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THE RELATIONSHIP BETWEEN CHILDHOOD AND ADULT TRAUMA AND THE SEVERITY OF PSYCHIATRIC SYMPTOMS IN ADULTS WITH SCHIZOPHRENIA IN UGANDA

A Dissertation submitted on 22 April 2021 to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in fulfilment of the requirements for the degree of MSc. Biostatistics & Epidemiology.

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Candidate Declaration

I [**Rufaro Catherine Samanga**] declare that this Dissertation is my own, unaided work. It is being submitted for the Degree of [**MSc. Epidemiology & Biostatistics**] at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

(Signature of candidate): 

Date: 22 April 2021

This declaration should appear on a separate page and each copy of the write-up should be individually signed by the candidate.

Dedication

I dedicate this research to my late father, Washington Samanga. *Ndinotenda Shumba,* for your commitment and investment into my education, for instilling in me a spirit of lifelong learning and most importantly, always believing in me even when I didn't believe in myself.
I love you. I miss you.

To my goddaughter, Buhle. You can have anything you want in this world, darling, so long as you give up the belief that you can't have it.

To every Black child who has come before me and who is yet to come.

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Abbreviations

ACE	Adverse Childhood Experiences
BCSS	Brief Core Schema Scales
CECA	Childhood Experience of Care and Abuse
CLEAR	Computerised Life Events Assessment Record
CLEFCQ	Childhood Life Events and Family Characteristics Questionnaire
CMIS	Childhood Maltreatment Interview Schedule
CNV	Copy number variant
CRDPSS	Clinician-Rated Dimensions of Psychosis Symptom Severity Scale
CTQ	Childhood Trauma Questionnaire
CTQ-SF	Childhood Trauma Questionnaire-Short Form
DAG	Directed Acyclic Graph
DS	Defeat Scale
EPSIS I	European Para-Suicide Interview Schedule I
FA	Fractional Anisotropic
GxE	Gene-environment
HPA	Hyperthalamic-pituitary-adrenal
LEC	Life Events Checklist
LEDS	Life Events and Difficulties Schedule
LMICs	Low-to-Middle-Income Countries
LTE	List of Threatening Experiences
MINI	Mini-International Neuropsychiatric Interview
PCA	Principal Component Analysis
PTSD	Post-traumatic Stress Disorder
RCT	Randomised Control Trial
SAM	Sympatho-adrenal Medullary
SAPS	Scale for the Assessment of Positive Symptoms
SCID-I	Structured Clinical Interview for DSM-IV Axis I Disorders
SCS	Social Comparison Scale
SGAs	Second-generation (atypical) antipsychotics
SMILE	Severe Mental Illness in HIV Endemic Uganda Study
WAYS	War-Affected Youths Survey
WMH	World Mental Health

Abstract

Background: Studies conducted in high and low-income countries suggest that childhood trauma is related to the onset of schizophrenia. A growing body of research mainly from high income countries suggests a relationship between recent adverse life events (adult trauma) and psychosis. However, there is a paucity of data of the effect of adult trauma schizophrenia symptoms in low-to-middle-income countries, especially African countries. This cross-sectional, secondary data analysis examined the effect of both childhood and adult traumatic events among cases with severe schizophrenia and the relationship between cumulative childhood and adult traumas on the severity of schizophrenia in a sample in Uganda.

Methods: Data were retrieved from the Severe Mental Illness in HIV Endemic Uganda cohort study. Cases with schizophrenia were recruited from the Butabika National Psychiatric Referral Hospital and the Masaka Regional Referral Hospital in Uganda. Childhood trauma was measured using the Childhood Trauma Questionnaire-Short Form and adult trauma was measured using the European Parasuicide Study Interview Schedule I. Adjusted left-censored regression and ordinal logistic regression models were employed to estimate individual and cumulative childhood and adult traumatic events in 314 patients with schizophrenia.

Results: The overall symptom severity score was significantly associated with overall adult trauma score ($p = 0.009$). Physical neglect, emotional and physical abuse during childhood contributed to the severity of specific positive symptoms namely delusions, disorganized speech, and negative symptoms (restricted emotional expression or avolition). Sexual abuse during adulthood was associated with severe hallucinations (OR 18.52, 95 % CI 1.93; 178.28). Adherence to oral psychiatric medication was associated with severe disorganised speech (OR 3.51, CI 1.25–9.82) while a higher BMI was associated with severe delusions (OR 0.92, CI - 0.154–0.014). Comorbid depression was associated with severe hallucinations (OR 2.28, CI 1.05–4.92). Cumulative adult traumas increased the odds of severe schizophrenia, especially hallucinations, delusions and abnormal psychomotor behavior in a dose-response manner.

Conclusion: Adult trauma is significantly associated with the prognosis of schizophrenia. Specific sub-types of childhood trauma were also implicated in prognosis with regards to both positive and negative symptoms. This knowledge is useful in designing future studies and treatment approaches to patients with severe mental illness where both early-life and recent

life adversities should be screened for and managed. Future work should look into the effect of adult traumatic events other than physical and sexual abuse. Furthermore, studies investigating the differential effect of childhood and adult trauma among patients with comorbid psychiatric disorders will be of tremendous value.

Chapter 1: Introduction

1.1. Background

1.1.1. Schizophrenia

Schizophrenia is a chronic psychiatric illness that is characterized by positive and negative symptoms. Positive symptoms include hallucinations and delusions while negative symptoms include blunted affect, avolition, asociality, alogia, anhedonia and cognitive impairment (Kirkpatrick *et al.,* 2011).

1.1.1.1. Diagnosis

The Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders-IV Axis I (SCID I) is one of the semi-structured assessment tools used to clinically diagnose a range of psychiatric illnesses including schizophrenia (Lobbestael *et al.,* 2011).

According to SCID I criteria, the diagnosis of schizophrenia occurs firstly with the presence of specific symptoms that have been experienced for at least a month and cannot be attributed to other psychiatric or medical conditions (McCormick and Flaum, 2005). Secondly, these symptoms have to result in significant functional impairment for a period of at least six months (McCormick and Flaum, 2005).

The Clinician-Rated Dimensions of Psychosis Symptom Severity Scale (CRDPSS) is an 8-item measurement tool used to assess the symptom severity of delusions, hallucinations, disorganized speech, abnormal psychomotor behaviour, negative symptoms, cognitive impairment, depression, and mania, in psychiatric disorders (CRDPSS; American Psychiatric Association, 2014). Each item is assessed on a 5-point scale which ranges from the absence of the symptom entirely to its severe presence (CRDPSS; American Psychiatric Association, 2014).

1.1.1.2. Aetiology

Over the past few years, genetic studies have focused on elucidating the cause of schizophrenia (Hilker *et al.,* 2018; Henriksen *et al.,* 2017; Tandon *et al.,* 2008). Landmark genome-wide studies have elucidated that genetic factors account for at least 80 percent of the heritability of the psychiatric illness (Van Os *et al.,* 2008; Hilker *et al.,* 2018).

Copy number variants (CNVs) have been strongly implicated in the genetic aetiology of schizophrenia while genome-wide association studies have found a little over 100 risk loci for schizophrenia with thousands of variants mediating the heritability (Tansey and Hill, 2018; Marshall *et al.,* 2017).

Other studies, on the other hand, have sought to determine the nature of the interactions between the underlying genetic predisposition and non-genetic or environmental factors (Matheson *et al.,* 2011). Existing models which have identified prominent causal pathways resulting in the development of schizophrenia, suggest that an underlying genetic risk is heightened by various environmental factors including childhood trauma, viral infections, lowered prenatal vitamin D exposure, social defeat, maternal nutrition and cannabis use, among others (Davis *et al.,* 2016). Studies conducted over the years have suggested that exposure to these environmental factors earlier on in life, may heighten the risk of the development of schizophrenia while exposure at a later stage is thought to affect symptom onset and severity (Matheson *et al.,* 2011; Welham *et al.,* 2009; Cannon *et al.,* 2003).

