significantly as a function of moderator variables, including study design and sampling methodology (Douglas, Guy, & Hart, 2009). A literature review (Walsh, Buchanan, & Fahy, 2002) and later meta-analysis (Fazel, Gulati, Linsell, Geddes, & Grann, 2009) agree that there is an increased risk of violence amongst individuals with schizophrenia, although variance in risk may be mediated by factors such as substance abuse co-morbidity. **It is clear from the available evidence that not all individuals with psychosis perpetrate violence, leading researchers to consider specific factors affecting the risk of violence perpetration within this population.** The suggestion that individuals with schizophrenia are more at risk of perpetrating violence than normal controls has led researchers to consider specific symptoms of psychosis. Some studies have suggested that one route to violence in psychosis is suffering acute symptoms (Volavka, 2013), and that more severe psychotic symptoms may be linked to greater violence (Fresán et al., 2005). Recent reviews have suggested that the content of psychotic symptomology may be relevant. For example, a review of the association between auditory hallucinations and violence did not find a direct association between the experience of command hallucinations and violent behaviour; however there was some evidence that hearing voices involving violence was a risk factor (Bjorkly, 2002). Similarly, a study investigating the content of hallucinations and delusions in individuals with psychosis found that violent participants experienced more negative emotions in perceived voices and held more persecutory delusions than non-violent participants (Cheung, Schweitzer, Crowley, & Tuckwell, 1997) .

Adverse experiences in childhood may not only increase the risk of psychosis but also affect the experience and content of psychotic symptoms. Early **maltreatment** has been found to be particularly associated with positive symptoms, including persecutory ideation (Freeman & Fowler, 2009) and

hallucinatory experiences (Read, Perry, Moskowitz, & Connolly, 2001). Neurodevelopmental models suggest that the experience of extreme stressors during periods of neurological development can result in an increase in the sensitivity of the hypothalamic-pituitary-adrenal (HPA) axis and an exaggerated autonomic response to perceived threats, which can persist into adulthood (Heim et al., 2002), several authors have suggested that this heightened stress response may contribute to or reinforce paranoid ideation in individuals with psychosis (Read, Fosse, Moskowitz, & Perry, 2014). Dysregulation of the HPA axis is associated with abnormalities in the neurotransmitter dopamine (including increased dopamine receptor density and dopamine release), an excess of dopamine is classically associated with schizophrenic illnesses (Guillin, Abi-Dargham, & Laruelle, 2007). Responses to trauma can also include symptoms such as dissociation, including the possible externalisation of traumatic memories (Moskowitz, Read, Farrelly, Rudegeair, & Williams, 2009), cognitive models of psychosis posit that a traumatic memory (for example the perpetrator calling a victim of childhood sexual abuse a slut) may be misattributed to an external event in the present (faulty source-monitoring) as a defence mechanism to prevent reliving the initial trauma (Read et al., 2005). It is possible that psychological responses to early maltreatment (which may be adaptive at the time) are mediated by neurochemical changes resulting in an increased vulnerability to persecutory delusions or hallucinations. Traumagenic neurodevelopmental models of psychosis suggest that the heightened physiological response to stress evident in numerous studies of individuals with psychosis can be caused by childhood trauma, partially accounting for the relationship between early child maltreatment and symptoms of psychosis in adulthood (Read et al., 2001). The combination of the heightened stress response associated with childhood maltreatment and processes such as dissociation or faulty source monitoring as a response to traumatic memories may plausibly increase the vulnerability of an individual with psychosis to experiencing persecutory delusions or hallucinations including negative or violent themes.

While early maltreatment has been established as a risk factor for violence in the general population, given the above evidence that such maltreatment may be particularly associated with persecutory experiences in individuals with psychosis it is possible that childhood maltreatment has a particular association with risk in this population.

Objectives

This review aimed to systematically review and quantitatively investigate the relationship between experiences of abuse or maltreatment in childhood and risk of perpetrating violence in individuals with psychosis.

Methods

A protocol (unpublished) was produced before the commencement of the review and detailed the following information:

Inclusion/exclusion criteria

Population: Children or adults with psychosis or clinically significant psychotic symptoms evidenced by a formal diagnosis or identification of symptoms (using DSM or ICD criteria) by a relevant professional specialised in the area of schizophrenia, schizoaffective disorder, delusional disorder, psychosis not otherwise specified, psychotic depression etc. Mixed samples including patients without psychosis (e.g. participants defined as severe mental illness or including other diagnoses), samples of organic psychosis or samples consisting entirely of substance related disorders were excluded.

Exposure: Experience of childhood maltreatment, including physical or sexual abuse or any form of neglect. Identified by (retrospective) self-report, informant report or official records.

Comparator: No exposure to child maltreatment OR different degrees of exposure.

Outcome: Violence to others, defined as acts of physical aggression directed towards other people, property or animals. Identified by self-report, informant report, formal records or criminal sanction. Self-harm and suicide were not the focus of this review, as distinct risk factors may be implicated in the aetiology of self-injurious behaviour.

Study types: Cohort, cross-sectional and case-control designs studies were included. Review, evidence synthesis, opinion papers (e.g. editorials, commentaries etc.) qualitative studies and single-case experimental designs were excluded.

Search Strategy

The following bibliographic databases and thesis portals were searched (without date restriction) by the first author on 12th November 2015: Applied Social Sciences Index and Abstracts (ASSIA), Embase, Medline, PsychArticles, PsychInfo, ProQuest, DART EThesis. Search terms were drawn from available literature including previous meta-analyses and expanded within electronic databases to identify potential synonyms or useful related terms. The following search terms were used to capture main themes:

Childhood maltreatment inclusive terms: (child abuse) OR (child maltreatment) OR (abandonment) OR (child neglect) OR (emotional abuse) OR (failure to thrive) OR (physical abuse) OR (sexual abuse) OR (verbal abuse) OR (child welfare) OR (victim*) OR (crime victim) OR (battered child syndrome) OR (trauma)

Violence inclusive terms: (violen*) OR (antisocial behavio*) OR (dangerousness) OR (torture) OR (homicide) OR (murder) OR (fighting) OR (attack) OR (conflict) OR (cruelty) OR (agonistic behavio*) OR (aggress*)

Psychosis inclusive terms: (psychosis) OR (psychotic) OR (capgras) OR (cotard) OR (hallucin*) OR (paranoi*) OR (schizophren*) OR (delusion*)

The above search strategy was verified by the third author (SC).

