Data supplement to Petros et al. Impact of childhood trauma on risk of relapse requiring psychiatric hospital admission for psychosis. Br J Psychiatry doi: 10.1192/bjp.bp.115.176636

**Supplement DS1: Methods**

Relevant studies were identified by searching the following electronic databases: PsychINFO (from 1806 to February 2015); Medline (from 1946 to February 2015); Ovid MEDLINE(R) In-Process and Other Non-Indexed Citations; and EMBASE (from 1974 to February 2015). Both titles (ti) and abstracts (ab) were incorporated into the search. The following terms were inputted into the systematic database search using the Boolean Operator "OR": 1) TRAUMA: abuse*.ab,ti.; maltreat*.ab,ti; neglect*.ab,ti.; trauma*.ab,ti.; advers*.ab,ti.; 2) DIAGNOSIS: bipolar.ab,ti.; psychot*.ab,ti.; psychos*.ab,ti.; schizophren*.ab,ti.; schizoaff*.ab,ti.; 3) RELAPSE: outcome.ab,ti.; hospital*.ab,ti.; relapse.ab,ti. 4) DEVELOPMENTAL PERIOD: child*.ab,ti. Using the Boolean Operator "AND" the four themes; trauma, diagnosis, relapse and developmental period were combined to run the conclusive search.

Data were extracted from the included studies systematically by one researcher (N.P.) and validated by two others (E.F., E.K.) (see DS2). A database was compiled to include characteristics of each study and variables that contribute to outcome. One of the authors was contacted to clarify data collection methods and results.

**Inclusion and Exclusion Criteria**

The following inclusion criteria applied to the included studies: 1) study participants: I) had experienced at least one episode of psychosis; II) have a diagnosis (identified using standard diagnostic system (e.g. DSM IV and ICD 10), which must be specified) of either schizophrenia-spectrum disorder or an affective disorder with reported psychotic symptoms i.e. bipolar affective disorder; III) were aged between 18-65 years; IV) childhood trauma (CT) occurred at ≤17 years; 2) follow-up occurred at ≥6 months after onset to allow for examination of relapse; 3) outcome, relapse or episode of illness is defined as psychiatric hospitalisation (i.e. admission (yes/no), number of admissions or duration of admission). Exclusion criteria were: 1) a diagnosis of psychosis as a result of an organic or substance-induced cause; 2) outcome not explicitly defined as psychiatric hospitalisation due to relapse of psychotic illness; 3) no explicit measurement of the relationship between CT and relapse requiring psychiatric hospitalisation for psychosis; 5) articles that included a subset/overlap of a sample from an included paper. Only peer-reviewed papers published in English were considered for review.

**Quality Assessment**

The Quality Assessment Tool used within this report is provided in (Table DS1) and the overall score for each study is provided in Table DS3. Each study was assessed on the following criteria: selection bias; measurement of CT; measurement of psychosis; measurement of relapse/outcome; adjustment for confounds; and reliability and validity of data collection methods. Studies that utilised semi-structured interviews to collect data on CT were given a higher score compared to those that used self-report measures, owing to the objective and comprehensive assessment that can be obtained via interviews. Self-report questionnaires may lead to underreporting[1]. Furthermore, they rely on an individual's subjective perception of an event, and hence may be subject to false positives and negatives.

Efforts were made to ensure that the quality assessment was in line with the criteria set by the Effective Public Health Practice Project (EPHPP) – Quality Assessment Tool for Quantitative Studies (http://www.ephpp.ca/tools.html). Two of the researchers (E.F., E.K.) independently assessed the quality of each of the included studies and a consensus score was subsequently reached. This report was prepared with reference to the MOOSE guidelines[2] for the systematic review of observational studies (Table DS2).