Over the past ten years or more, studies have examined gene-environment (GxE) interactions in psychosis (Van Os *et al.,* 2008; Ayhan *et al.,* 2016; Hosak & Hosakova, 2015). For example, Featherstone and colleagues suggest that there may be synergism between genes and the environment that result in the "sensitization" of the mesolimbic dopamine neurotransmission which is key in the development of schizophrenia (Featherstone *et al.,* 2007; Collip *et al.*, 2008; Van Os *et al.,* 2008; Nikolaus *et al.,* 2019).

What is also particularly interesting about G×E interactions is that environmental factors may induce epigenetic (non-genetic influences on gene expression) changes. These changes result from promoter DNA methylation affecting gene expression in neural systems that are relevant for psychosis (European Network of Schizophrenia, 2008). Thus, there is consensus that schizophrenia is caused by complex GxE interactions (Davis *et al.,* 2016).

As specific interest in early childhood trauma and psychosis has grown over the years, numerous studies have attempted to show a specific link between childhood trauma and clinical symptoms of schizophrenia (Şahin *et al.,* 2013; Daalman *et al.,* 2012; Álvarez *et al.,* 2015). Several mechanistic pathways have been postulated with regards to the link between childhood trauma and schizophrenia including the hypothesis that traumatic experiences may result in structural and neuro-chemical anomalies in the brain and nervous system, thereby affecting the function of the hypothalamus-pituitary-adrenal axis, which plays a role in stress response (Pruessner *et al.,* 2017).

1.1.1.3. Prevalence of schizophrenia

Although schizophrenia was ranked as one of the 25 leading causes of disability in 2013, the lifetime and point prevalence of the illness are low (Vos *et al.,* 2013). The median lifetime prevalence of schizophrenia is 4 individuals for every 1000 individuals of the population whilst the point prevalence ranges between 2.6 to 6.7 individuals for every 1000 individuals of the population (World Health Organization, 2001).

The prevalence of schizophrenia on the African continent, let alone individual African countries, is poorly documented. Of the few studies that do exist, one has described the burden of major psychiatric disorders including schizophrenia to be between 4 to 5 million Africans (Saha *et al.,* 2005). Additionally, McGrath and colleagues suggest that reported schizophrenia prevalence estimates are often conflicting due to the heterogeneous and complex nature of the disorder (McGrath *et al.,* 2008).

Prevalence data for schizophrenia in Uganda is admittedly lacking. There have been no nationally representative prevalence studies that have been carried out as yet. However, there have been a few small-scale studies which give some indication of the burden of the psychotic disorder in the country. In a study evaluating the prevalence of psychotic disorders among first treatment contact patients at Uganda's Butabika National Psychiatric Referral Hospital, 62.7 percent of the patients had a psychotic disorder with 51.08 percent having presented with a schizophrenia spectrum disorder (Mwesiga *et al.,* 2020). Additionally, a recent secondary data analysis conducted on the national health surveillance database found that among the common mental and neurological disorders in Uganda, between 2012 and 2016, 11 people per 10 000 of the population were diagnosed with schizophrenia (Alitubeera *et al.,* 2020).

Current schizophrenia prevalence data in South Africa, a middle-income country, is also lacking. Dated census estimates project that 1 percent of the South African population suffers from schizophrenia, amounting to approximately 500 000 people (Trump & Hugo, 2006; Saayman, 2010). In spite of the landmark 2009 South African Stress and Health study, the first large-scale population-based survey of common mental disorders in the country, schizophrenia was not accounted for in the 12-month and lifetime prevalence rates of psychiatric disorders including: anxiety disorders, mood disorders, impulse control disorders and substance use disorders (Herman *et al.,* 2009).

Valuable research on schizophrenia has also been conducted in Ethiopia. Kebede and colleagues investigated major socio-demographic correlates of schizophrenia, and their interactions, in a rural population of Ethiopia (Kebede *et al.,* 2004). The findings of the study showed that the socio-demographic correlates of schizophrenia in that rural population were similar to those found in studies conducted in developed countries (Kebede *et al.,* 2004). Furthermore, the findings also uncovered significant interactions between age, sex, marital status, area of residence and education as correlates of schizophrenia (Kebede *et al.,* 2004).

1.1.2. Childhood trauma

Childhood trauma is defined as any adverse experience that occurs before the age of 18 years. It is inclusive of physical, psychological, sexual and emotional abuse, the loss or divorce of a parent, physical and emotional neglect as well as bullying (Sacchi *et al.,* 2017).

1.1.2.1. Assessment of childhood trauma

There are several tools which can be used to assess childhood trauma retrospectively and these are broadly categorised into either interview-based or self-report instruments (Roy & Perry, 2004).

A few examples of interview-based instruments include the Childhood Experience of Care and Abuse (CECA), the Childhood Life Events and Family Characteristics Questionnaire (CLEFCQ) and Childhood Maltreatment Interview Schedule (CMIS), while the self-report instruments include the Adverse Childhood Experiences (ACE) Questionnaire and Childhood Trauma Questionnaire (CTQ) (Roy & Perry, 2004). The ACE Questionnaire is a 10-item instrument, most notably used in the World Mental Health Survey, that measures three

domains of childhood adversities including abuse, neglect and household dysfunction (Cheong *et al.,* 2017).

The more commonly used self-report tool is the CTQ which was first proposed by Bernstein and colleagues in 1994. The original self-administered 70-item tool assesses four key areas of childhood maltreatment including physical and emotional abuse, emotional neglect, sexual abuse and physical neglect, using a 5-point Likert scale ranging from “Never True” to “Very Often True” (Bernstein *et al.,* 2003). A short form of the CTQ (CTQ-SF) comprising 28 items was proposed almost a decade later and found to have adequate validity in both clinical and non-referred groups (Bernstein *et al.,* 2003). The CTQ has since been modified and translated to various languages in different study settings including China, Germany, Brazil and several others (Grassi-Oliveira *et al.,* 2014; He *et al.,* 2019; Karos *et al.,* 2014). In one Nigerian study, the factor structure, validity, reliability, and gender measurement invariance of Bernstein’s CTQ was compared to that of Gerdner and Allgulander’s more recent CTQ with the latter having exhibited a better fit among Nigerian adolescents in high school (Aloba *et al.,* 2020). Kinyanda and colleagues, through a local adaptation process, have translated the CTQ into both the Luganda and Luo languages for use in several studies in Uganda (Mugisha *et al.,* 2015a; Mugisha *et al.,* 2015b).

What has been of interest to clinicians is whether there is agreement between retrospective and prospective measures of childhood trauma. Initially, public health professionals have made use of the tools interchangeably and assumed that the tools effectively identify the same individuals (Baldwin *et al.,* 2019).

However, Baldwin and colleagues conducted a meta-analysis of 16 unique studies which suggested that there was poor agreement between prospective and retrospective measures of childhood trauma (Baldwin *et al.,* 2019). While agreement was higher when interviews with participants were conducted instead of self-administered questionnaires, the researchers suggested that there are different risk pathways to psychosis development in children who are prospectively identified as having experienced childhood trauma compared to adults who have retrospectively reported having experienced childhood trauma *(*Baldwin *et al.,* 2019).

Additionally, researchers have also highlighted the issue of recall bias which is often encountered during the retrospective measurement of childhood trauma (Susser & Widom, 2012). Recall bias is introduced when one fails to accurately recall the details of the trauma

one has experienced. This can be due to any number of reasons including current emotional state and certain amnesias associated with trauma (Susser & Widom, 2012).

