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Title: Sexual trauma increases the risk of developing psychosis in an ultra high risk

('prodromal") population

Running title: Trauma and psychosis risk in UHR individuals

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# Abstract

Studies indicate a high prevalence of childhood trauma in patient cohorts with established psychotic disorder and in those at risk of developing psychosis. A causal link between childhood trauma and development of psychosis has been proposed. We aimed to examine the association between experience of childhood trauma and the development of a psychotic disorder in a large "Ultra High Risk" (UHR) for psychosis cohort. The data was collected as part of a longitudinal cohort study of all UHR patients recruited to research studies at the PACE clinic between 1993 and 2006. Baseline data was collected at recruitment to these studies. The participants completed a comprehensive follow-up assessment battery (mean time to follow-up, 7.5 years, range 2.4 to 14.9 years), which included the Childhood Trauma Questionnaire (CTQ), a self-report questionnaire that assesses experience of childhood trauma. The outcome of interest was transition to a psychotic disorder during the follow-up period. Data was available on 233 individuals. Total CTQ trauma score was not associated with transition to psychosis. Of the individual trauma types, only sexual abuse was associated with transition to psychosis (p=0.02). The association remained when adjusting for potential confounding factors. Those with high sexual abuse scores were estimated to have a transition risk 2-4 times that of those with low scores. The findings suggest that sexual trauma may be an important contributing factor in development of psychosis for some individuals.

Keywords: Trauma; psychosis; ultra high risk

#### Introduction

Interest in the relationship between trauma and psychosis has been prompted by a number of research findings and clinical observations. First, the proportion of individuals with a psychotic disorder who have reported experiencing previous trauma is very high <sup>1, 2</sup>. Previous experience of trauma appears to be related to the severity of psychotic symptoms <sup>3, 4</sup> and have a negative impact on outcome and course of these disorders <sup>5, 6</sup>. Second, general population studies have demonstrated an association between early trauma and development of both psychotic-like experiences <sup>7</sup> and psychotic disorder <sup>8-10</sup>. This has led some authors to postulate an aetiological role for trauma in the development of psychotic disorders <sup>11</sup>.

Longitudinal studies are especially important to help address potential confounding factors in the observed cross-sectional relationship between previous trauma and psychosis. Given that the development of a psychotic disorder is a relatively rare event, cohort studies have often focused on psychotic symptoms and not on disorder <sup>12-14</sup>. When studies have investigated psychotic disorder as an outcome, the number of available cases has been low and the measures used to diagnose psychosis relatively broad <sup>8, 10</sup>. The measures of trauma used in these studies have also been relatively crude in the context of large epidemiological studies. A number of research groups have investigated longitudinal prospective data on the outcome of childhood abuse in relation to developing a psychotic disorder. A group from Melbourne reported significantly higher odds of developing schizophrenia and other psychotic disorders in individuals who had documented childhood sexual abuse compared to a matched control population <sup>15</sup>, although there are also null findings from this group <sup>16</sup>. Janssen

and colleagues reported an increased risk of later experiencing a psychotic disorder in a general population sample if individuals reported baseline childhood abuse (all abuse types) <sup>7</sup>. The populations and follow-up times in these studies are quite different but they do suggest a possible relationship between early abuse and the development of a psychotic disorder <sup>7, 16</sup>. Indeed a recent meta-analysis of a combination of study designs reported significant associations between adversity and psychosis with an overall effect of OR =  $2.78^{17}$ . The positive association was found for sexual abuse, physical abuse, bullying and emotional abuse but not the death of a parent <sup>17</sup>.