Data collection process

Study data were extracted using a pre-defined pro-forma. The following data items were extracted from each study:

- Population
- Total sample size
- Definition and measurement of psychosis
- Definition and measurement of childhood maltreatment
- Level of measurement of childhood maltreatment

- Definition and measurement of violence
- Level of measurement of violence
- Dichotomous data – maltreated and non-maltreated sample sizes and number of events in each group
- Continuous data – maltreated and non-maltreated sample sizes and means and standard deviations in each group
- Correlational data – total sample size and Pearson's r

Data extraction was completed by the primary author, all studies were independently reviewed by a second assessor (E Baldwin, PhD, CPsychol, AFBPsS) to assess inter-rater reliability using Cohen's Kappa, agreement was perfect for data extraction ($\kappa=1$).

Risk of bias in individual studies

Risk of bias in individual studies was assessed using a predefined pro-forma. This pro-forma was designed to consider risk of bias both at the study level and at the outcome level, in line with the PRISMA guidelines for reporting systematic reviews and meta-analyses (Moher, Liberati, Tetzlaff, & Altman, 2009). Data extracted to assess the risk of study level bias included items relating to: selection bias; Detection and performance bias; attrition bias and reporting bias. In order to consider potential bias at the outcome level, quality assessment also recorded whether or not childhood **maltreatment** was the primary independent or grouping variable, and whether or not risk of violence was the primary outcome measure. The following information relating to potential sources of bias was recorded for all studies:

- What was the study design?
- What was the sampling methodology?
- What were the study's inclusion and exclusion criteria?
- What was the group allocation methodology?
- What were the sources of information (interview or file review)?
- Was collateral evidence relating to violence and childhood **maltreatment** collected?
- Were assessors blind?
- How was missing data identified and treated?
- Comprehensiveness of result reporting
- Was the reporting clear (was any of the above information unavailable)?
- Was childhood **maltreatment** the primary independent/grouping variable?
- Was risk of violence the primary dependent/outcome variable?

Where retrieved studies vary substantially in risk of bias, sensitivity analyses were planned to assess any influence on effect sizes.

The assessment of risk of bias was completed by the primary author, 100% of studies were independently reviewed by a second assessor (E Baldwin, PhD, CPsychol, AFBPsS) to assess inter-rater reliability. Initial inter-rater reliability was very good ($\kappa=0.85$, 95% CI = 0.74 – 0.97). The only discrepancies related to judgements of clarity of reporting. To resolve this discrepancy ‘clarity of reporting’ was operationalised to refer more specifically to whether or not all other information regarding quality assessment was available, using this criterion agreement was perfect.

Summary measures

Data were compared to consider the presence or absence of childhood maltreatment on the presence or absence of violence to others (e.g. a dichotomous comparison) in the form of (logged) odds ratios (ORs).

An OR represents the odds that an outcome will occur (in this instance violence) in an exposed group (those who experienced childhood maltreatment) compared to the odds that this outcome will occur in the absence of this exposure. The natural logarithm of ORs is taken for the purpose of comparison as the sampling distribution of untransformed ORs is positively skewed.

There is evidence that negative outcomes may be more severe in cases of complex or repeated abuse (e.g. a cumulative effect; see Suliman et al., 2009). However, there is limited consistency in the measurement of childhood maltreatment in the available literature and information surrounding the severity, frequency or complexity of abuse experiences may be unreported (May-Chahal & Cawson, 2005). For this reason, and given that childhood maltreatment and violence measurements have an inherent true zero value (i.e. the absence of maltreatment/violent behaviour), a dichotomous summary measure was selected. This provides an estimate of the impact of the presence or absence of abuse on violence perpetration, but limits the sensitivity of the analysis as it does not include the (relative) impact of severe or repeated abuse.

Where studies employed a continuous measurement of violence risk, the means and standard deviations of the measure within maltreated and non-maltreated groups were extracted. This information was

standardised to cohen's d which was then transformed to (logged) ORs (see appendix A for data transformation equations, drawn from (Borenstein, 2011)).

Where studies reported a correlation between a continuous measure of childhood maltreatment and a continuous measure violence, the total sample size and pearson's r were extracted. This statistic was then transformed to cohen's d and finally to (logged) ORs (see appendix A).

Where studies reported individual effects of different forms of abuse (e.g. physical abuse, sexual abuse etc.) on violence risk, these were combined to provide a single estimate of the effect of any abuse for the main analysis (see appendix A).

Synthesis of results

As the data transformation described above precluded entering raw data into the meta-analysis, the generic inverse variance method (which allows for direct comparison of effect sizes and standard errors) was used to compare (logged) ORs. This method of comparison weights studies according to the inverse of the variance of the effect estimate, so larger studies (with smaller standard errors) are given more weight in the analysis. Due to the number of variables known to influence violence in psychosis (e.g substance misuse; familial support etc.), there may be true variance in effect sizes between studies and as such random effects models were planned for main analyses. All analyses and figures were generated using Review Manager (Collaboration, 2014).

Heterogeneity between effect estimates was assessed both with X^2 statistics (Cochran's Q) and I^2 percentages, to provide a measure of the significance of any differences (X^2) and a sensitive analysis of the degree of variation (I^2).

Risk of bias across studies

Risk of publication bias across studies was considered visually using funnel plots and assessed statistically using Egger's test, which considers whether a funnel plot is significantly asymmetrical

using a regression equation of the normalised effect estimate against precision (Egger, Smith, Schneider, & Minder, 1997).

Planned additional analyses

An a-priori sensitivity analysis was planned to assess the influence of data transformation on pooled effect size.

Results

Study selection

Initial searching identified 6488 references; 989 duplicates and 852 clearly irrelevant references were excluded after scanning the titles. After reviewing abstracts and full texts, 4636 did not meet the inclusion criteria. Thirteen potentially relevant studies were identified, two used identical samples to other (included) studies. In the case of over-lapping samples the paper with the greater focus on variables of interest (childhood maltreatment and violence) was retained. Figure 1. details the selection process.

Study characteristics and clinical heterogeneity

As identified in Table 1, studies were identified from five countries, and involved both in- and out-patient samples including male and female participants. In this way the combined sample was representative of a variety of individuals with psychosis.

The ages of participants varied between studies, including child, adolescent and adult samples (see Table 1.). This review was conducted to consider the hypothesis that psychotic symptoms which develop in part as a consequence of experiencing early **maltreatment** may contain more negative or persecutory themes or be associated with higher levels of hostility and so increase the risk of violence (see rationale). Given that all samples included patients with fully expressed psychotic symptoms

(confirmed by a formal diagnosis), all samples were considered in the analysis of main effects. However differences between younger and older samples were investigated in a post-hoc sub-group analysis (see additional analyses, section).