Furthermore, Widom and colleagues have highlighted the underreporting or inconsistent reporting of childhood trauma due to either the social desirability or psychological burden that accompanies having to disclose trauma (Widom *et al.,* 2015). The type of misclassification that results from the underreporting or inconsistent reporting of trauma has been shown to result in biased study estimates that tend towards a null association (Widom *et al.,* 2015). In a number of studies, the retrospective recall of trauma has been acknowledged as a limitation (Colman *et al.,* 2016; Scott *et al.,* 2012; Hardt & Rutter, 2004; Susser & Widom, 2012).

1.1.3. Adult trauma

Adult trauma, also referred to as post-childhood trauma, proximal stressors or adverse life events, encompasses situations or occurrences which bring about a negative change in personal circumstances and involve an element of threat (Beards *et al*., 2013). Various stress-vulnerability models have proposed that stressful life events may play a role in the onset and exacerbation of psychosis. However, there have been mixed findings with studies investigating the role of stressful life events in the onset and course of schizophrenia due to methodological issues (Horan *et al*., 2005).

1.1.3.1. Assessment of adult trauma

A researcher-administered List of Threatening Experiences (LTE) questionnaire is one of the more frequently used 12-item tools used to assess stressful life events (Hosang *et al.,* 2010). However, one of the main criticisms of this tool has been its low internal consistency despite its high test-test reliability (Motrico *et al.,* 2013).

Additionally, the Life Events Checklist (LEC) is another self-report tool used for the assessment of adult trauma and is more commonly used to facilitate the diagnosis of PTSD (Bae *et al.,* 2008). The tool measures traumatic events or exposures which range from natural disasters and car accidents to physical and sexual abuse.

The Life Events and Difficulties Schedule (LEDS), on the other hand, has been considered the gold standard in measuring major stressful life events and superior to the checklist

approaches (Spence *et al.,* 2015). However, the tool is labour-intensive and also requires between 1-2 hours to administer. As a result, the Computerised Life Events Assessment Record (CLEAR) was investigated in a study conducted by Spence and colleagues in 2015 where the authors sought to improve upon the LEDS by developing a more sophisticated and digital approach to measuring life events (Spence *et al.,* 2015).

An alternative tool which has been used by Kinyanda and colleagues in past studies conducted in Uganda, involved modifying items derived from the Life Events and History module of the European Parasuicide Study Interview Schedule I (EPSIS 1) in order to collect data on specific adverse life events (Kinyanda *et al.,* 2005). Additionally, the modified tool was translated to Luganda, the primary language of Uganda.

1.1.4. Childhood and adult trauma and psychosis studies in Uganda

As a result of the two-decade-long civil conflict in the northern parts of Uganda, a review of the existing literature reveals that studies conducted thereafter have largely focused on the burden, impact and treatment of PTSD and depression among former child soldiers (Mugisha *et al.,* 2015a; Ovuga *et al.,* 2008; Ertl *et al.,* 2011). There is a paucity of studies on childhood trauma and recent life stressors as exposures leading to psychosis. However, there have been a few studies that have assessed the relationship between different types of war experiences and psychotic symptoms associated with PTSD (Amone-P'Olak & Nyeko, 2014). In a notable longitudinal cohort study titled the War-Affected Youths Survey (WAYS), a significant relationship was found between war experiences and psychotic symptoms with recommendations that trauma experienced during war be considered as a potential risk factor for psychotic symptoms among affected youths in post-conflict settings (Amone-P'Olak & Nyeko, 2014).

1.1.5. HIV/AIDS prevalence and severe mental illness in Uganda

Mental, neurological and substance use disorders in Uganda have been shown to be exacerbated by a number of factors including HIV/AIDS prevalence (Mugisha *et al.,* 2015a). Thus, it is important to highlight the various studies evaluating the impact of HIV/AIDS prevalence on severe mental illnesses. Kinyanda and colleagues have especially led the way in terms of investigating the effects of HIV/AIDS on mental illnesses including major depressive disorder, bipolar disorder and schizophrenia. In a 2009 study investigating emotional and behavioural disorders in HIV seropositive adolescents in urban Uganda, the results revealed

more than half of the sample, of which 60.9 percent of the patients had HIV/AIDS stages III and IV, experienced anxiety, depression, somatisation, seizures, mania and HIV-associated progressive encephalopathy (Musisi & Kinyanda, 2009). Furthermore, a 2011 study sought to examine the seroprevalence of HIV and risk factors for HIV infection among first-time psychiatric admissions in Uganda (Maling *et al.,* 2011). The results of the study confirmed that HIV prevalence (18.4 percent) (95 % CI, 13.8–23.0 %) is high among patients with severe mental illness and that HIV further adds to the burden of mental illness in Sub-Saharan African countries with an already high HIV prevalence (Maling *et al.,* 2011). More recently, the 2019 CHAKA study investigated the rates, types and co-occurrence of emotional and behavioural disorders among perinatally HIV-infected youth in Uganda (Kinyanda *et al.,* 2019). Among the 1339 children and adolescents attending HIV youth clinics for care, the prevalence of any DSM-5-based psychiatric disorder (generalized anxiety disorder, social anxiety disorder, separation anxiety disorder, major depressive disorder, attention deficit hyperactivity disorder, oppositional defiant disorder and conduct disorder) was approximately (17.4 percent) (95 % CI, 15.4–19.5 %) (Kinyanda *et al.,* 2019). The study went on to conclude that there was a significant burden of psychiatric disorders among the children and adolescents living with HIV (Kinyanda *et al.,* 2019).

Chapter 2: Literature Review

2.1. Conceptual frameworks for trauma and psychosis

Due to the causal factors of psychosis being both genetic and environmental, much work has been conducted to develop appropriate and integrated biopsychosocial models. Chief among these are the traumagenic neurodevelopmental model, neural diathesis-stress model, biopsychosocial model and social defeat hypothesis. Conceptually, these models underpin the understanding of the relationship between childhood and adult trauma and psychosis, which will be explored further in this review of existing literature.

2.1.1. Traumagenic Neurodevelopmental model

Seminal papers published by Weinberger, Murray and Lewis in 1987 laid the foundation for the current models that map out the complex development of schizophrenia. These authors initially put forward a purely neurodevelopmental theory which posited that a singular prenatal event could interfere with the maturation process of the brain during key neurodevelopmental stages and ultimately lead to the development of schizophrenia later on in life (Murray and Lewis, 1987; Weinberger, 1987). This became popularly known as the “single hit theory” of schizophrenia.

However, over time it became apparent that the model could not adequately account for features in schizophrenia such as the longitudinal changes in brain volume and thus research then focused its effort into delineating “secondary hits” or perturbations which would address the gaps in the model (Davis *et al.,* 2016). Similarly, the “two hit theory” of schizophrenia eventually proved limiting and it is for this reason that Read and colleagues argued that the traumagenic neurodevelopmental model is a better integrated model (Read *et al.,* 2014).

The traumagenic neurodevelopmental model attempts to partially explain the link between trauma and psychosis by integrating both psychological and biological processes (Read *et al.,* 2014). Broadly, the model suggests that the heightened response to stress that is often

reported in individuals with psychosis, including those with schizophrenia, stems from key neurodevelopmental changes which occur in the brain as a result of experiencing trauma earlier on in life (Read *et al.,* 2014).

Following their 2005 review, Rapoport and colleagues present an update to the neurodevelopmental model of schizophrenia, which suggests that the disorder is the product of abnormal neurodevelopmental processes which precede the onset of the disorder (Rapoport *et al.,* 2005; Rapoport *et al.,* 2012). The authors include recent studies which potentially modify or expand the existing neurodevelopmental model through the review of longitudinal whole-population studies, gene expression studies, placental pathology as well as multi-modal brain imaging studies (Rapport *et al.,* 2012).

2.1.2. Neural Diathesis-Stress model

This model was initially proposed in 1997 by Walker and Diforio, and updated in 2008 by Walker *et al,* and is primarily centered on the exposure to stress as shown in the diagram below (Pruessner *et al.,* 2017). The premise of this model is founded on evidence which has shown that exposure to stress stimulates numerous neurobiological systems including the sympatho-adrenal medullary (SAM) system and hyperthalamic-pituitary-adrenal (HPA) axis (Pruessner *et al.,* 2017).