**References**

1. Finkelhor D, Araji S, Baron L, Browne A, Peters SD, Wyatt GE. A sourcebook on child sexual abuse. Sage Publications, 1986.
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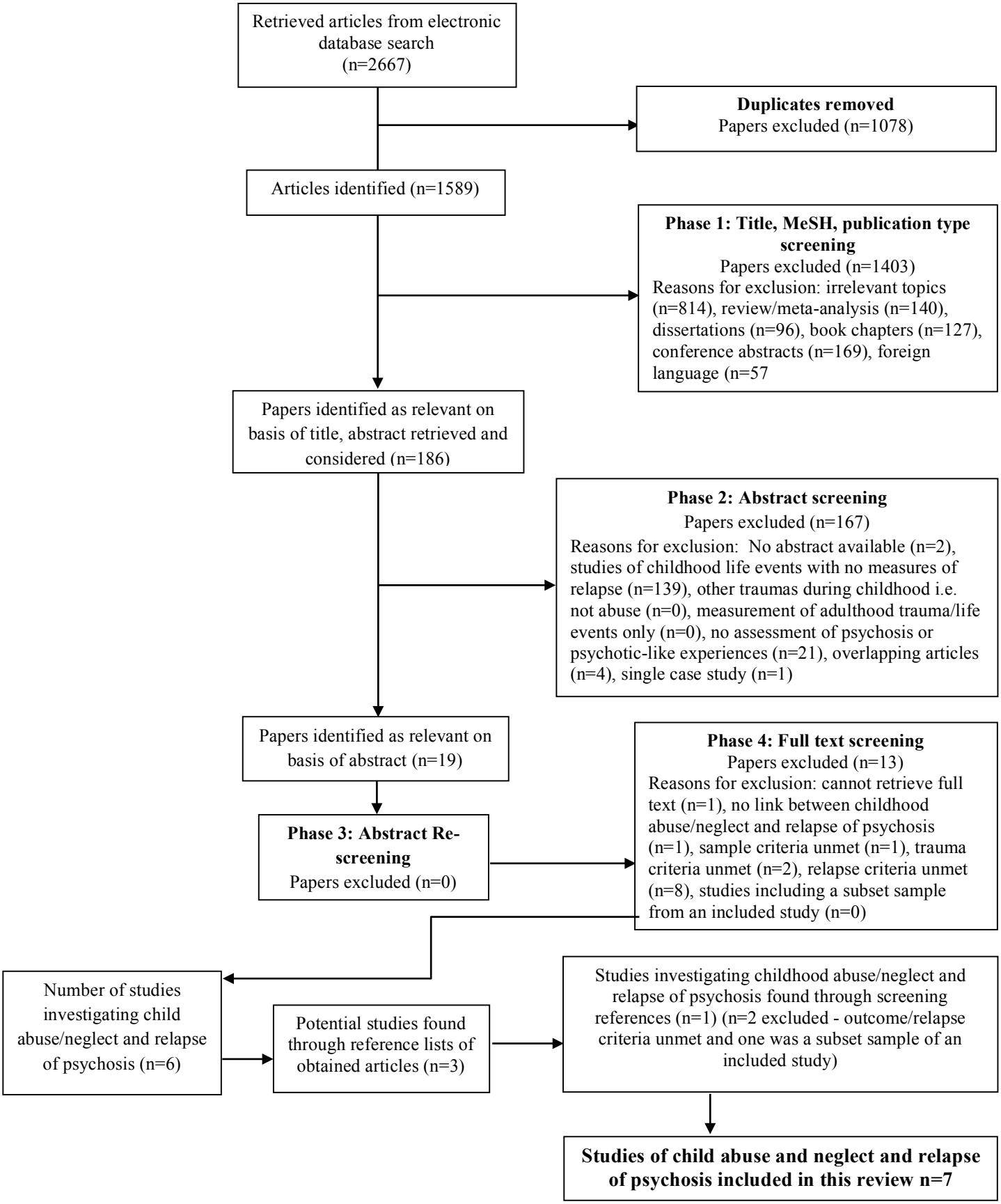


**Fig. DS1 FLOW DIAGRAM: IDENTIFICATION, SCREENING, ELIGIBILITY AND INCLUSION OF DATA SOURCES FOR THE REVIEW**

**Supplement DS2 DATABASE HEADINGS FOR DATA EXTRACTION**

- Ovid result number
- Web-link to article
- Author
- Year
- Title
- Location
- Study design
- Sample size
- Number of dropouts
- Mean age
- Ethnicity
- Marital status
- Socioeconomic status
- Diagnostic groups included
- Treatment status
- Control group included
- Sample size with and without history of trauma
- Recruitment procedure
- Diagnostic tool
- Psychosis measures
- Inclusion and exclusion criteria
- Trauma groups included
- Definition of trauma
- Childhood trauma measures
- Follow-up period
- Main outcome considered
- Definition of relapse
- Source of outcome/relapse data
- Statistic model
- Reliability and validity of measures considered
- Adjustment for confounders
- Main findings
- Univariate analysis findings
- Multivariate analysis findings
- Methodological quality assessment score