As expected, the definition and measurement of childhood maltreatment also varied between studies, although almost all included experiences of physical or sexual abuse as indicators of maltreatment (with one exception (Lysaker, Wright, Clements, & Plascak-Hallberg, 2002), which considered only physical abuse).

All identified studies were designed to identify factors associated with the risk of perpetrating violence against others, and as such included an assessment of the participant's risk or history of perpetrating violence against others as an outcome variable. One study (Fawzi, Fawzi, & Fouad, 2013) considered violence perpetrated specifically against parents, all others considered more general violence risk. Notably, the largest identified study (Swanson et al., 2006) considered actual violence perpetrated over a 6-month period, in contrast with other studies which considered lifetime history or risk (see also risk of bias within studies).

It is perhaps notable that six (Goldstein, 2003; Khalid, Ford, & Maughan, 2012; Kumari et al., 2014; Ross, Maximon, Kusumi, & Lurie, 2013; Samardžić, Nikolić, Grbeša, Simonović, & Milenković, 2010; Spidel, Lecomte, Greaves, Sahlstrom, & Yuille, 2010) of the eleven studies reported statistically non-significant effects (assuming a probability level of 0.05), only one of which came from an unpublished source (Goldstein, 2003).

Within study risk of bias

See table 2. for a summary of study limitations.

All included Studies were either of a cross-sectional (Bosqui et al., 2014; Lysaker et al., 2002; Ross et al., 2013) or case-control (Clare, Bailey, & Clark, 2000; Fawzi et al., 2013; Goldstein, 2003; Khalid et al., 2012; Kumari et al., 2014; Samardžić et al., 2010; Swanson et al., 2006) design. Whilst dates were not restricted during searching, all included studies were dated between 2000 and 2014.

The majority of studies employed convenience sampling of patients admitted to in or outpatient services during a certain time period. The only exception (Swanson et al., 2006) analysed baseline data from a randomised trial designed to assess the cost effectiveness of antipsychotic medication which included participants referred from 57 sites across the United States. While this larger study was designed to be representative of a diverse sample of individuals with psychosis; cases referred excluded treatment resistant disorders, schizoaffective disorders and patients suffering their first episode of psychotic symptoms. In this sense the results may not be generalisable to all individuals with psychotic illnesses. As previously discussed (see Study characteristics and clinical heterogeneity) this study assessed violence by looking at actual perpetration over a 6-month period, in contrast to all other studies which considered more general or lifetime risk. For these reasons a post-hoc sensitivity analysis was conducted to consider whether this variation resulted in significant differences between effect sizes.

Three studies (Bosqui et al., 2014; Lysaker et al., 2002; Samardžić et al., 2010) excluded patients suffering acute or severe symptoms during the study period. One study (Fawzi et al., 2013) designed to investigate intra-familial violence included only patients living with both biological parents. As the quality of family relationships and support may impact the clinical presentation of psychotic illnesses (e.g. Bolton, Gooding, Kapur, Barrowclough, & Tarrier, 2007) the generalisability of the results to individuals with psychosis more generally may be questioned.

Inherent issues in investigating childhood **abuse** are small or uneven sample sizes, and these were evident in all included studies, potentially reducing the power of statistical analyses. In particular, five studies (Bosqui et al., 2014; Clare et al., 2000; Kumari et al., 2014; Lysaker et al., 2002; Samardžić et al., 2010) had a total sample size of less than 50 (the minimum sample size to achieve 80% power in the analysis of mean differences between groups assuming a medium effect size (Faul, Erdfelder, Lang, & Buchner, 2007). Given the substantial variation in sample sizes, a post-hoc sensitivity analysis was conducted to consider whether this variation resulted in significant differences between effect sizes.

In terms of potential confounding factors in the aetiology of violence, eight studies (Bosqui et al., 2014; Fawzi et al., 2013; Goldstein, 2003; Khalid et al., 2012; Lysaker et al., 2002; Samardžić et al., 2010;

Spidel et al., 2010; Swanson et al., 2006) explicitly excluded patients with intellectual disability, and five (Bosqui et al., 2014; Fawzi et al., 2013; Kumari et al., 2014; Lysaker et al., 2002; Spidel et al., 2010) excluded patients with organic or neurological conditions. Five studies (Clare et al., 2000; Fawzi et al., 2013; Kumari et al., 2014; Samardžić et al., 2010; Spidel et al., 2010) listed substance misuse as an exclusion criterion, and one (Kumari et al., 2014) excluded patients diagnosed with co-morbid antisocial personality disorder. The exclusion of patients suffering co-morbid disorders or misusing illicit substances may increase the validity of the results, in that they can be more confidently linked to childhood **maltreatment**. However, both co-morbid disorders and substance misuse may plausibly moderate the relationship between childhood maltreatment and violence in individuals with psychosis. Unfortunately none of the retrieved studies were designed to consider moderating variables in this relationship.

Three studies (Clare et al., 2000; Goldstein, 2003; Khalid et al., 2012) analysed information from patient files without direct interview, these studies all involved child/adolescent samples. The reliance on secondary data allows for inclusion of patients who may have been unable or unwilling to consent to interview. However limiting the identification of childhood **maltreatment** and violent behaviour to file information may underestimate the incidence of these factors. Of the remaining studies; four (Bosqui et al., 2014; Fawzi et al., 2013; Kumari et al., 2014; Ross et al., 2013) sought collateral evidence of violence (file review or informant interview) to support interview data and two (Kumari et al., 2014; Ross et al., 2013) sought evidence to support childhood maltreatment data.

In no study were assessors blind to group allocation during assessments. Three studies (Khalid et al., 2012; Kumari et al., 2014; Samardžić et al., 2010) included groups of patients without psychotic illnesses, only data relating to subgroups of patients with psychosis was included in the analysis. All other case-control studies (Clare et al., 2000; Fawzi et al., 2013; Goldstein, 2003; Swanson et al., 2006) allocated participants to groups on the basis of history of violence (present or absent), only one study (Goldstein, 2003) matched participants (according to age and gender).

In all studies, violence was the primary outcome variable. However in only two cases (Bosqui et al., 2014; Samardžić et al., 2010) was the study designed specifically to investigate the influence of childhood **maltreatment**. Both of these studies measured negative childhood experiences and violence risk on continuous scales, neither considered the influence of other factors on this relationship. All other studies included childhood **maltreatment** as one of a number of variables potentially influencing violence.

In all studies the statistical analysis (relating to childhood **maltreatment**) was appropriate and was reported in full.

Synthesis of results

An overall analysis of the effect of any childhood **maltreatment** on violence in all samples suggested a significant overall model (K = 11, N = 2215, Z = 7.04, $p < 0.00001$) with a pooled OR of 2.46 (95% CI = 1.91 – 3.16).