The HPA axis has garnered more attention in the study of psychopathology because of the long-term effects of stress exposure which have been implicated in the onset and symptomology of psychiatric illnesses including schizophrenia and bipolar disorder (Sinclair *et al.,* 2012).

The HPA axis releases glucocorticoids which have the potential to alter brain function and structure (Frodl & O'Keane*,* 2013). Glucocorticoids have been known to alter the activity of certain neurotransmitter systems and neuronal functioning which have long been implicated in the pathophysiology of psychosis and major depression (Frodl & O'Keane*,* 2013).

However, critics of the model initially challenged the model's assumption that individuals suffering from psychosis were overexposed to stress whereas it was more likely that a genetic predisposition just made them more 'vulnerable' to stress (Read *et al.,* 2001).

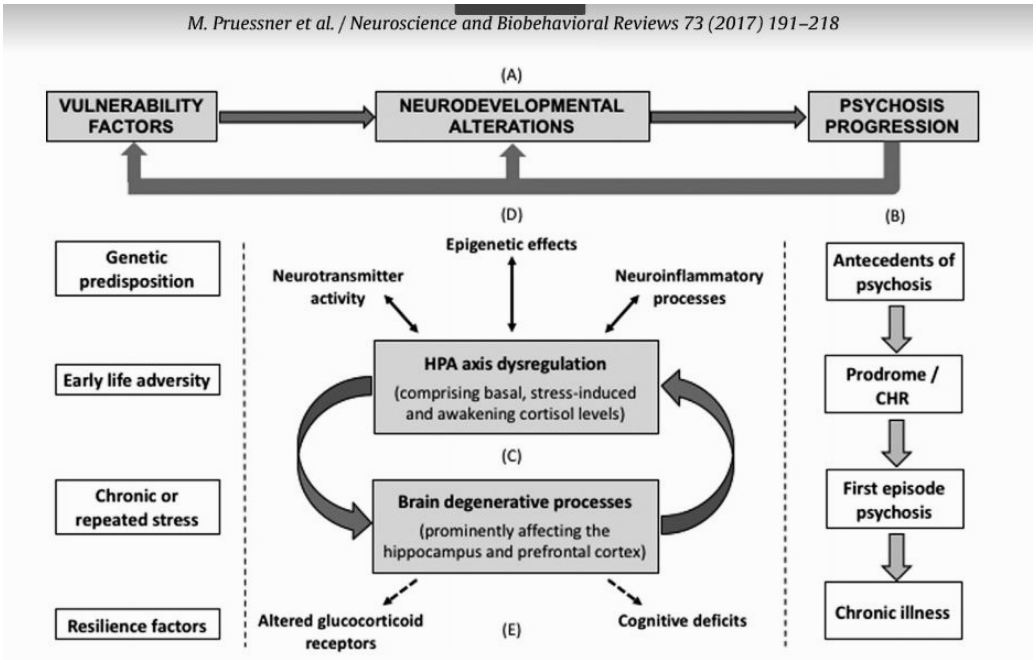


Diagram: Pruessner *et al.,* 2017

For years, research conducted focused almost exclusively on the genetic architecture and heritability of the disease, further propelled by advances in molecular, technological and statistical methodologies (Henriksen *et al.,* 2017). As a result, key causal environmental factors have been neglected.

2.1.3. Biopsychosocial model

While the biopsychosocial model already existed in the 1950s, with the term “biopsychosocial” having been coined by neurologist and psychiatrist Roy Grinker, it was George Engel who popularised the model decades later in what has now become the central dogma in contemporary psychiatry (Ghaemi, 2009; Engel, 1977).

The biopsychosocial model seeks to reconcile the biological mechanisms underlying psychosis with both psychological and social factors by considering four factors: the individual, the individual’s social context, the social context of the broader health care system as well as the physician-patient relationship (McCutcheon, 2006). While the model has become the conceptual premise for a more holistic approach to the treatment of psychiatric disorders, disorders which have often been misunderstood by a strictly biomedical model, many scholars have advocated for an expanded and more integrated model which takes into

consideration strides made in neuroscience, the range of causes for psychiatric disorders, the classification of such psychiatric disorders as well as effective treatment strategies (Davies & Roache, 2017; Lehman *et al.,* 2017; Brenner, 2016).

2.1.4. Social Defeat Hypothesis

In 2005, the social defeat hypothesis was proposed. The hypothesis suggests that prolonged exposure to social defeat, the negative experience of being excluded from the majority group, results in the sensitization of the mesolimbic dopamine system which ultimately leads to the development of schizophrenia (Selten and Cantor-Graae, 2005). According to the authors, social defeat is the common denominator across the five major risk factors of schizophrenia which include urban upbringing, migration, childhood trauma, low intelligence and drug abuse (Selten and Cantor-Graae, 2005).

Admittedly, social defeat is difficult to measure and thus the vast majority of epidemiological studies have focused on defeated and non-defeated groups instead of individuals. However, the use of questionnaires such as the Social Comparison Scale (SCS), the Defeat Scale (DS), and the Brief Core Schema Scales (BCSS) have proved useful alternative measurement tools (Selten *et al.,* 2013).

2.2. Childhood trauma and psychosis

An emerging field of research has been investigating the relationship between childhood trauma experienced by individuals and their risk of developing psychosis later in life. Whilst the influence of genetics on psychosis has been well-studied, research highlights the equally important influence of environmental factors such as developmental trauma, cannabis use, minority group position and growing up in an urban environment (Isvoranu *et al.,* 2016; Vaucher *et al.,* 2018; Vassos *et al.,* 2012).

Thus, childhood trauma has been identified as a potential risk factor in the development of psychosis later on in life and found to be related to psychotic symptoms including paranoia, hallucinations and delusions (Read *et al.,* 2005; Isvoranu *et al.,* 2016, Mall *et al.,* 2019).

Interestingly, the development of psychosis or the presence of psychotic symptoms has not been limited to adults who have experienced adversities during their childhood. A 2011 longitudinal study followed a nationally representative cohort of young twins in the UK and their exposure to maltreatment by an adult, bullying by their peers and involvement in accidents (Arseneault *et al.,* 2011). Participants were recruited at the age of 5 and follow-up assessments conducted at ages 7, 10 and 12 to verify the presence of any psychotic symptoms by clinicians (Arseneault *et al.,* 2011).

Furthermore, studies have also attempted to not only link childhood trauma to psychosis in general, but specific subtypes of childhood trauma (e.g. sexual or physical abuse) to specific psychiatric disorders namely Schizophrenic Spectrum Disorders, Bipolar Disorder and Major Depressive Disorder (Bruni *et al.,* 2018).

2.2.1. Childhood trauma and schizophrenia

Research conducted in high-income countries suggests that there is an association between childhood trauma and schizophrenia (Larsson *et al.,* 2013, Bruni *et al.,* 2018; Hardy *et al.,* 2016). However, there is a notable paucity of similar data in LMICs (Mall *et al.,* 2019).

More specifically, several studies have linked childhood trauma to the development and onset of schizophrenia, the course of the psychiatric disorder as well as the existence of a dose-response relationship between the number of childhood adversities experienced and the severity of clinical symptoms (Carbone *et al.,* 2019; Li *et al.,* 2015).

In a collaborative study by Mørkved and colleagues which recruited patients from Norway and Austria, results suggested that patients suffering from schizophrenia were more likely to have experienced childhood trauma compared to individuals suffering from other mental illnesses (Mørkved *et al.,* 2017).

Larsson and colleagues found a higher prevalence of childhood trauma, particularly physical abuse and neglect, among patients suffering from schizophrenia spectrum disorder compared to patients with affective disorder (Larsson *et al.,* 2013). Bruni and colleagues found that loneliness, psychological and physical abuse as well as escape from home were more frequently occurring in patients with schizophrenia spectrum disorders compared to those with major depressive disorder or bipolar disorder (Bruni *et al.,* 2018).