**Table DS1 QUALITY ASSESSMENT**

| Quality Assessment | Brown, G. et al 2005 | Alvarez M.-J. et al (2011) | Larsson S. et al (2013) | Conus P. et al (2010) | Cutajar M.C. et al (2010) | Schenkel L.S. et al (2005) | Garno J.L. et al., (2005) |
|---|---|---|---|---|---|---|---|
| **Selection Bias** | | | | | | | |
| **(1) What percentage of selected individuals agreed to participate?** | | | | | | | |
| 0 Less than 50% of participants, or not reported or not applicable. | 0 | | | 0 | 0 | 0 | |
| 1 50-69% of participants. | | | | | | | |
| 2 70-100% of participants. | | 2 | 2 | | | | 2 |
| **(2) What is the sample size?** | | | | | | | |
| 0 Less than 50 subjects in each group | | 0 | 0 | 0 | 0 | 0 | 0 |
| 1 At least 50 subjects in each group | | | | | | | |
| 2 At least 100 cases and controls or sample size calculation indicating adequate statistical power | 2 | | | | | | |
| **Measurement of Childhood Trauma** | | | | | | | |
| **(3) What was the quality of the childhood trauma measurement tool?** | | | | | | | |
| 0 Audit screening tool/clinical note screening | | | | 0 | | | |
| 1 Self-report checklist measure | | 1 | 1 | | | | 1 |
| 2 Semi-structured interview, observer-rated instrument or official records e.g. police | 2 | | | | 2 | 2 | |
| **Measurement of Psychosis** | | | | | | | |
| **(4) How was psychosis measured?** | | | | | | | |
| 0 Clinician-only diagnosis | | 0 | | | 0 | | |
| 1 Structured assessment by trained research worker, or self-report measure for psychotic-like experiences | | | | | | | |
| 2 Structured assessment by clinician | 2 | | 2 | 2 | | 2 | 2 |
| **Confounding** | | | | | | | |
| **(5) Was there an assessment of confounding in the analysis?** | | | | | | | |
| 0 No adjustment for confounders | 0 | 0 | | | 0 | 0 | 0 |
| 1 Adjustment for basic demographics e.g. age, gender, ethnicity, socioeconomic status | | | 1 | 1 | | | |
| 2 Potential confounders were measured and adjusted for in the analysis e.g. adjustment of basic demographics and other risk factors such as urbanicity, drug/alcohol use, social support | | | | | | | |
| **Measurement of Relapse/outcome** | | | | | | | |
| **(6) How was outcome/relapse measured?** | | | | | | | |
| 0 No details provided | | | | | | | |
| 1 Self-report data | 1 | | 1 | | | | 1 |
| 2 Medical records | | 2 | | 2 | 2 | 2 | |
| **Data Collection Methods** | | | | | | | |
| **(7) Were data collection tools shown to be valid?** | | | | | | | |
| 0 Cannot tell/unclear | | | | | 0 | 0 | |
| 1 Not shown to be valid / no description of validity | 1 | | | | | | |
| 2 Measurements shown to be valid either through assessment of validity or described/referenced from previous studies | | 2 | 2 | 2 | | | 2 |
| **(8) Were data collection tools shown to be reliable?** | | | | | | | |
| 0 Cannot tell/unclear | | | | | 0 | | |
| 1 Not shown to be reliable / no description of reliability | | | | | | | |
| 2 Measurements shown to be reliable either through assessment of reliability or described/ referenced from previous studies | 2 | 2 | 2 | 2 | | 2 | 2 |
| **TOTAL SCORE** | **10** | **9** | **11** | **9** | **4** | **8** | **10** |