There was no statistical heterogeneity between effect sizes ($\tau = 0.00$; $X^2 = 8.87$, $df = 10$, $p = 0.54$, $I^2 = 0\%$). See figure 2. for a forest plot of the main effects.

Assuming that acts of violence are a relatively rare event within individuals with psychosis, the pooled OR would transform to a risk ratio of 2.018 (see appendix A for transformation assumptions and equation). This would suggest that individuals with psychosis who reported childhood **maltreatment** were roughly twice as likely to perpetrate violence against others as those reporting no **maltreatment** across all samples.

Additional Analyses

Sensitivity analyses

A planned sensitivity analysis was carried out to consider whether the process of transforming effect sizes to ORs, or combining ORs to form a single estimate, had an influence on the overall analysis. Excluding all transformed data resulted in a slightly larger pooled effect estimate of 3.02 (95% CI =

1.92 – 4.75; K = 5; N = 531). If transformed ORs, combined ORs and untransformed ORs were considered as separate subgroups, there would be no statistical differences between them ($X^2 = 1.84$, $df = 2$, $p = 0.40$, $I^2 = 0\%$).

In light of the risk of bias assessment, a post-hoc sensitivity analysis was also conducted to consider whether the inclusion of studies with smaller samples had influenced the results. Excluding all studies with a sample size of less than 50 had very little impact on the overall effect size (pooled OR excluding studies with under 50 participants = 2.34, 95% CI = 1.70 – 3.22; K = 6; N = 2031).

An unplanned analysis was conducted to consider whether or not the single study measuring actual violence occurring over a six month period (Swanson et al., 2006) varied significantly from the majority of studies which used lifetime risk of violence as an outcome measure.

This analysis suggested that the pooled odds ratio for studies considering lifetime violence risk would be 3.06 (95% CI = 2.11 – 4.43; N = 805), where the odds ratio for the single study considering 6-month perpetration was 1.89 (95% CI = 1.35 – 2.65; N = 1410).

Subgroup comparisons

Age of participants

The pooled odds ratio for all studies involving child or adolescent samples was 3.12 (95% CI = 1.99 – 4.90; K = 5; N = 542). The comparable odds ratio for adult samples only was 2.21 (95% CI = 1.64 – 2.99; K = 6; N = 1673). Whilst there was some variance between these subgroups, these differences did not approach statistical significance ($X^2 = 1.54$, $df = 1$, $p = 0.21$, $I^2 = 35.2\%$). See figure 3. for a forest plot of the subgroup analysis.

Risk of bias across studies

A funnel plot was constructed plotting effect sizes (X axis) and the standard error of the log OR (Y axis) to examine publication bias (see figure 4.).

There was some evidence of A-symmetry, and Egger's regression co-efficient was significant ($t = 2.8048$, $p < 0.05$). Therefore it is possible that smaller studies with non-significant results were undetected, authors were not contacted directly to request any unpublished findings, although databases including academic theses were included.

It is perhaps notable that the largest study included had a notably smaller effect size (see post-hoc subgroup analyses) plausibly attributed to method variance. Excluding this study would render Egger's test non-significant ($t = 0.1904$, $P > 0.05$), and as such variations in methodology may partially account for this finding.

Discussion

This is the first meta-analysis to consider the influence of childhood abuse on risk of violence in a diverse sample of individuals with psychosis. Across all samples, the risk of violence in patients reporting childhood **maltreatment** was greater than in control groups. **The available evidence supports a descriptive relationship between early experiences of abuse and the risk of perpetrating violence in individuals with psychosis**, this finding is consistent with the hypothesis that individuals who have experienced **maltreatment** in childhood are more likely to experience psychotic symptoms involving derogatory themes or a sense of persecution, which may be associated with an increased risk of violence. **However this hypothesis is in need of empirical testing**, the available evidence does not allow for an analysis of the relationship between **maltreatment**, individual psychotic symptoms and violence and so the mechanism of this association remains unclear. **There is, however, an established body of evidence identifying that individuals who experience maltreatment in childhood are more likely to develop symptoms of psychosis in adulthood.**

The majority of identified studies were not specifically designed to investigate the relationship between early **maltreatment** and violence in individuals with psychosis. No study analysed mediating or moderating variables in this relationship, and so the extent to which the increased risk is associated with particular symptoms of psychosis or confounding variables is unknown.

Childhood abuse is an established risk factor for violence in normal populations (Lansford et al., 2007). A review of early abuse and self-injurious behaviour has suggested that this relationship is largely explained by the development of mental disorder (Klonsky & Moyer, 2008). Theorised mechanisms for the relationship between early **maltreatment** and later violence include disruptions to neurological development, particularly altered emotional processing and stress reactivity, in combination with risky health behaviours (e.g. substance misuse Repetti, Taylor, & Seeman, 2002). Similar factors are implicated in traumagenic developmental models of psychotic symptoms (Read et al., 2014; Read et al., 2001) and may be associated **with** an increased sense of threat or persecution. It is plausible that the relationship between early **maltreatment** and violence is mediated by the development of psychotic symptoms in this population, particularly given the suggestion that early **maltreatment** is associated with positive symptoms with persecutory or negative themes (Reiff, Castille, Muenzenmaier, & Link, 2012). In this sense, childhood abuse may not only relate to general reactive or emotive violence but potentially to psychotically motivated violence. Tentative support for this hypothesis is suggested by two of the included (Fazel et al., 2009; Swanson et al., 2006) which report increased positive symptoms (as well as childhood **maltreatment**) in violent groups, although the co-occurrence of these factors was not reported. **It is also important to recognise that while the current review identifies an increased risk of violence perpetration among individuals with psychosis who have experienced maltreatment in childhood, all identified studies included participants with symptoms of psychosis and early experiences of abuse who have never been violent. It is clear that childhood maltreatment is not the only factor influencing violence risk among individuals with psychosis, and research designed to identify protective factors may help to inform preventative strategies or strength-based interventions.**

Given the devastating impact of violence influenced by psychotic symptoms (to the victim, perpetrator and wider society), understanding risk factors and developing preventative strategies is of paramount importance. This review would suggest that experiencing early abuse roughly doubles the risk of violence in individuals with psychosis. Research designed to consider this relationship in more depth, in particular the relationship between early abuse, specific symptoms of psychosis and violence, may help to guide risk assessments and preventative strategies.