A case-control study looked at the association between childhood trauma and fractional anisotropic (FA) values, the level of myelination and organization of brain tract fibres which are underlying components of brain connections (Asmal *et al.,* 2018). The results of the study suggested that individuals with schizophrenia, who had been exposed to high levels of childhood trauma, had lower FA values than the controls who were also exposed to high levels of childhood trauma. Thus, connectivity in several regions of the brain was affected in individuals with lower FA values due to the disruption of white matter pathways involved in the development of schizophrenia (Asmal *et al.,* 2018).

Studies have also shown significant associations between specific subtypes of childhood trauma and symptoms of schizophrenia. Childhood emotional neglect and abuse were found to be associated with higher scores on the Scale for the Assessment of Positive Symptoms (SAPS) in patients with first-episode schizophrenia. A review examining trauma and schizophrenia found that in one study, the relative risk of patients with schizophrenia who had been sexually abused compared to the controls, was 1.2 times higher (Ücok and Bikmaz, 2007; Morgan and Fisher, 2007).

Another study examining the association between trauma, persecutory ideation and verbal hallucinations found that childhood sexual abuse was associated with psychotic-like experiences (Freeman and Fowler, 2009). In a 2016 study, Hardy and colleagues found that childhood sexual abuse was linked to auditory hallucinations while childhood emotional abuse was specifically associated with delusions (Hardy *et al.,* 2016).

In a more recent case-control study conducted by Mall and colleagues among the Xhosa people in the Western Cape region of South Africa, it was found that the odds of schizophrenia were 2.44 times higher among those who experienced any trauma than among those who reported no traumatic experiences. Additionally, the odds of developing schizophrenia were considerably higher in individuals who had experienced physical or emotional abuse (OR 1.59, CI 1.28–1.97), neglect (OR 1.39, CI 1.16–1.68), and sexual abuse (OR 1.22, CI 1.03–1.45) compared to those individuals who had not (Mall *et al.,* 2019).

2.2.1.1. Childhood trauma and schizophrenia prognosis

Several studies have suggested that childhood trauma is also associated with illness trajectory in psychosis. A number of theories have been posited as to how overall childhood trauma and its specific subtypes increase the severity of specific symptoms experienced by patients with schizophrenia (Bailey *et al.,* 2018). A systematic review and meta-analysis conducted by Bailey and colleagues found that among those suffering from psychosis, childhood trauma was significantly correlated with severity of hallucinations and delusions (Bailey *et al.,* 2018).

Another study evaluated gender differences in childhood trauma and the association with symptom severity in psychosis over a period of two years. Multiple linear regression analyses found that severe emotional abuse was a strong predictor for positive symptom severity ($p = 0.003$) in male patients while emotional neglect was also found to be a strong predictor for negative symptom severity ($p = 0.006$) (Pruessner *et al.,* 2019).

Furthermore, McCabe and colleagues examined the relationship between childhood trauma and the clinical and cognitive features of schizophrenia and found that positive symptom severity was associated with childhood trauma (McCabe *et al.,* 2012).

2.2.1.2. Sex differences in childhood trauma and schizophrenia

It is well established that sex differences exist in the development of schizophrenia (Kocsis-Bogár and Forintos, 2018). Higher incidence rates of schizophrenia, earlier age of onset, increased negative symptoms and cognitive impairment as well as the unfavourable progression of the illness, are associated more with men than women due, in part, to the protective role of both oestrogen and oxytocin (Canuso and Pandina, 2007; Eranti *et al.,* 2013).

As it pertains to the role of trauma and the development of schizophrenia, there are studies which have found an association between childhood trauma and symptom severity to be much stronger and more pronounced in women than in men while other studies have failed to show any differences between the sexes altogether (Cutajar *et al.,* 2010; Shevlin *et al.,* 2015).

Moreover, a 2009 study found that severe physical and sexual abuse precipitated the onset of first-episode psychosis. A follow-up study led by Gayer-Anderson in 2015, found that women who had been exposed to physical abuse during their childhood, were four times more likely to develop psychosis in adulthood compared to those who were not exposed to physical abuse during their childhood (Gayer-Anderson *et al.,* 2015; Fisher *et al.,* 2009). There was no clear association found between physical abuse during childhood and the onset of psychosis in men, however (Gayer-Anderson *et al.,* 2015).

2.2.1.3. Cannabis use, childhood trauma and schizophrenia

Both childhood trauma and cannabis use are considered risk-modifying factors for schizophrenia.

While few studies have investigated their individual effects on schizophrenia, even fewer studies have examined how the two environmental factors interact with each other in schizophrenia (Baudin *et al.,* 2016).

It is well established that cannabis use greatly impacts the course of schizophrenia, with patients who have used cannabis during their adolescence being susceptible to longer and more frequent hospitalizations as a result (Manrique-Garcia *et al.,* 2014).

A 2012 study by Schimmelmann and colleagues suggested that cannabis use is associated with worse functional outcomes while two other studies showed that first-episode psychosis patients, who either decrease or stop their cannabis use entirely, improve their overall global functioning (Schimmelmann *et al.,* 2012; Faber *et al.,* 2012; Stone *et al.,* 2014).

Following several studies which have found higher cannabis use among children who have experienced trauma, including a longitudinal study spanning 25 years, it has been suggested that childhood trauma sensitises individuals to the psychotomimetic effects of cannabis use (Baudin *et al.,* 2016; Fergusson *et al.,* 2008).

2.3. Recent adverse life events and psychosis

Stress-vulnerability models have posited that stressful life events may trigger the onset of psychosis or exacerbate its symptoms (Horan *et al.,* 2005).

In a meta-analysis conducted by Beards and colleagues, it was found that patients with psychosis were three times more likely to have been exposed to recent adverse life events compared to controls (Beards *et al.,* 2013).

The main effect of recent adverse life events appears to be the exacerbation of psychotic symptoms as opposed to the onset of psychosis according to several critical reviews (Norman & Malla, 1993; Day *et al.,* 1987). In what was then perhaps a landmark study, Brown assessed the cumulative frequency of adverse life events between periods of stability and symptom exacerbation and the results seemed to suggest that adverse life events preceded psychotic episodes (Brown, 1968).

Another study replicated the findings of Brown's study and showed that there was an increase in the number of stressful life events reported by patients in the three weeks prior to the onset of psychotic symptoms (Day *et al.,* 1987).

2.3.1. Recent adverse life events and schizophrenia

Research points towards adverse or stressful life events potentially exacerbating clinical symptoms of schizophrenia although the mechanisms through which this occurs remain unclear (Horan *et al.,* 2005).

Much of the research carried out towards the end of the 20th century laid the foundational work for what is known about the association between stressful life events and the development of psychosis, especially schizophrenia. However, just as Norman & Malla pointed out in 1993 already, several rigorous literature reviews conducted by the likes of Rabkin and Tennant in 1980 and 1985 respectively, agreed that the evidence for the association between stressful life events and psychosis was weak (Norman & Malla, 1993).

2.4. Research question

What relationship does childhood trauma and recent adverse life events (adult trauma) have on the severity of psychiatric symptoms experienced by people with schizophrenia in Uganda between 2017-2018?

2.5. Justification for study

In light of the paucity of data in Africa on childhood and adult trauma and their relationship with schizophrenia, understanding the possible pathways involved between childhood and adult trauma and schizophrenia, will allow for an understanding of prognosis of schizophrenia and how this can be further exacerbated by trauma. This may lead to interventions that specifically target trauma and its consequences. Research such as this is therefore critical within the context of resource-limited settings in African countries as it has the potential to elucidate key risk factors that may impact the development of psychotic disorders such as schizophrenia in this instance.