A population in which this association has not yet been well investigated is the "Ultra High Risk" (UHR) or putatively prodromal population <sup>18, 19</sup>. There may be important factors that are different in these individuals to population cohorts, for example the fact they are seeking help from services for mental health problems. Recent research in clinical high risk samples has demonstrated high rates of previous abuse in these patients <sup>20</sup>. Our group has previously reported data suggesting an association between previous experience of sexual trauma specifically and subsequent "transition" to a frank psychotic disorder <sup>21</sup>, but not with overall trauma or other types of trauma. This was an interesting finding but the study was conducted in a relatively small sample and only examined psychosis outcome over a short-term follow-up. Recent studies <sup>22-</sup> <sup>25</sup> have demonstrated that the risk of psychotic illness is not limited to the first 12 months and longer follow-up is necessary to thoroughly investigate the relationship between potential risk factors and development of psychosis. Our previous study also did not employ a structured participant-rated instrument of trauma.

In the current study we aimed to further investigate the relationship between experience of childhood/adolescent trauma and transition to psychotic disorder in an independent and much larger UHR sample, using a structured trauma instrument and with a longer follow-up period. Based on our previous finding, we hypothesized that sexual trauma specifically would predict transition to psychosis in this population.

# Method

#### Setting and sample

The data for this study was collected as part of a longitudinal cohort study which attempted to follow-up all UHR individuals who participated in research studies at the PACE (Personal Assessment and Clinical Evaluation) clinic between 1993 and 2006. The PACE clinic is a specialist "at risk" clinic for young people who meet the UHR for developing psychosis criteria. The catchment area of the service includes northwestern metropolitan Melbourne, Australia. Young people (aged 15-30 years) were eligible for treatment at PACE if they met at least one of three UHR groups: (1) Attenuated Psychotic Symptoms (APS). Presence of attenuated (subthreshold for a diagnosis of a psychotic disorder) psychotic symptoms within the previous 12 months. (2) Brief Limited Intermittent Psychotic Symptoms (BLIPS): history of brief self limited psychotic symptoms which spontaneously resolve (within 7 days) in the previous 12 months. (3) Trait group (FH): genetic vulnerability to psychotic disorder (either schizotypal personality disorder or family history of psychotic disorder in a first degree relative) and a drop in functioning over the past 12 months. The full criteria can be found in Yung and colleagues <sup>26</sup>. Exclusion criteria for PACE are: presence of a current or past psychotic disorder; known organic cause for

presentation, and past neuroleptic exposure equivalent to a total continuous haloperidol dose of >50 mg.

The overall cohort consisted of all 416 subjects who participated in research studies between 1993 and 2006. Seven research studies were conducted over this period, three of which were intervention studies (Risperidone + CBT v Needs based intervention; Risperidone + CBT v Placebo + CBT v Placebo + Standard Treatment; Lithium v Treatment as usual). Further details of the follow-up of the cohort are described in detail elsewhere <sup>25</sup>. In summary, the participants had research data collected throughout their initial individual research study including at baseline. They were then invited to complete a comprehensive assessment follow-up battery (completed between July 2008 and July 2009), including an assessment of psychopathology, functioning and previous trauma. The focus of this paper is on one particular measure, which was collected at this follow-up time point, the Childhood Trauma Questionnaire (CTQ), for which data was collected on 233 subjects.

#### Measures

#### 1) Experience of childhood trauma

The brief Childhood Trauma Questionnaire (CTQ) <sup>27</sup> was completed at the follow-up time point. The CTQ is a 28-item self-report questionnaire that assesses the experience of specific early traumatic events "as a child and as a teenager". Each CTQ item is scored on a 1-5 scale with 1 representing "never true" and 5 representing "very often true". The CTQ has 5 subscales (physical abuse, sexual abuse, emotional abuse, physical neglect and emotional neglect) and also provides a total score for all trauma. The score of each subscale is simply the sum of the 5 abuse specific items and

the total score is the sum of all 25 items with three validity items excluded. The definitions of abuse and neglect used in the CTQ have been outlined previously by the authors <sup>27</sup>. More information on the CTQ can be found in <sup>27</sup>.