**Table DS2 MOOSE CHECKLIST(1)**

| ITEM | REPORTED | NOTES |
|---|---|---|
| **Background** | | |
| Problem definition | ☑ | See introduction |
| Hypothesis statement | ☑ | See introduction |
| Description of study outcomes | ☑ | See methods |
| Type of exposure | ☑ | See methods |
| Type of study designs used | ☑ | See methods |
| Study population | ☑ | See methods |
| **Search strategy** | | |
| Qualification of searchers | ☑ | Investigators with BSc and MSc |
| Search strategy (time and key-words) | ☑ | See methods |
| Effort to include all available studies | ☑ | Included contact with authors, see acknowledgements |
| Database and registries searched | ☑ | See methods |
| Search software | ☒ | None used |
| Use of hand search | ☑ | Included cross-checking of references of obtained articles |
| List of citations included and excluded | ☑ | Details of the literature search process are outlined in the flow chart. The citation list is available upon request |
| Articles not in English language | ☑ | Excluded |
| Abstract and unpublished studies | ☑ | Excluded |
| **Methods** | | |
| Description of relevance of studies included | ☑ | See methods |
| Rationale for the selection of studies | ☑ | Data extracted from each of the studies were relevant to the population characteristics, study design, exposure, outcome, and possible effect modifiers of the association. |
| Classification and coding of data | ☑ | Multiple raters, blinding and inter-rater reliability. |
| Assessment of confounding | ☑ | Potential confounders discussed |
| Assessment of study quality | ☑ | See methods and Supplementary Material 1 |
| Assessment of heterogeneity | ☑ | Heterogeneity of the 7 studies were not explored quantitatively, however the methodological variances and outcomes were discussed |
| Description of statistical methods | ☒ | Not applicable none used |
| Provision of appropriate table and figures | ☑ | See methods |
| **Results** | ☑ | |
| Graphic with individual study estimates and overall estimate | ☒ | Not applicable – meta-analysis not performed |
| Table with descriptive information of each study | ☑ | See methods |
| Results of sensitivity testing | ☒ | Not applicable – meta-analysis not performed, only 7 studies were available, hence sensitivity analysis was not deemed appropriate |
| Indication of statistical uncertainty in findings | ☒ | Not applicable – meta-analysis not |

| | | |
|---|---|---|
| | | performed |
| **Discussion** | | |
| Quantitative Assessment of bias | ☒ | Not applicable – meta-analysis not performed |
| Justification for exclusion | ☑ | All studies were excluded based on the pre-defined inclusion criteria. |
| Assessment of quality | ☑ | See discussion |
| **Conclusions** | | |
| Consideration of alternative explanations | ☑ | See discussion |
| Generalization of the conclusions | ☑ | See discussion |
| Guidelines for future research | ☑ | See discussion |
| Disclosure of funding source | ☑ | Included |

1.Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA*. 2000; **283** (15): 2008-12.

**Supplement DS3 Results**

The electronic search identified 1589 articles using human participants only, published during 1980-2014, once duplicates (n=1078) were removed (see Fig. DS1) . These articles were drawn from the databases; Embase (n=1013), Ovid MEDLINE (n=73) and PsychINFO (n=503). Additional studies were identified through screening full texts of articles.

Of the seven studies included in this report, most used a case-only design and applied cross-sectional, retrospective methods to compare psychiatric hospitalisations in participants with pre-existing psychosis either with or without a history of CT (see Table 1 and Table DS3). One study[1] included a general population control group; however only cases with psychosis were considered within this report owing to the focus on relapse of a pre-existing disorder. One study did not report comparisons between abused and non-abused groups[2]. Four studies included participants with an affective psychosis only; three studies included patients with both affective and non-affective psychotic disorders. One study included some patients with drug-induced psychosis[1], although the number of these individuals was not specified, it was likely to be small. Hence, the paper continued to be included in the review.

The majority of the total sample of participants (from all of the identified studies (n=946) had an affective psychotic disorder (n=758), rather than a non-affective psychotic disorder (n=188) and the majority of the total sample were men (62%). Ethnicity was not reported in most of the studies, two reported that approximately 25% of their sample were non-white or from ethnic minority backgrounds[3,4]. The estimated mean age amongst the total population (including the general population sample with history of abuse in Cutajar et al.[1] was 36.8 years. Mean duration of illness for all of the included studies was not estimated as this was not widely reported. At least 44.1% (n=418) of the total sample examined reported to have experienced childhood trauma; one of the studies[2] did not report the number of exposed participants.