2.6. Aim and objectives

2.6.1. Aim

To determine whether childhood trauma and adult trauma have a relationship with the psychiatric symptoms experienced by people with schizophrenia in their adulthood.

2.6.2. Objectives

Objective 1:

To describe the severity of schizophrenia symptoms experienced by the study participants using the Clinician-Rated Dimensions of Psychosis Symptom Severity (CRDPSS) scale.

Objective 2:

To examine separately the impact of childhood and adult traumatic events on the severity of symptoms as measured by the CRDPSS.

Objective 3:

To develop a cumulative model for both childhood and adult traumatic events to determine whether multiple traumas have an additive effect on the severity of schizophrenia symptoms as measured by the CRDPSS.

Chapter 3: Methodology

3.1. Primary study

3.1.1. Study design

The primary study that forms the basis of this research report is the Severe Mental Illness in HIV Endemic Uganda (SMILE) cohort study which examined the relationship between risky sexual behaviour and HIV prevalence in individuals suffering from severe mental illnesses (major depressive disorder, bipolar disorder and schizophrenia). The SMILE study was conducted from 15 January 2018 to 30 August 2020 and provided several opportunities for secondary data analysis.

The SMILE study was conducted in central and south-western Uganda at both the Butabika National Psychiatric Referral Hospital (situated 10km East of Kampala) and the Masaka Regional Referral Hospital (Birungi 2017, pers. comm). The Butabika National Psychiatric Referral Hospital is a 600-bed capacity mental facility with specialised services for substance use disorders, a forensic ward, a specialised child and adolescent mental health unit as well as specialised occupational therapy and psychotherapy units. The Masaka Regional Referral Hospital is a 540-bed capacity facility that offers a range of medical services expected from a regional referral facility in addition to providing nutritional support for children and a dedicated mental health unit. One thousand respondents were recruited from the mental health out-patient departments of both hospitals over a 6-month period and followed up for at least 12 months with assessments carried out every three months (Birungi 2017, pers. comm).

3.1.2. Study population

Individuals aged at least 18 years old who were admitted to either the Butabika National Psychiatric Referral Hospital or the Masaka Regional Referral Hospital in Uganda between 2017 and 2018.

3.1.3. Eligibility criteria

3.1.3.1. Inclusion criteria

Patients were included in the primary study if they met the following criteria: 1) minimum age of 18 years; 2) registered with the mental health outpatient clinic at either Butabika National Psychiatric Referral Hospital or Masaka Regional Referral Hospitals; 3) resided within a 15km radius of the study clinic; 4) had one of three severe mental illnesses namely bipolar affective disorder, schizophrenia and recurrent major depressive disorder; 5) understood either English or Luganda (the predominant local language spoken in central and southwestern Uganda and the language to which the study instruments were translated); 6) consented to participate in the study or 7) obtained surrogate consent (from a legally authorised and acceptable representative of the patient) and 8) had insight. The study did not specifically assess for insight as is the focus of several previous studies on schizophrenia (García-Cabeza *et al.,* 2018; Dam, 2006; Lincoln *et al.,* 2017) but excluded persons who were unable to engage with the research process for any reason that may include having severe psychiatric symptoms, sensory or cognitive impairment or being physically too sick.

3.1.4. Measures, Study variables and Procedures

3.1.4.1. Measures

3.1.4.1.1. Interview-based standardized questionnaires

Data collection of exposure and outcome variables was conducted in the primary cohort study using the following interview-based standardized questionnaires presented in Table 1 and all of which have been appended to this research report. The three main data collection tools were the childhood trauma questionnaire-short form (CTQ-SF), the Clinician-Rated Dimensions of Psychosis Symptom Severity (CRDPSS) and the European Para Suicide Interview Schedule I (EPSIS I) as presented below.

3.1.4.1.2. Local adaptation of psychosocial assessment scales

The psychosocial assessment scales were taken through a local adaptation process that consisted of the following: i) separate forward and back translation by teams of mental health professionals and lay people conversant with both English and the local language of translation (Luganda); ii) a consensus workshop where translation teams derived the versions of the data collection tools with the most acceptable internal validity; and iii) assessed the data collection tool with patients with SMIs to refine the terminology in order to enhance clarity (Birungi 2017, pers. comm).

Table 1. Interview-based standardized questionnaires used to collect primary data

Data collection tool	**Domains examined**
Childhood Trauma Questionnaire-Short Form (Bernstein and Fink, 1998)	Examines adverse events during childhood
Clinician-Rated Dimensions of Psychosis Symptom Severity (CRDPSS; American Psychiatric Association, 2014)	Examines severity of psychosis symptoms
European Para Suicide Interview Schedule I (Kerkhof *et al.,* 1989)	Examines physical and sexual abuses during adulthood.

3.1.4.1.2.1. Childhood Trauma Questionnaire-Short Form

The CTQ is a 28-item tool which measures childhood trauma (physical abuse, physical neglect, emotional abuse, emotional neglect, sexual abuse) in addition to a minimization/denial scale. The CTQ makes use of a Likert scale where 1 = Never true, 2 = Rarely true, 3 = Sometimes true, 4 = Often true and 5 = Very often true. Exactly 10 items on the 28-item tool were reverse scored.

Both the overall childhood trauma score and mean scores for individual trauma types were computed.

Internal validity and Reliability

The CTQ has been previously validated by Kinyanda and colleagues in the Ugandan context using the local adaptation process described above in 3.1.4.1.2. The Cronbach's alpha for the CTQ was found to be 0.88 (Kinyanda *et al.,* 2017).

3.1.4.1.2.2. Clinician-Rated Dimensions of Psychosis Symptom Severity

The CRDPSS is an 8-item measurement tool used to assess the symptom severity of delusions, hallucinations, disorganized speech, abnormal psychomotor behaviour, negative symptoms, cognitive impairment, depression, and mania, in psychiatric disorders (CRDPSS; American Psychiatric Association, 2014). Each item is assessed on a 5-point Likert scale where 0 = Not present, 1 = Equivocal, 2 = Present and mild, 3 = Present and moderate and 4 = Present and severe.

Both the overall symptom severity score and the mean scores for five out of the possible eight sub-scales were computed separately. The primary SMILE cohort study only collected data for these five sub-scales (hallucinations, delusions, disorganized speech, negative symptoms/avolition and abnormal psychomotor behaviour.

Internal validity and Reliability

The CRDPSS questionnaire was used for the first time in a Ugandan setting in the SMILE study. The results of this primary study will be able to better comment on the validity indices of the data collection tool.

3.1.4.1.2.3. European Para Suicide Interview Schedule I

The modified EPSIS I used by Kinyanda and colleagues measured negative life events including physical and sexual abuse experienced during adulthood in two time periods: later in life (from onset of adulthood at age 18 to 12 months before the study commenced) and the last 12 months (Kinyanda *et al.,* 2005). The EPSIS I a binary scale where patients answered either 1 = Yes and 2 = No.

The overall adult trauma score and mean scores for individual trauma types were computed separately.

Internal validity and Reliability

The EPSIS I was first used in a Ugandan setting by Kinyanda and colleagues and taken through the local adaptation process described above in 3.1.4.1.2. The Cronbach's alpha for the EPSIS I was found to be 0.82 (Kinyanda *et al.,* 2011).

3.1.5.1. Study variables

The main exposure variables of interest were *childhood trauma and *adult trauma. As per the primary cohort study, childhood trauma was defined in the secondary study as physical, emotional and sexual abuse, physical and emotional neglect experienced prior to the age of 18 years.

A minimization/denial scale designed to assess any bias introduced by way of minimizing the degree of childhood trauma experienced was also included as an additional variable. Cut-off scores were not used with childhood trauma so as to keep the variable continuous and allow for the determining of any dose-response relationship with the outcome.