2) Psychosis status: The main outcome of interest in this study was transition to psychotic disorder. Transition status information was derived from both i) the assessments performed during the follow-up period of the original individual research studies and ii) at the long-term follow-up interview. Transition to psychosis status was determined by the Comprehensive Assessment of At Risk Mental States (CAARMS)  $^{28}$  using previously published cut-off points for psychosis threshold  $^{18, 29}$  except for the earliest research participants (n = 59) where cut-off scores on the Brief Psychiatric Rating Scale (BPRS)  $^{30}$  and Comprehensive Assessment of Symptoms and History (CASH)  $^{31}$  were used in the original research studies to determine psychosis threshold and is therefore considered equivalent  $^{25}$ .

# **Covariates**

A number of factors known or suspected to be associated with transition to psychosis were included as covariates. The first set of covariates was based on previous research in this cohort into factors known to be associated with transition to psychosis, namely duration of untreated symptoms, year of entry into the clinic (with four levels: 1993-1997, 1998-2000, 2001-2003, 2004-2006) and baseline functioning <sup>25, 26</sup>. Duration of symptoms prior to treatment at PACE was assessed with the CAARMS. Functioning level at baseline in this cohort was assessed using the Global Assessment of Functioning (GAF) <sup>32</sup>. A number of other factors that may be related to experience of

trauma and transition were also considered as possible confounding variables and were included as covariates in the analysis if the data were available. These were age, gender and educational level (as measure of general intellectual functioning). These were assessed at baseline using a demographic interview. We also included measures of baseline (i.e. when the individual was first assessed for the original research study) psychopathology and quality of life as an additional set of covariates. Negative symptoms, depression and other psychiatric symptomatology were assessed using the Schedule for the Assessment of Negative Symptoms (SANS) <sup>33</sup>, the Hamilton Rating Scale for Depression (HRSD) <sup>34</sup>, and the BPRS <sup>30</sup> respectively. Quality of life was assessed using the Quality of Life Scale (QLS) <sup>35</sup>.

# Procedure

A tracking system previously used in a long term follow-up study of first episode psychosis patients was used to locate and re-contact participants in this cohort <sup>36</sup>. If participants did not consent to a face-to-face assessment, they were asked if they would consent to a brief telephone or written assessment, enabling a minimal set of clinical and functional outcome data to be collected. The interview consisted of a battery of psychopathological and neuropsychological assessments. These are outlined in full elsewhere <sup>25, 26</sup>. The CTQ was performed only at face-to-face interview and in one instance by a written assessment. It was available in 233 of the 271 (86.0%) individuals in the cohort who were interviewed or provided written information at follow-up (38 refused or did not complete this and the others provided information over the telephone). The flow of participants in the study is shown in Figure 1. All subjects gave written consent for both the original research study and the follow-up interview. The study was approved by the Melbourne Health research and ethics committee.

[Insert Figure 1 here]

# Statistical analysis

We compared the baseline data of those in the cohort who did not complete a CTQ to those who did using simple chi squared and T-tests. Survival analysis, using Cox regression, was applied to investigate the association between the CTQ scores and risk of transition to psychosis. The analysis was carried out with and without covariates. Each covariate was considered separately apart from those found to be associated with transition to psychosis in this cohort (baseline GAF, year of entry to PACE and time between symptom onset and first contact with PACE). The CTQ scores were treated as continuous variables. As an additional secondary analysis we added the other individual trauma type scores as covariates in the analysis of each specific trauma type and transition to try to further examine the specificity of any relationship to individual trauma type. As an alternative analysis, CTQ scores were also converted into categorical variables by choosing cut off points corresponding to tertiles. This was done for all subscales and the total score, except the sexual abuse subscale for which nearly three-quarters of the subjects had the minimum score (i.e. 5). For this subscale, the three groups formed were: a score of 5, a score of 6-11 and a score of 12-25. The formation of the three groups is similar to the categorization of trauma as none/mild, moderate to severe and severe to extreme used in previous studies <sup>37</sup>. Some of the cohort subjects were randomised to intervention trials in their past research participation at PACE and therefore received non-standard (trial)

treatments. In order to account for this treatment factor, the analysis was conducted for all subjects as well as for the subjects who received standard treatment or "treatment as usual". Results were essentially the same for both groups, so only the results for all subjects are presented. All analyses were performed using S-PLUS 6.1 for Windows and SPSS version 18.