A cut-off for hospitalisation history was used in three of the studies - 2 years[5], 18 months[6] and 5 years[3]. In four of the included studies, data on RRPH-P was obtained via the screening of patient clinical records/case registers, and the remaining articles relied upon information collected via semi-structured/clinical interviews (see Table DS3. Data on childhood trauma was collected retrospectively for all but one of the studies[1](20) which extracted data from police records of childhood abuse. Well-known self-report checklist measures to assess experiences of childhood trauma (e.g. Childhood Trauma Questionnaire (CTQ)[7], Traumatic Life Events Questionnaire (TLEQ)[8] – see Table 3) were used in three of the studies. All of the studies used standardised criteria e.g. DSM-IV/ICD-10[9,10] to ascertain diagnosis.

Given the limited available data in this area, studies were not excluded on the basis of quality score (see Table DS3). In general, areas in which the included studies received high scores were: 1) the measurement of psychosis, with most studies establishing patient diagnosis using structured assessments performed by clinicians; 2) the measurement of relapse; medical records were used in four of the studies to establish RRPH; 3) the reliability of

the data collection tools; most studies either demonstrated reliability of measures via assessment (e.g. inter-rater reliability) or by providing a reference of previous work.

Three out of seven studies included in this review did not find a significant difference in RRPH in patients with pre-existing psychosis between those with a history of childhood trauma and those without[1,3,4]. Cutajar et al. reported no significant difference in the number of admissions between individuals with or without a history of childhood sexual abuse. Garno and colleagues did note increased past year rapid cycling in individuals with a history of childhood emotional abuse (OR 5.61 (95% CI 2.01-15.70), physical abuse (OR 4.04 (95% CI 1.44-11.31) and emotional neglect (OR 4.04 (95% CI 1.44-11.31) in a sample of patients with bipolar affective disorder[3]. However, whether this rapid cycling had resulted in hospitalisation or involved symptoms of psychosis was not specified. Brown et al.[4] found that individuals with a history of any type of childhood abuse were more likely to be admitted to psychiatric hospital involuntarily at index episode (i.e. time of recruitment into the study) compared to those with no abuse (p=0.029, OR=2.37, CI 1.10-5.14). Involuntary hospitalisation may reflect the severity of the particular episode but it does not supply an insight into other relapse events or the course of illness experienced by these individuals with a history of childhood abuse. A significant difference in the number of hospitalisations or number of days spent in hospital in the past 5 years was not revealed between those with a history of childhood abuse and those without. Furthermore, in their report Brown and colleagues did not distinguish between hospitalisations required for substance use and those required for psychiatric reasons. Brown et al.[4] did report that patients with a history of physical abuse had an increased probability of a rapid cycling pattern of illness compared to those without trauma histories (p=0.047, OR=1.96, CI 1.01-3.79). However, the presence of psychotic symptoms during the rapid cycling episodes and whether hospitalisation was required was not clearly indicated. Additionally, the increase in rapid cycling amongst the individuals with a history of physical abuse no longer remained significant when analysis was restricted to men only, who constituted 90.9% of the total sample. The sample included in Brown et al. overlapped with another study by Bauer et al.[11] (identified through reference screening), however the latter included a smaller sample size and thus was excluded from this review.

**References**


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**Table DS3 SAMPLE, TRAUMA AND STUDY CHARACTERISTICS AND MAIN FINDINGS**