In comparing child and adult samples, there was no evidence that the risk associated with early abuse was diminished in the adult sample. There are several potential co-variables which may be influencing this finding, in particular the current analysis was not able to control for re-victimisation in adulthood. Both being a victim of childhood abuse and suffering from a psychotic disorder have been established as risk factors for violent and sexual victimisation in adulthood (de Zulueta, 2006; Fitzgerald et al., 2005) and being a victim in adulthood has been shown to predict violence in patients with psychosis (Swanson et al., 2006). Also, while in all samples the primary diagnosis was a psychotic disorder, it was not possible to analyse the influence of childhood abuse on co-morbid diagnoses (e.g. antisocial or borderline personality traits).

The current analysis considered only bivariate relationships, and so was not sensitive enough to consider the relationships between early **maltreatment** and the above potential co-variables. However, by limiting the included studies to those recording *childhood* victimisation, it is plausible that abuse may predate other potential risk factors. In this sense childhood abuse may underlie several risk factors in populations with psychosis, and these findings support the consideration of early abuse in treatment and risk management strategies.

This analysis identifies a clear need for further research into this area. In particular, the majority of available studies did not consider childhood maltreatment or neglect as a primary independent (or grouping) variable, and as such the identification of childhood abuse was often limited to recording its presence or absence. Given that this analysis would suggest that early maltreatment has a significant impact on the risk of violence in individuals with psychosis, future studies would benefit from considering in more detail the influence of types and frequency/duration of abuse and neglect on risk of violence specifically within this population. In order to understand the mechanisms of this relationship, studies exploring the associations between early experiences; specific symptoms or experiences of individuals with psychosis and behaviour including violence are necessary.

The current results highlight the importance of identifying childhood experiences of abuse and neglect in clients of mental health services presenting with possible symptoms of psychosis, both to facilitate

meaningful formulations and develop comprehensive treatment plans. This may be particularly relevant to early intervention for psychosis programmes, where identification of child maltreatment may help to formulate treatment plans addressing the sequelae of early trauma, which may feasibly have a preventative effect. While childhood experiences are typically identified as a static or unchangeable factor in risk assessment tools, a fuller understanding of the mechanisms by which risk is increased may help to identify dynamic factors as meaningful treatment targets. For example, some interventions have been demonstrated to attenuate the heightened stress response notable in individuals who have experienced trauma (see e.g. Olf, de Vries, Güzelcan, Assies, & Gersons, 2007), the current review would imply that such interventions may plausibly reduce risk of violence in individuals with psychosis. The current review also emphasises the significant negative consequences of childhood maltreatment, and the primary preventative implications are clear.

While the mechanism requires further explanation, the above analysis suggests that there is a consistent relationship between early abuse and violence within individuals with psychosis. Predicting (and addressing) the risk of violence perpetrated by individuals with psychosis is complicated by the rarity of such events, however the available evidence suggests that considering the influence of early experiences on this risk may be a useful avenue of future research. In particular considering the influence of early experiences on specific symptoms of psychosis may allow for the identification of more dynamic sequelae of abuse in individuals with psychosis, which may represent valid treatment targets for interventions designed to reduce risk.

Limitations

In keeping with the majority of research into victimisation, studies collecting primary data relied on retrospective reports of childhood experiences, and all studies were of a case-control or cross-sectional design. While several sought collateral evidence to support patient reports, this methodology is vulnerable to recollection bias. While these methodologies do not allow for definitive causal relationships to be identified, there is some evidence that reports of childhood abuse remain relatively stable among individuals with psychosis, and are not affected by the severity of psychotic symptoms

(Fisher et al., 2009). However, larger scale longitudinal research (e.g. birth cohort studies) would address these limitations.

As discussed above, the methodology of included studies did not allow for an analysis of moderating or mediating variables, specific types of **maltreatment**, or the relative influence of more severe or repeated abuse in childhood. Whilst it may be inferred that the presence of early abuse relates to enduring post-traumatic symptoms (and associated behaviours), none of the identified studies considered current symptomology in relationship to earlier abuse.

The majority of included studies were not specifically designed to investigate the influence of early abuse on violence in patients with psychosis, and rather identified general risk factors for violence in this population. The studies frequently employed convenience sampling, resulting in small and uneven group sizes. Despite this there was very little statistical heterogeneity in the main analysis, however the findings would suggest a clear need for research specifically addressing the influence of early experiences on risk of violence in individuals with psychosis.

This analysis did not address the influence of early maltreatment on the risk of self-harm in individuals with psychosis, given that different factors may influence this relationship (see e.g. Gray et al., 2003). However, it is well-established that there is a high prevalence of suicidal ideation, self-injurious behaviour and attempted suicide in this population (Taylor, Hutton, & Wood, 2014), and as such future reviews may benefit from considering the influence of early maltreatment on violence generally in individuals with psychosis, in particular to consider the possibility of shared variance in the risk of harm to self and harm to others.

Conclusions

The results suggest that individuals with psychosis who had been victims of maltreatment in childhood were approximately twice as likely to be violent as individuals with psychosis who had not been victims. This finding was consistent across diverse samples of patients with psychosis.

The results were not able to establish the influence of co-variables on this relationship, and are limited by the relative rarity of studies addressing childhood abuse as a risk factor for violence in psychosis (in comparison to other mental disorders).

The consistency of the results would suggest that the relationship between childhood abuse and violence may be particularly salient in populations diagnosed of psychosis, and should be considered in risk assessments and interventions.

Theoretically, the relationship between childhood trauma and violence in populations with psychosis may be associated with the impact of early **maltreatment** on psychotic experiences. Future research may benefit from addressing the relationship between early abuse and psychotically motivated or extraordinary violence, and specific symptoms of psychosis.

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Table 1. Characteristics of identified studies and extracted data

Study and country of origin	Population and total sample size	Psychosis measurement (psychometric)	Childhood maltreatment measurement (psychometric)	Violence measurement (psychometric)	Maltreated N	Control N	Extracted statistic (95% CI)	log OR(SE)	P *
Bosqui et al 2014 Northern Ireland	Male and female in- and outpatients aged 18-70 N = 41	DSM-IV diagnosis	Physical, emotional or sexual abuse, physical and emotional neglect (CTQ)	Risk of violence (HCR20V2)	NA	NA	r = 0.41 (0.12 – 0.64)	1.6307 (0.7753)	0.0351
Clare, Bailey & Clark 2000 UK	Male and female in- and outpatients aged 12-18 N = 39	ICD-10 diagnosis	Physical, emotional or sexual abuse evidenced by file review	History of violence evidenced by formal sanction	PA=9 SA=8	PA=30 SA=31	OR(PA) =10.00 (1.67 – 59.99) OR(SA) = 2.1 (0.43 – 10.17)	1.5223 (0.7598)	0.0448
Fawzi et al 2013 Egypt	Male outpatients aged 13-19 N = 150	DSM-IV diagnosis (SCID) (PANSS)	Physical, emotional or sexual abuse, physical and emotional neglect (CTQ)	Physical or verbal abuse towards parents (APQ)	74	76	OR = 4.47 (2.21 – 9.02)	1.4973 (0.3582)	< 0.001
Goldstein 2003 USA	Male and female inpatients aged 13-17 N = 60	Diagnosis of psychosis NOS in medical records	Physical abuse, verbal abuse, sexual abuse, and neglect evidenced by file review	Verbal and physical aggression against people or objects evidenced by file review	28	32	OR = 2.26 (0.80 - 6.36)	0.8148 (0.5285)	0.123