# Results

#### Sample description

For the sample concerned in this analysis (i.e. the 233 subjects who provided the CTQ data), the time to follow-up ranged from 2.4 to 14.9 years with a mean of 7.0 years (SD 3.2). The number of subjects known to have developed a psychotic disorder was 55. The 1-year transition rate was 12.4% (95% CI, 8.1 - 16.6), 3-year rate was 18.9% (95% CI 13.7 – 23.8) and 5-year transition rate was 22.8% (95% CI, 17.0 – 28.2).

The characteristics of the sample are shown in Table 1 along with those individuals from the overall cohort who did not complete the CTQ. Those who had CTQ data were younger and more likely to be female than those who did not have CTQ data. They were also more likely to come from more recent PACE cohorts. Otherwise they were no different in terms of baseline symptomatology between the two groups (see Table 1).

### Reported levels of trauma

The average total CTQ score was 47.8 (SD 18.4). The average scores for the 5 subscales were respectively: emotional abuse 11.9 (SD 5.5); physical abuse 8.5 (SD 4.8); sexual abuse 7.5 (SD 5.4); emotional neglect 12.0 (SD 5.2) and physical neglect 7.9 (SD 3.2). Females scored significantly higher than males on the total CTQ score and the emotional abuse and sexual abuse subscale scores.

# Survival analysis investigating relationship between trauma and transition to psychosis

The results of the Cox regression analysis relating past trauma to transition to a frank psychotic disorder are shown in Table 2. Hazards Ratios (HR) in the table refer to a change hazard ratio for a one-point difference in the subscale CTQ score concerned and therefore are correspondingly small. The total CTQ score was not significantly associated with transition to psychosis (p=0.24). Of the individual trauma types, only sexual abuse was related to transition to psychosis (p=0.02). The three covariates, year of entry to PACE, baseline GAF score and time between symptom onset and first contact with PACE were found to be significant predictors of transition in the analysis of the entire cohort <sup>25, 26</sup> and therefore the Cox regression was also carried out with all these three as covariates considered together. The significant relationship between sexual abuse and transition remained and was strengthened when adjusting for these particular variables (p=0.003) (Table 2). The relationship also remained significant when adjusting for other covariates. The relationship between sexual trauma and transition remained significant but was attenuated when the other types of trauma

were adjusted for in the secondary analysis (see Table in supplementary material). Results were similar when analyzing the CTQ measures as categorical variables (no abuse/mild, moderate and severe) and so for this analysis the continuous data are reported.

[Insert Table 2 here]

#### *Relationship of CTQ sexual abuse scores and transition to psychosis.*

The relationship between CTQ sexual abuse scores and risk of transition to psychosis was further delineated by describing the relationship in terms of both hazards ratios and estimated transition rates. Hazards ratios represent the rate an event (e.g. development of psychosis) happens in one group compared to another. The hazard ratios of a transition to psychosis if scoring 15 and 25 on the CTQ sexual abuse subscale as opposed to 5 are reported in Table 3. Note that 5 is the minimum possible score for sexual abuse (no abuse), 25 is the maximum possible score and 15 is the middle value between these two extremes and were chosen to illustrate the relationship between sexual abuse and transition. The numbers of individuals scoring 5 (no sexual abuse) was 167, between 6 and 11 was 31 and between 12 and 25 was 33. The hazards ratio of transition to psychosis for a subject with a score of 5 and a score of 25 about 4 times that of a subject with a score of 5.