| Authors, Location | N/ Mean Age (SD)/ Illness Stage, Average Years Since Onset/ Follow-Up Period | CT Prevalence (n=History/n=No-History) | CT Measurement | Relapse Measurement | Source Of Outcome Data | Quality Score (Max 16) | Main Findings |
|---|---|---|---|---|---|---|---|
| **Alvarez et al. (2011), Spain*** | 102 (54m/48f; BPD n=40; SZ n=52; SAD n=10) / 39.4 (10.4) / CP, 15yrs / N/A | 83/19 | TLEQ (Kubany and Haynes, 2001); Distressing Event Questionnaire (DEQ) (Kubany, 2001) | Number of admissions to acute psychiatric unit, partial or day hospitalisations | Clinical data | 9 | **Individuals with a history of childhood psychological abuse had more hospital admissions (n=2.05 (2.40 (SD) in the last two years compared to their non-psychologically abused counterparts (n=1.08 (1.42 (SD), P=0.028). This relationship between psychological abuse and number of admissions was significant in patients with bipolar disorder only (n=2.93 (3.22) v n=1.31 (1.49), P = 0.035)** |
| Larsson et al. (2013), Norway | 141 (56m/85f; BPDI n=103; BPDII n=26; BPDNOS n=12) / 32.4 (11.5) / CP, 11yrs / N/A | Not specified | CTQ (Bernstein et al., 1994) | Number of psychiatric hospitalisations | The Structured Clinical Interview for DSM-IV (SCID) and semi structured clinical interview | 11 | Emotional abuse/neglect revised factor score was negatively associated with number of hospitalisations (β= -0.33, p=0.003), the higher the score the less number of hospitalisations |
| **Schenkel et al. (2005), USA*** | 40 (25m/15f; SZ n=21; SAD n=19) / 41.9 (10.7) / CP, 20yrs / N/A | 18/22 | Coded as present or absent based on information from medical charts and from the clinical interview (frequency and severity coded) | Number of psychiatric hospitalisations | Clinical data and structured interview (not specified) | 8 | **Individuals with a history of childhood maltreatment had a significantly greater number of previous hospitalisations compared those without a history of childhood maltreatment (t=2.72, p=<0.05)** |
| Garno et al. (2005), USA | 100 (51m/49f; BPDI n=73; BPDII n=27) / 41.1 (13.1) / CP, 23yrs / N/A | 51/48 | CTQ (Bernstein et al., 1994) | Lifetime psychiatric hospitalisations | SCID and semi-structured interview developed by the authors | 10 | No significant difference in number of admissions between individuals with or without a history of childhood abuse (t=0.661, p=0.510) |
| Conus et al. (2010), Australia | 118 (71m/47f; BPDI-FEPM n=118) / 22.4 (3.2) / EP, 18mths / 18mths (retrospective file audit) | 29/89 | Early Psychosis File Questionnaire (EPFQ) (Conus et al., 2007) – clinical file audit tool | Admitted to hospital (dichotomous) and number of psychiatric hospitalisations | EPFQ (Conus et al., 2007) | 9 | Individuals with a history of childhood sexual/physical abuse were less likely to have a hospital admission during the 18 month follow-up period (p = 0.041, OR = 0.56, 95% CI: 0.32–0.98) |
| Cutajar et al. (2010), Australia | 115 (31m/84f; SZ n=73; OP n=42) / 33.7 (11.1) / CP, 15yrs / N/A | 78/37 | Screening of Police Surgeons Office and Victorian Institute of Forensic Medicine for sexual abuse cases | Number and duration of psychiatric hospitalisations | Victorian Psychiatric Case Register | 4 | Mean number (4.58 vs 3.5, p=0.47) and duration of hospitalisations were not significantly different between individuals with schizophrenia and a history of childhood sexual abuse and non-abuse cases with schizophrenia |
| Brown et al. (2005), USA | 330 (330m/30f; BPDI n=286; BPDII n=44) / 46.6 (10) / CP, 26yrs / 5yrs | 159/171 | Semi-structured interview (Bauer et al., 1997) | Number and duration of psychiatric hospitalisations | SCID and a battery of interview and self-report instruments (Bauer et al., 1997) | 10 | No significant difference in number (p=0.59) or duration (p=0.47) of hospitalisations (for psychiatric reasons/substance use) in the last 5 years between those with or without a history of childhood sexual/physical abuse |

BPD = bipolar affective disorder; SZ = schizophrenia; SAD = schizoaffective disorder; CP = Chronic Psychosis; BPDI = bipolar affective disorder type 1; BPDII = bipolar affective disorder type 2; BPDNOS = bipolar affective disorder not otherwise specified; BPDI-FEPM = bipolar affective disorder type 1 - first episode of psychotic mania; EP = Early Psychosis; OP = other psychoses not specified