Khalid, Ford & Maughan	Male and female inpatients aged 7-18									
2012	N = 1558 (psychotic subgroup = 212)	ICD-10 diagnosis	Exposure to physical or sexual abuse evidenced by file review	Actual physical aggression evidenced by file review	17	195	OR = 1.67 (0.61 – 4.55)	0.5119 (0.5121)	0.322	
UK										
Kumari et al,	Male in and outpatients aged 18-55	DSM-IV diagnosis								
2014	N = 57 (psychotic subgroup = 28)	(SCID)	Exposure to physical abuse; sexual abuse; neglect; extreme poverty etc. evidenced by file review	Actual acts of violence evidenced by file review	17	11	OR = 3.21 (0.66 – 15.59)	1.1658 (0.8065)	0.149	
UK		(PANSS)								
Lysaker et al	Male outpatients aged 18+	DSM-IV diagnosis								
2002	N = 36	(SCID)	Physical abuse (CAQ)	Behavioural and attitudinal hostility (BDHI: Physical aggression scale)	NA	NA	r = 0.39 (0.07 – 0.64)	1.5364 (0.7535)	0.041	
USA		(PANSS)								
Ross et al	Male and female outpatients aged 4-15	DSM-IV diagnosis								
2013	N = 81	(Adapted SCID)	Victim of any abuse, evidenced by file review	Any act of physical aggression towards others evidenced by file review	8	73	OR = 3.26 (0.62 – 17.21)	1.1809 (0.7216)	0.102	
USA										
(Samardžić et al., 2010) Samardžić et al	Male and female outpatients aged 18+									
2010	N = 113 (psychotic subgroup = 40)	ICD-10 diagnosis	Physical, sexual and emotional abuse; witnessing DV; neglect and loss of family members (ACE)	Behavioural and attitudinal hostility (BDHI: Physical aggression scale)	NA	NA	r = 0.36 (0.05 – 0.60)	1.3998 (0.7245)	0.053	
Serbia										

Spidel et al 2010 Canada	Male and female outpatients aged 18+ N = 118	Consulted a medical professional for psychotic symptoms for the first time in the two years preceding the study	Physical, emotional or sexual abuse, physical and emotional neglect (CTQ)	History of physical violence <i>MOAS (physical violence scale)</i>	NA	NA	$r = 0.31$ (0.14 – 0.46)	1.1828 (0.6846)	0.084
Swanson et al 2006 USA	Male and female in- and out- patients aged 18-65 N = 1410	DSM-IV diagnosis (SCID) (PANSS)	Exposure to physical or sexual abuse	Actual physical aggression over a 6 month period identified by the MacArthur community violence interview	PA=278 SA=284	PA = 1130 SA = 1122	OR(PA) =1.82 (1.34 – 2.46) OR(SA) = 1.97 (1.46 – 2.66)	0.6371 (0.1730)	< 0.001

Abbreviations:

ACE = Adverse childhood experiences questionnaire (Felitti et al., 1998)

APQ = Abused parent questionnaire (Ghanizadeh & Jafari, 2010)

BDHI = Buss-Durkee Hostility Inventory (Buss & Durkee, 1957)

CTQ = Childhood trauma questionnaire (Bernstein, 1998)

HCR20v2 = Historical, Clinical, Risk management (Webster, 1997)

MOAS = Modified Overt Aggression Scale (Kay, Wolkenfeld, & Murrill, 1988)

PA = Physical Abuse

PANSS = Positive and negative syndrome scale (Kay, Flszbein, & Opfer, 1987)

SA = Sexual Abuse

SCID = Structured clinical interview for DSM-IV Axis I disorders (First, Spitzer, Gibbon, & Williams, 1995)

SCL-90 = The Symptom Checklist – 90 (Derogatis, 1994)

* See appendix A for equation used to calculate p value (Altman & Bland, 2011).

Table 2. Summary of limitations within studies

Study	Excluded first episode/acute symptoms	Excluded patients not living with biological parents	Excluded patients not suitable for antipsychotic medication	Did not exclude patients on the basis of substance misuse	Lack of matching between violent and non-violent groups	Small sample size (N < 50)	Data extracted from case file only	Assessment of childhood adversity self-report only	Assessment of violence self-report only	Primary aim of study not to investigate childhood abuse
Bosqui et al, 2014	◆			◆	N/A	◆		◆		*
Clare et al, 2000					◆	◆	◆			◆ *
Fawzi et al, 2013	◆	◆			◆			◆		◆ *
Goldstein, 2003				◆			◆			◆
Khalid et al, 2012				◆	◆		◆			◆
Kumari et al, 2014					◆	◆				◆
Lysaker et al, 2002	◆			◆	N/A	◆		◆	◆	◆ *
Ross et al, 2013				◆	◆					◆
Samardzic et al, 2010	◆				◆	◆		◆	◆	◆
Spidel et al, 2010					N/A			◆	◆	
Swanson et al, 2006	◆		◆	◆	◆			◆		◆ *

Note. ◆ = limitation applies to study; * = effect size statistically significant (P<0.05)

Small sample defined as below the necessary N to achieve 80% power assuming a medium effect size