The estimated 3-year transition rates as obtained from Cox regression are shown in Figure 1. The 3-year transition rates were chosen as the majority of transitions in the cohort occurred within this time frame. Similar increased risks were found using 5 or 10-year transition rates but with larger confidence intervals.

[Insert Table 3 here]

[Insert Figure 2 here]

# Discussion

## Summary of the results

We report a positive association between experience of childhood sexual abuse and transition to a psychotic disorder in a UHR cohort - the higher the sexual abuse score, the higher the risk of transition to a psychotic disorder in the medium to long term. This was not the case for other types of trauma or total trauma score.

## Comparison with previous studies

The CTQ trauma scores from our sample appear similar to those reported from samples of patients with schizophrenia. This is the case for the individual abuse types <sup>37, 38</sup> as well as the total score <sup>37</sup>. The degree of reported trauma in our study is also considerably higher than those reported in community samples, for example Scher *et al.* <sup>39</sup> found a mean total score of 31.8 (SD 11.2) in their sample of over 1000 individuals. This suggests relatively high levels of previous trauma in a sample that meet UHR criteria, regardless if they later develop a psychotic disorder.

Two previous large general population epidemiological studies have reported a similar association between previous sexual trauma and psychosis <sup>9, 10</sup>. However, in both these studies the relationship was not limited to sexual trauma alone and extended to other types of trauma. Prospective longitudinal studies of the experience of trauma have also reported a specific relationship between sexual trauma and development of a psychotic disorder <sup>15</sup>, as well as a relationship for trauma more generally <sup>7, 16</sup>. However, none of these longitudinal studies have specifically examined

the UHR population, which may represent those more likely to present to services early with psychotic symptoms. Only our group has previously examined the association in an UHR population, with similar findings that sexual trauma was a risk factor for transition <sup>21</sup>. This would benefit from replication in at risk samples from other research groups.

# Why is sexual trauma particularly related to transition to psychosis in this population?

There are a number of theories for why trauma in general may cause psychosis. For example, biological models of how trauma might impact on psychosis include heightened sensitivity to stress through aberrant activation of the Hypothalamic-Pituitary- Adrenal (HPA) axis stress-diathesis model <sup>40</sup>. Dysregulation of the HPA axis may contribute to, or interact with, the dopaminergic abnormalities that are thought to be important in psychotic disorders <sup>40</sup>. There is some evidence that there is already HPA axis impairment in UHR samples <sup>41</sup>, although it is not know how this relates to past trauma. Psychological models highlight that exposure to trauma during childhood may sensitize people for the later exposure to daily life stress <sup>42</sup>, perhaps through the development of negative cognitive schemas <sup>43</sup> altered stress sensitivity <sup>44</sup>, difficulties in source monitoring internal events and externalising biases as results of traumatic events. Others have highlighted the importance of post-traumatic intrusions <sup>43</sup>. These theories are not mutually exclusive and a model combining the biological sensitization and the formation of cognitive schemas seems appealing. In the UHR population it is worth noting that individuals are already experiencing symptoms and

the additional history of abuse may be influential in the appraisal of symptoms or their consequences.

It is of particular interest that the relationship between previous trauma and development of a psychotic disorder was only found for sexual trauma and not all types of trauma. The above models have often not discriminated between the types of trauma experienced. Authors that have postulated a specific link between sexual trauma and psychosis have proposed that early sexual trauma may lead to a disruption of "internal anchors" of the sense of self, resulting from dissociative detachment, which may particularly augment psychological mechanisms involved in psychosis symptom formation <sup>45 46</sup>. However, there has been limited research into levels of dissociation in UHR samples, either associated with trauma or not. Related to this potential mechanism, others have suggested that sexual trauma may represent a more repeated or severe form of abuse and have reported an increased risk in those who experience more severe or intrusive forms of this abuse <sup>15</sup>. In our study those scoring highest on the CTQ sexual abuse questionnaire had the highest risk of developing a psychotic disorder but we were unable to demonstrate a clear link to severity or duration of abuse given the nature of the questionnaire. Others have suggested that sexual abuse might predispose to psychosis via deficits in metacognition or theory of mind which might be psychological sequelae of the abuse <sup>47,48</sup>. Further work should endeavour to investigate this relationship and the specific role of sexual trauma in symptom formation and development.