*Studies highlighted in bold show significant positive relationship

## Supplement DS4 Discussion

### Methodological Issues

An important limitation across the reviewed studies is the small sample size, which can limit the ability to systematically explore the potential dose-response relationship between CT and psychosis relapse, as well as effects of different types of CT, their severity and frequencies. A further common feature across most of the reviewed articles was the lack of homogeneity within and between the samples in terms of diagnosis and stage (e.g. first episode/chronic) or duration of illness. Amongst the studies that reported a significant association[1,2], one included affective psychotic disorders only, whilst the other included both affective and non-affective psychotic disorders. Researching individuals at a similar stage of illness would help to minimise the potential confounding effect of illness chronicity on outcome. Research on recent SLEs and relapse suggests that the influence of these events may vary depending on the stage of psychotic illness[3,4], which may also be the case in relation to childhood adversity. The variability in the samples prevents clear comparison between each study, particularly in relation to course and long-term outcome. Six of the studies sampled the participants based upon the presence of their psychosis; however, Cutajar et al.[5] sampled individuals based upon abuse history and then estimated the prevalence of psychosis cases within the abused sample. Sampling differences may have also influenced the demographic characteristics of the sample as one study used a veteran only population consisting of just 9% women, which makes it difficult to generalize beyond this population group[6].

The different methodologies used to extract information on history of CT between the seven studies (see Table DS3) make it difficult to compare, contrast and draw conclusions from the evidence. We know from previous life event studies that it is vital to measure the nature, frequency and severity of adverse experiences[7,8], as this may suggest what dose of CT is tolerable before the poorer outcome can be predicted. The timing of events is also crucial, specifically in the case of childhood events, as neuroimaging research has revealed that experiences of CT can initiate different changes within the brain depending on the development period in which they occur[9-11]. These important factors were not considered consistently across the reviewed studies and owing to the spread of methodological variations and the noted limitations, it is important that the findings are therefore interpreted with caution. A further potential limitation is related to inaccurate categorisation of events, which may limit the reliability of the data; some of the studies recounted abuse as either absent or present in cases where details of the events were unclear.

Within this review, all but one study[12] which used police records, included retrospective measures to assess experiences of childhood abuse, which limits their ability to infer cause and effect on the long-term outcome of psychotic illness. The use of retrospective methods alone can be problematic in any study of CT given the often long temporal gap between the event/s and the measurement. Perhaps, this is particularly challenging in patients with psychosis because of the risk of poor event-recall (i.e. over or underreporting) owing to effort after meaning effects[13], cognitive deficits due to neurodevelopmental[14] and disease processes[15] and medication effects[16].

The varied methods used to extract information on RRPH-P (either self-report or clinical record screening) also make it difficult to compare and make inferences from the findings (see Table DS3). Relapse information was mostly collected through the screening of clinical/case notes, however three of the studies[1,6,17] utilised structured clinical and semi-structured interviews and self-report instruments to collect data on frequency and duration of hospitalisations, which again could be considered unreliable due to problems with recall. Furthermore, the benefit of extracting outcome data through screening notes also enables researchers to access information on patients who are less likely to engage with clinical research, such as those with chronic psychosis, limiting sample selection bias.

Whilst two of the studies reviewed found CT to be a risk factor for RRPH-P, they are limited by the lack of adequate consideration of potential confounders, for example use of cannabis[18]. Comorbid diagnoses, e.g. post-traumatic stress disorder (PTSD) and borderline personality disorder (BPD) and treatment status (e.g. compliance with medication) were also not recorded or considered in all of the studies, but are especially important when examining relapse. Furthermore, the mental and affective state of the victims of CT at the time of event recall could have influenced their ability to recollect early life experiences; the presence of symptoms at recall were assessed in the majority of the papers included in the review[1,2,17,19], although not necessarily controlled for in their analysis. However, evidence does suggest the validity and sufficient reliability over time of reports of CT amongst adults with psychosis, moreover, these reports are not influenced by psychopathology at the time of recall[20]. Additionally, interviewers or outcome data-collectors were not blinded in any of the studies, thus the data recording could have been subject to bias.

It is also worth noting that the studies examined in this review were carried out in different countries, each with their own criteria, thresholds and protocols for hospitalisation, limiting comparability and generalizability.

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