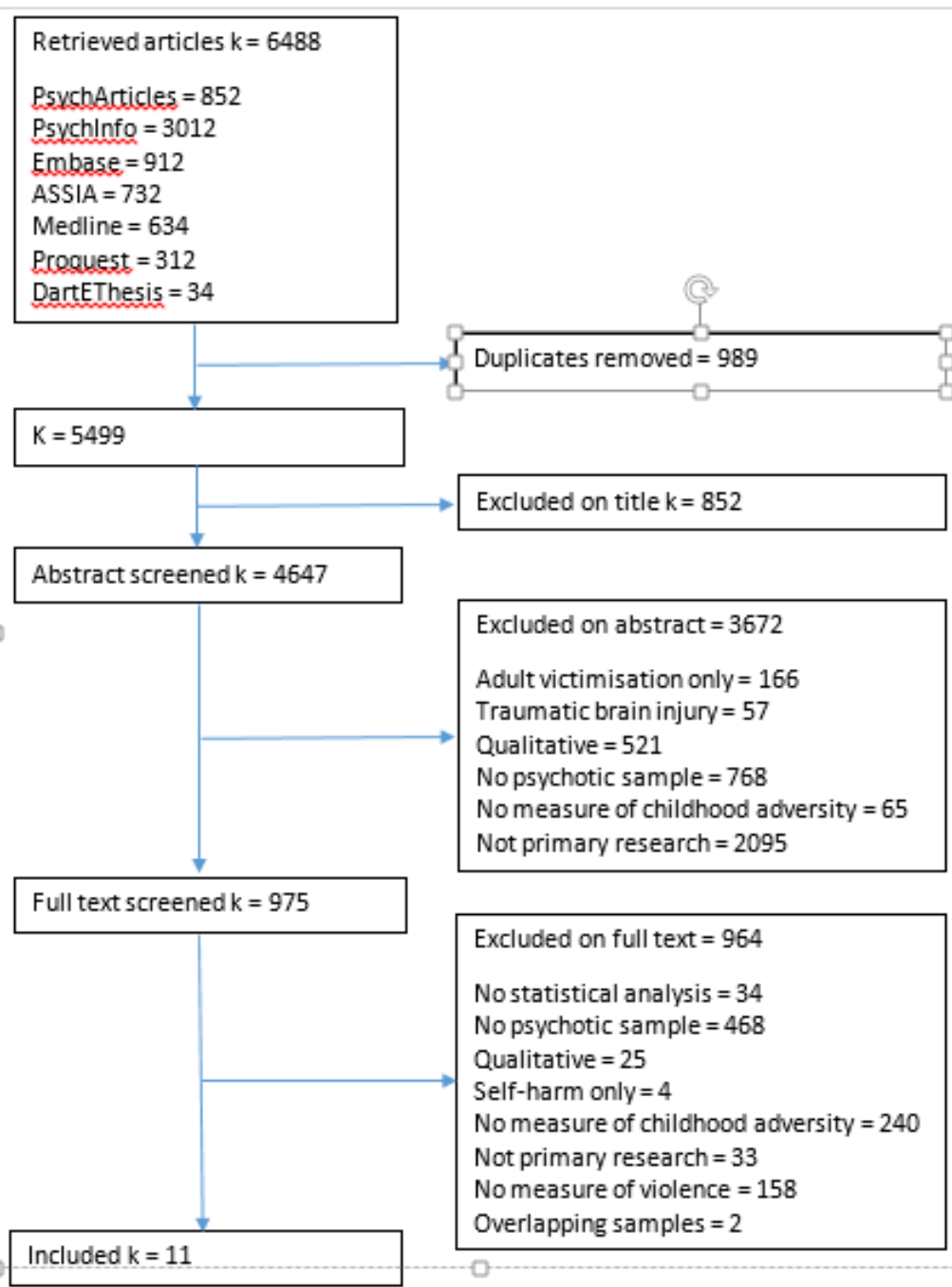


Figure 1. flowchart of studies excluded by eligibility screening

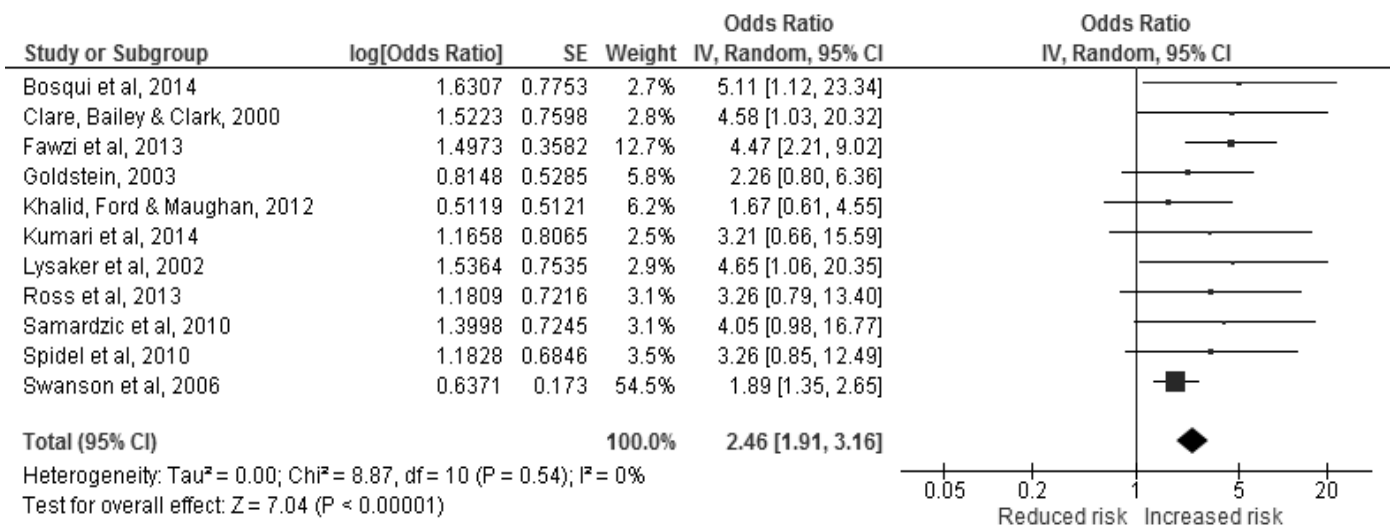


Figure 2. Forest plot of influence of any childhood maltreatment on violence to others