## Strengths and Limitations

The strengths of the study are the large sample size (the largest sample from a single site and comparable in size to the largest multisite collaborations), the long follow-up time and the comprehensive diagnostic interview data obtained both at follow-up and baseline. The study has a number of limitations. The CTQ completed in the study is a retrospective rating of trauma completed at follow-up and in this respect we cannot be sure that the trauma happened before the transition to psychosis. However, the wording of most items refers to experiences occurring over a period of time when the subjects were young (and the questionnaire specifically asks about experiences that happened when they were "growing up as a child or teenager"), so it is reasonable to assume that the majority of trauma experience had already occurred before any psychotic episodes or even symptoms. However, 17 of the 55 transition cases in our sample did occur before the age of 18 so we cannot discount that some of the trauma occurred after the onset of psychosis. It is also worth noting that with this data we cannot address the important question as to whether the past trauma alone or the interaction of trauma with existing sub-threshold psychotic symptoms is particularly important 49, 50.

A second limitation inherent to long-term follow-up studies that include assessing retrospective events is recall bias. This might have introduced some error into recording of previously experienced trauma as well as previously experienced symptoms. There is the possibility of an "effort after meaning" response with regard to trauma in those who experienced a psychotic disorder. However, a recent study suggests that retrospective reports of abuse in those with psychosis may be not be overly influenced by illness characteristics or current psychopathology <sup>51</sup>. We are also

aware that the numbers of individuals who experienced significant sexual abuse was relatively low and the results would benefit from replication in large samples.

It is also worth noting that that the study is different to a population cohort study as individuals did receive treatment that may have affected their risk of transition to psychosis. It could be for example that individuals who were most affected by traumatic experiences may also be more likely to respond well to these interventions which might suggest that the associations presented could be an under-estimated compared to what might be found in a cohort who had not received any treatment.

## Clinical implications

Our results suggest high levels of trauma in the UHR population, a finding we have previously reported along with other research groups <sup>20, 21</sup>. The relationship between sexual trauma and development of psychosis in this particular population has a number of clinical implications: first, we should be routinely assessing previous sexual trauma in the "at risk" population, as it may pose an increased risk for transition to a psychotic disorder. It has been reported that previous abuse is often not well assessed in psychiatric clinics <sup>52</sup> and that this should be an important part of the overall assessment process. Second, addressing the sequelae of sexual trauma may be a focus of early intervention strategies and approaches in these clinics to preventing individuals developing a frank psychotic disorder, or at least the particularly negative outcome related to having both a psychotic disorder and previous trauma <sup>53, 54</sup>. Examples of approaches might be working directly with the dissociative experiences in response to trauma using psychological techniques such as coping strategies, body awareness/mindfulness techniques and stress management. Challenging any

externalised attributional biases, which may have been developed or exacerbated by previous trauma, may also reduce the risk of symptom development or entrenchment. Third, attempts to enhance prediction of who within the UHR group is at additional increased risk of developing a psychotic disorder may consider using sexual trauma in these models.

# **Conclusions**

Longitudinal data from a cohort of individuals at ultra high risk for developing a psychotic disorder suggest a relationship between experience of sexual abuse and the medium to long-term development of a psychotic disorder. Further studies are needed to understand the mechanisms by which previous traumatic experiences, especially sexual trauma, predispose at risk individuals to developing a psychotic disorder.