Adult trauma was defined as both physical and sexual abuse experienced from the age of 18 years until 12 months before the commencement of the primary cohort study. The adult trauma score for both physical and sexual abuse was comprised of the number of items to which the participant responded affirmatively ("yes").

Additional explanatory variables included in the data analyses included: *age, *sex, *education level and *study site.

The main outcome of interest was the severity of schizophrenia symptoms experienced (hallucinations, delusions, disorganized speech, abnormal psychomotor behaviour and restricted emotional expression/avolition) as determined by the CRDPSS questionnaire. The overall CRDPSS score was used with the outcome variable subsequently treated as continuous.

The following variables were also included in the descriptive studies: **adherence (to taking oral psychiatric medication), **"ever had depression" and **"lifetime number of depressive episodes". Adherence was measured using a standardized tool evaluating psychiatric history. Patients were

asked to answer “yes” or “no” to whether they had missed taking their psychiatric medication in the 3 days prior to being assessed. “Ever had depression” was measured as a “yes” or “no” response to ever having felt “down, sad, empty or hopeless” for most of a given day while the “lifetime number of depressive episodes” was measured by the number of depressive episodes experienced in the patient’s lifetime up until they took part in the study.

Given the extensive literature which has suggested that **alcohol abuse and the use of illicit substances such as **heroin, **cocaine, **khat, **kubab and **cannabis, either affect the onset or course of schizophrenia, the intention was to include these variables in the analyses as confounders. However, due to missing data, these variables were subsequently omitted. **HIV serostatus was also considered as a potential explanatory variable but was omitted from the final models as there was no evidence of association with the severity score.

* explanatory variables included in models regardless of statistical significance
** potential explanatory variables to be included in models but omitted due to very few positive responses, many missing values or no evidence of association with the outcome.

3.1.6.1. Procedures

3.1.6.1.1. Recruitment of study participants

A sub-register was created that comprised all active patients with SMIs who were attending the mental health out-patient clinics at both Butabika Hospital and Masaka Hospital. From the sub-register at Butabika Hospital, a random sample of 800 patients was selected and from the sub-register at Masaka Hospital, a random sample of 400 patients was elected using a table of random numbers. Participants were recruited on the basis of having met the inclusion criteria of the study (Birungi 2017, pers. comm).

3.1.6.1.2. Diagnosis of schizophrenia

Schizophrenia was diagnosed using the Structured Clinical Interview for DSM-5 Axis I Disorders (SCID-5; American Psychiatric Association, 2017) by psychiatric nurses and clinical officers who were supervised by Dr Caroline Birungi, a trained psychiatrist and principal investigator of the SMILE study. The diagnosis was carried out by a psychiatrist and the data obtained from a patient chart review. The structured diagnostic assessment instrument, the Mini-International Neuropsychiatric Interview (MINI), provided a diagnosis of psychosis (Birungi 2017, pers. comm).

3.1.6.1.3. Interviewing of study participants

Data for this study were obtained through an interview using standardised and structured questionnaires that were administered by trained psychiatric nurses and clinical officers who were supervised by psychiatrist, Dr Carol Birungi, who is undertaking her PhD in the same project. Additional information such as the provisional psychiatric diagnosis was obtained from patient chart reviews. Biological indices such as HIV and syphilis serostatuses were determined in the laboratory on a venous blood sample taken from each patient (Birungi 2017, pers. comm).

3.1.6.1.4. Collection of clinical and laboratory data

HIV seroprevalence

HIV status was diagnosed through serology on a sample of venous blood. If a patient confirmed a positive status at the initial interview, they were required to provide an HIV certificate as evidence thereof. If a patient claimed to be negative or uncertain of their status, a blood sample was taken by a trained psychiatric nurse and subsequently tested at a laboratory (Birungi 2017, pers. comm).

Substance abuse

A urine sample was taken by a trained psychiatric nurse and tested at a laboratory to evaluate substance abuse in the form of cannabis, heroin, cocaine and amphetamines (Birungi 2017, pers. comm).

3.2. Secondary study

3.2.1. Study design

This study, the focus of the research report, was a secondary analysis of data collected from the SMILE study. It had a cross-sectional study design and entailed a detailed analysis of the data collected as it pertained to respondents suffering specifically from schizophrenia.

The following methodological approaches were followed for the secondary study.

3.2.1.1. Directed acyclic graph (DAG) of childhood and adult trauma pathways involved in the development of schizophrenia

A DAG was produced to conceptually map out and evaluate the possible multiple pathways involved between childhood trauma, adult trauma and schizophrenia as well as known confounders, potential interactions and mediators. As shown below in Figure 1, childhood and adult trauma are seen to be independent risk factors for both depression and schizophrenia as health outcomes. Age, sex, urbanicity, education level, substance abuse and alcohol use are well documented confounders in the independent associations between childhood and adult trauma and the development of schizophrenia.

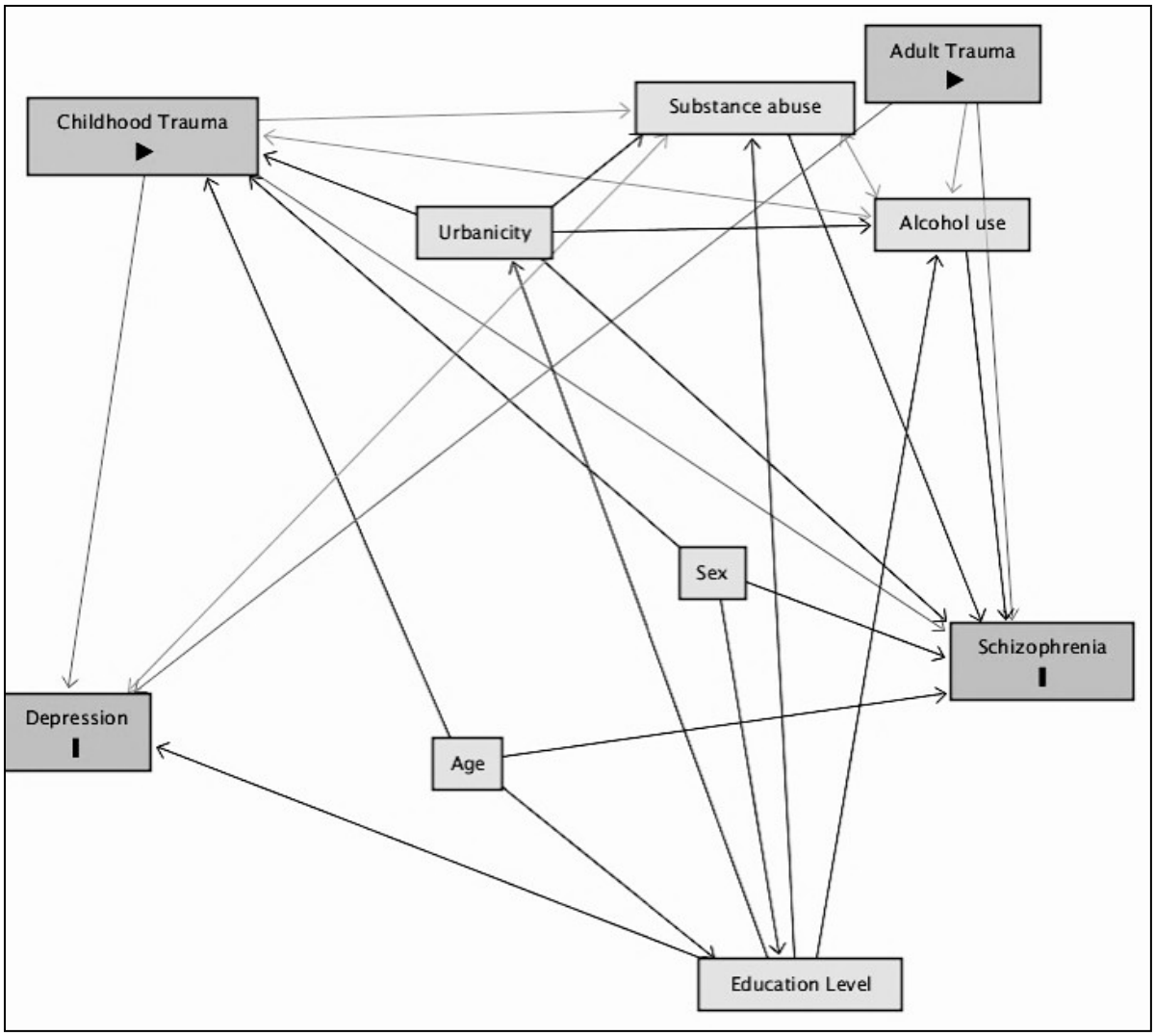


Figure 1. Directed acyclic graph (DAG) depicting potential pathways in schizophrenia development. Childhood and adult trauma are exposures, schizophrenia is the outcome of interest, depression is a possible effect modifier, and age, sex, education, urbanicity, substance and alcohol use are all potential confounders. To adjust for confounding, conditioning on confounding variables was carried out to close biasing pathways.