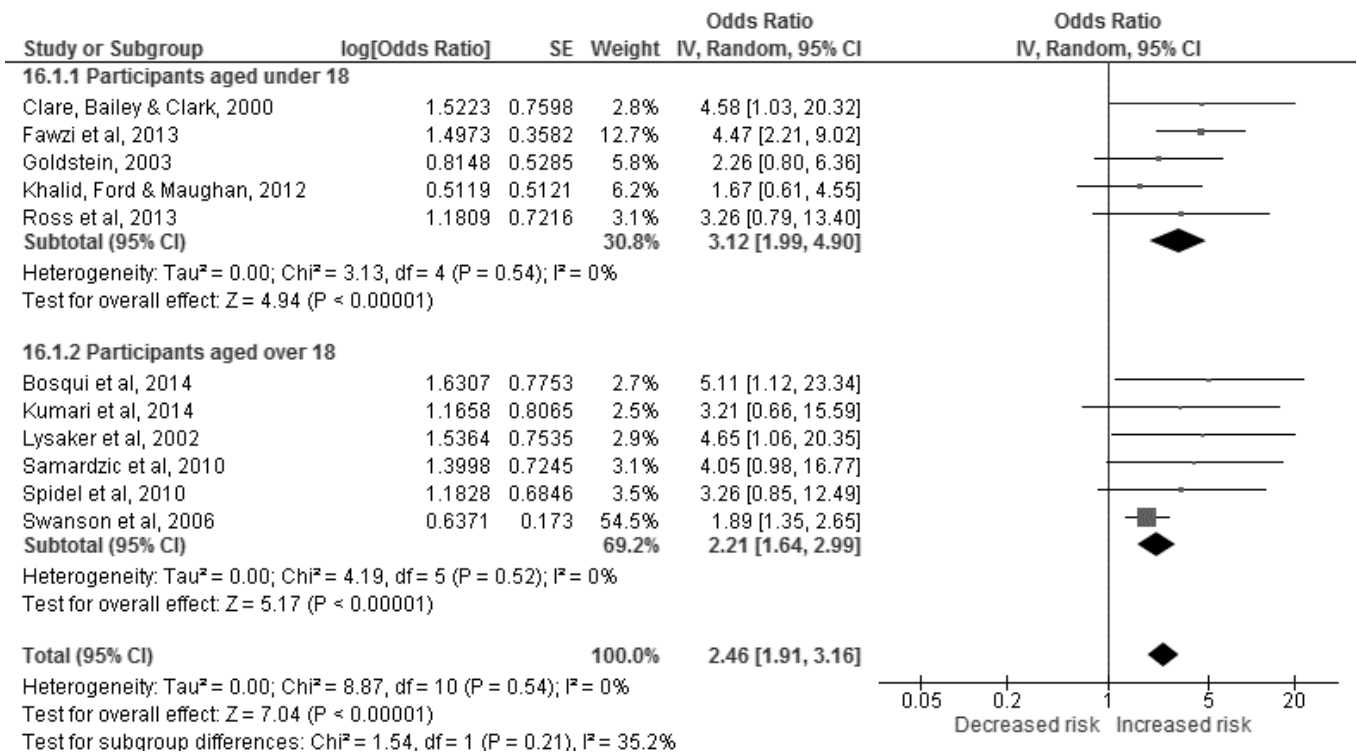


Figure 3. Forest plot of comparison of participants aged under or over 18

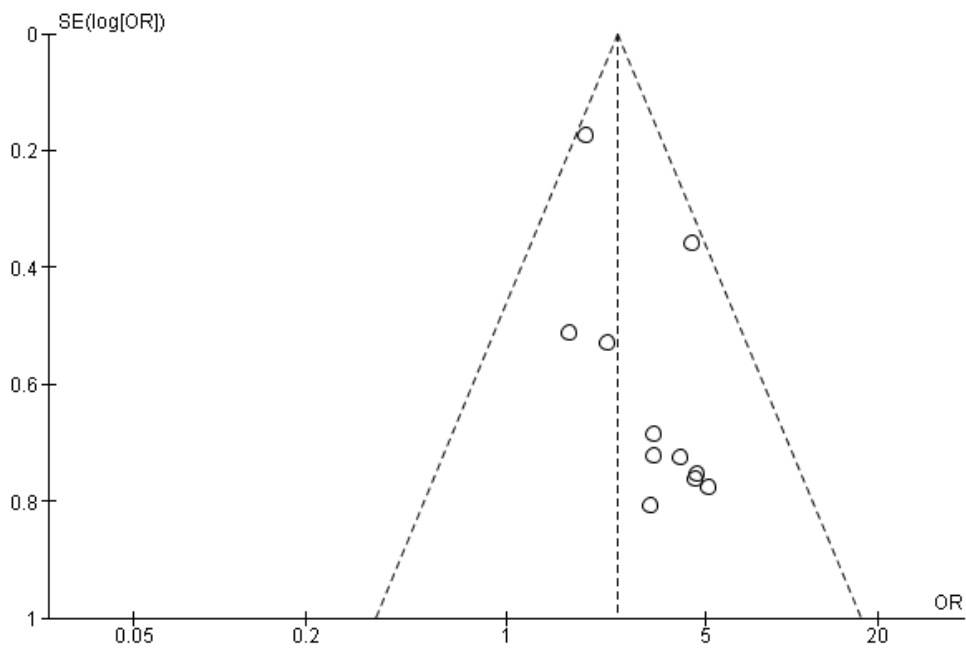


Figure 4. Funnel plot of effect size and standard error

Appendix A – Equations used for effect size calculation and data transformation

Transforming r (correlation) to d (mean effect size):

$$d = \frac{2r}{\sqrt{1-r^2}}$$

Transforming V_r (the variance of r) to V_d (the variance of d):

$$V_d = \frac{4V_r}{(1-r^2)^3}$$

Transforming d to the log Odds Ratio:

$$\text{LogOddsRatio} = d \frac{\pi}{\sqrt{3}}$$

Transforming V_d (the variance of d) to the variance of the logged odds ratio:

$$V_{\text{LogOddsRatio}} = V_d \frac{\pi^2}{3}$$

Calculating the combined effect size (\bar{Y}) of two (non-independent) subgroups within the same study:

$$\bar{Y} = \frac{1}{2} (Y_1 + Y_2)$$

Calculating the combined variance of two (non-independent) subgroups within the same study:

In order to calculate the variance of the combined effect estimate, the actual co-occurrence of forms of abuse (drawn from the published literature; Rosenberg et al, 2007; Felitti et al, 1998; Read et al, 2003) was used to estimate the correlation of the variances and incorporated into the calculation

$$V_{\bar{Y}} = \frac{1}{4}(V_{Y_1} + V_{Y_2} + 2r\sqrt{V_{Y_1}}\sqrt{V_{Y_2}})$$

Where $V_{\bar{Y}}$ = combined variance; V_{Y_1} = variance of effect size 1; V_{Y_2} = variance of effect size 2 and r = the correlation of the variance of effect sizes.

Transforming odds ratio (OR) to risk ratio (RR):

$$RR = \frac{OR}{[1 - P_{ref} + (P_{ref} \times OR)]}$$

Where P_{ref} = the prevalence of the outcome in the reference (or control) group. **While estimates vary as to the prevalence of violence perpetration in individuals with psychosis, population studies in the UK have reported a prevalence of 13.5% in a combined sample of 23444 participants (Coid, Ullrich, Bebbington, Fazel & Keers, 2016), similarly a longitudinal study reported a prevalence of 15% perpetuating or engaging in any threatening or physically violent behaviour during the prior year in a sample of individuals with psychosis (Langeveld et al., 2014). For the purposes of the transformation of OR to RR, an estimated prevalence of 15% was used for the reference group.**