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# **Conflicts of Interest:**

None

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|                    |   | Availability of CTQ data |       |       |       |                                    |  |  |
|--------------------|---|--------------------------|-------|-------|-------|------------------------------------|--|--|
|                    |   | Yes                      |       | No    |       |                                    |  |  |
|                    |   | Count                    | %     | Count | %     | Chi-<br>square<br>test p-<br>value |  |  |
| Baseline year      | 1993 – 1997   | 48                       | 20.6  | 79    | 43.2  |                                    |  |  |
|                    | 1998 - 2000   | 44                       | 18.9  | 33    | 18.0  | < 0.001                            |  |  |
|                    | 2001 - 2003   | 72                       | 30.9  | 43    | 23.5  | <0.001                             |  |  |
|                    | 2004 - 2006   | 69                       | 29.6  | 28    | 15.3  |                                    |  |  |
| Gender             | Male  | 96                       | 41.2  | 104   | 56.8  | 0.002                              |  |  |
|                    | Female  | 137                      | 58.8  | 79    | 43.2  | 0.002                              |  |  |
| Educational level  | Secondary education only or lower                                       | 177                      | 76.6  | 128   | 71.9  | 0.278                              |  |  |
|                    | Higher than secondary education   | 54                       | 23.4  | 50    | 28.1  |                                    |  |  |
| UHR Intake group # | Genetic vulnerability   | 29                       | 12.9  | 26    | 14.9  |                                    |  |  |
|                    | BLIPS   | 11                       | 4.9   | 12    | 6.9   | 0.35                               |  |  |
|                    | Attenuated Psychotic Symptoms   | 142                      | 63.4  | 95    | 54.6  | 0.55                               |  |  |
|                    | More than one intake group  | 42                       | 18.8  | 41    | 23.6  |                                    |  |  |
|                    |   | Mean                     | SD    | Mean  | SD    | T-test p-<br>value                 |  |  |
|                    | Age at baseline   | 18.5                     | 3.2   | 19.3  | 3.5   | 0.020                              |  |  |
|                    | Time between symptom onset and contact with first step to clinic (days) | 296.6                    | 428.9 | 380.3 | 677.5 | 0.161                              |  |  |
|                    | Time between symptom onset and first contact with clinic (days)         | 402.5                    | 480.4 | 500.9 | 862.4 | 0.184                              |  |  |
| Baseline           | GAF   | 58.4                     | 10.8  | 58.1  | 11.5  | 0.772                              |  |  |
| measures           | QLS Total   | 76.6                     | 22.5  | 73.9  | 20.1  | 0.197                              |  |  |
|                    | BPRS Total  | 47.0                     | 9.5   | 47.3  | 9.2   | 0.797                              |  |  |
|                    | BPRS Psychotic subscale   | 9.4                      | 3.0   | 9.5   | 2.9   | 0.731                              |  |  |
|                    | SANS Total  | 19.4                     | 12.9  | 20.6  | 12.7  | 0.375                              |  |  |

Table 1. Comparison between sample with data on the Childhood Trauma Questionnaire (CTQ) (n =233) and those without (n = 183)

Abbreviations: CTQ, Childhood Trauma Questionnaire; BLIPS, Brief Intermittent Psychotic Symptoms; GAF, Global Assessment of Functioning; QLS, Quality of Life Scale; BPRS, Brief Psychiatric Rating Scale; SANS, Scale for Assessment of Negative Symptoms

# total with data n=398

|                                |                                      | Unadjusted                   | Adjusted for covariates             |                              |                              |                              |  |
|--------------------------------|--------------------------------------|------------------------------|-------------------------------------|------------------------------|------------------------------|------------------------------|--|
|                                |                                      |                              | GAF/time to<br>clinic/entry<br>year | Gender                       | Age at<br>baseline           | Educational level            |  |
| CTQ<br>Emotional               | Hazards Ratio<br>(95% CI)<br>P value | 1.01<br>(0.96-1.06)<br>0.675 | 1.01<br>(0.96-1.06)<br>0.606        | 1.01<br>(0.96-1.06)<br>0.643 | 1.01<br>(0.96-1.06)<br>0.667 | 1.01<br>(0.96-1.07)<br>0.658 |  |
| Abuse subscale                 |                                      |                              |                                     |                              |                              |                              |  |
| CTQ Physical<br>Abuse subscale | Hazards Ratio<br>(95% CI)            | 1.04<br>(0.99-1.09)          | 1.04<br>(0.99-1.09)                 | 1.04<br>(0.99-1.09)          | 1.04<br>(0.99-1.09)          | 1.04<br>(0.99-1.09)          |  |
|                                | P value                              | 0.187                        | 0.149                               | 0.184                        | 0.189                        | 0.160                        |  |
| CTQ Sexual<br>Abuse subscale   | Hazards Ratio<br>(95% CI)            | 1.05<br>(1.01-1.09)          | 1.06<br>(1.01-1.10)                 | 1.05<br>(1.01-1.10)          | 1.05<br>(1.01-1.09)          | 1.08<br>(1.03-1.13)          |  |
|                                | P value                              | 0.023*                       | 0.003**                             | 0.017*                       | 0.023*                       | 0.035*                       |  |
| CTQ<br>Emotional               | Hazards Ratio<br>(95% CI)            | 1.01<br>(0.96-1.06)          | 1.01<br>(0.96-1.06)                 | 1.01<br>(0.96-1.06)          | 1.01<br>(0.96-1.06)          | 1.01<br>(0.96-1.07)          |  |
| Neglect<br>subscale            | P value                              | 0.734                        | 0.678                               | 0.728                        | 0.725                        | 0.776                        |  |
| CTQ Physical<br>Neglect        | Hazards Ratio<br>(95% CI)            | 0.98<br>(0.90-1.07)          | 0.98<br>(0.90-1.07)                 | 0.98<br>(0.90-1.07)          | 0.98<br>(0.89-1.07)          | 0.98<br>(0.88-1.08)          |  |
| subscale                       | P value                              | 0.675                        | 0.653                               | 0.682                        | 0.688                        | 0.618                        |  |
| CTQ total<br>score             | Hazards Ratio<br>(95% CI)            | 1.01<br>(0.99-1.02)          | 1.01<br>(0.99-1.02)                 | 1.01<br>(0.99-1.02)          | 1.01<br>(0.99-1.02)          | 1.01<br>(0.99-1.03)          |  |
|                                | P value                              | 0.241                        | 0.128                               | 0.224                        | 0.236                        | 0.260                        |  |

Table 2: Cox regression for CTQ subscales and total scores. The results are presented as hazard ratios and p values for unadjusted analysis and those adjusted for covariates.

Abbreviations: CI, Confidence Interval; CTQ, Childhood Trauma Questionnaire; GAF, Global Assessment of Functioning

\*p<0.05 \*\*p<0.01

Table 3. Hazard ratios for Childhood Trauma Questionnaire (CTQ) sexual abuse subscale scores unadjusted and adjusted for covariates known to be associated with transition to psychosis in the sample.

|                              |        | CTQ sexual abuse score |                               | CTQ sexual abuse score |                               |  |  |
|------------------------------|--------|------------------------|-------------------------------|------------------------|-------------------------------|--|--|
|                              |        | 15 vs. 5               |                               | 25 vs. 5               |                               |  |  |
| Adjustment<br>for Covariates | Number | Estimated hazard ratio | 95%<br>confidence<br>interval | Estimated hazard ratio | 95%<br>confidence<br>interval |  |  |
| No                           | 231    | 1.7                    | (1.1, 2.5)                    | 2.7                    | (1.2, 6.1)                    |  |  |
| Yes*                         | 210    | 2.1                    | (1.4, 3.3)                    | 4.5                    | (1.9, 11.1)                   |  |  |

\* Year of entry to PACE, baseline GAF and time between symptom onset and first contact with PACE are used as covariates.