3.2.1.2. Eligibility criteria

3.2.1.2.1. Inclusion criteria

Patients whose primary diagnosis was schizophrenia were included in the secondary study.

3.2.1.3. Sampling

All individuals with schizophrenia were selected and used as part of the study sample. The study investigated the association between the severity of schizophrenia symptoms and the childhood and adult trauma scores, separately and then jointly. The study further investigated the effect that the amount of trauma (dose) had on the severity of schizophrenia symptoms.

3.2.1.4. Sample size and power considerations

The primary cohort study recruited 1000 patients. The sample for the secondary study comprised of 314 patients whose primary diagnosis was schizophrenia. Based on the median value of several articles reporting the prevalence of childhood trauma, we assumed that 70 percent of the patients had been exposed to childhood trauma. This prevalence implied that 220 of the patients were exposed to childhood trauma and 94 of the patients were not exposed to childhood trauma.

We further assumed that the mean hallucination score was 2.04 with a standard deviation of 1.3 (Park *et al.,* 2016) among those who were not exposed to childhood trauma. Under this assumption, the secondary study had 80 percent power to detect a difference of 0.5 in the mean hallucination score as being statistically significant at the 5 percent level. The decision to use the overall CRDPSS score, with greater discrimination between participants than a particular dimension (such as hallucination), should have given the study greater power to detect as statistically significant the effect of childhood trauma. The power calculation was carried out for a binary exposure. In the analysis we used the exposure as a continuous variable. As pointed out by Royston *et al.,* (2006), this gives a considerable gain in power compared to treating the exposure as dichotomous.

3.2.1.5. Data collection

Baseline data from the SMILE study was provided by the MRC/UVRI/LSHTM Uganda unit. All patient/participant identifiers were removed. A data dictionary was then established and the data itself was stored on a password-protected online cloud.

3.2.1.6. Data analysis

All statistical analyses were conducted using Stata Release 16.1 (StataCorp., 2020). Descriptive statistics were used to firstly describe the demographic and clinical characteristics of the study population through the generation of summary statistics.

3.2.1.6.1. Objective 1

Scatter plots and summary statistics were generated in order to describe the severity of the symptoms experienced by patients diagnosed with schizophrenia. Overall symptom severity as well as the mean scores for individual symptom sub-types were evaluated.

A Cronbach's alpha was generated in order to determine whether the five sub-scales of the CRDPSS were measuring symptom severity as a common and singular construct. It was decided that a Cronbach's alpha of at least 0.6 would be an acceptable level of internal consistency among the five sub-scales measuring symptom severity. Thereafter, an overall CRDPSS score was derived as an average of the five sub-scales. While a Cronbach's alpha value of 0.7 and above has become somewhat of the norm when reporting the internal consistency of certain data collection tools, there is a range of alpha values which are considered acceptable. In a comprehensive review of the use of the Cronbach's alpha in science education, "acceptable" and/or "sufficient" alpha values have been reported as greater or equal to 0.45 while "acceptable alpha values are reported as greater than or equal to 0.6 (Taber, 2018). For instance, in a study investigating the attitudes of young children towards science, the authors cite the Cronbach's alpha as having "acceptable values of 0.7 or 0.6" (van Griethuijsen *et al.,* 2015). On the other hand, Kinyanda and colleagues determined a Cronbach's value of at least 0.4 to be acceptable in their analysis of major depressive disorder and suicidality in early HIV infection in semi-urban and rural Uganda (Kinyanda *et al.,* 2017).

3.2.1.6.2. Objective 2

For objective 2, tobit regression (or left-censored regression with lower limit set to zero) was used to investigate 1) the association between the overall childhood trauma score and the overall CRDPSS score 2) the association between the overall adult trauma score and the overall CRDPSS score. The assumptions of tobit regression are the following: i) data must be normally distributed and ii) homoskedasticity.

Ordinal logistic regression was then used to investigate 1) the association between the mean scores of individual childhood trauma sub-types and the severity of each of the CRDPSS sub-scales 2) the association between the individual adult trauma scores and the severity of each of the CRDPSS sub-scales. The assumptions of ordinal logistic regression are that the outcome variable is ordinal and that the proportional odds assumption holds i.e. the odds ratio for a "better" versus a "worse" outcome does not depend on which cut-off point is used in the ordinal outcome to denote "better" and "worse".

Bivariate analyses were first conducted between the response variable (overall CRDPSS score) and each potential explanatory variable. Explanatory variables that were significant using a liberal 20 percent cut-off were then included as potential explanatory variables in the full regression analysis where backward elimination was used with a 10 percent significance level for inclusion (Bursac *et al.,* 2008). The decision to use a cut-off of 20 percent was informed by an existing body of work on strategies around variable selection and adjusting for important confounders in regression analyses. For instance, Royston *et al.,* (1999) say that "the nominal p-value for a confounder should be larger than for a risk factor" in order to "ensure negligible 'residual confounding'" (Royston *et al.,* 1999). Additionally, Vittinghoff and colleagues say that, "If p-value driven selection is used, we recommend a liberal criterion, to rule out confounding more effectively: in particular only removing variables with p-values ≥ 0.2." The authors go on to further substantiate their assertions saying, "These liberal criteria are particularly important in small data sets, where even important confounders may not meet the usual $p<0.05$ criterion for statistical significance" (Vittinghoff *et al.,* 2012).

Furthermore, the backward elimination/selection approach, a form of stepwise regression, was used for variable selection as it is favoured when dealing with negative confounding. Again, Vittinghoff and colleagues say that, "The principal advantage of backward selection is that negatively confounded sets of variables are less likely to be omitted from the model, since the

complete set is included in the initial model" (Vittinghoff *et al.,* 2012). Similarly, Sun and colleagues favour automated backward elimination over bivariate analyses in variable selection because "the forward and stepwise regression are highly sensitive to specification of their stopping rules in the presence of confounding" (Sun *et al.,* 1999).

Interaction terms which were derived conceptually from the DAG presented in Figure 1, were considered for inclusion in the final model.

Cronbach's alpha values were generated for childhood and adult trauma scores as well as for the overall scores. Cronbach's alpha values that were found to be less than 0.6 provided evidence against childhood and adult trauma existing as singular or unidimensional constructs. As a result, principal component analysis (PCA) was conducted in order to determine the number of dimensions (components) there were to childhood and adult trauma as well as which variables to use to encompass said dimensions. Components which had eigenvalues greater than 1 were selected. Furthermore, among the selected components, only the variables with loadings greater than 0.1 were interpreted. There are no parametric assumptions for PCA beyond the need for the variables involved to be quantitative or at least ordinal.

3.2.1.6.3. Objective 3

For objective 3, tobit (or left-censored regression with lower limit set to zero) and ordinal logistic regression were employed to develop a model that predicted the additive effect of the number of traumatic events experienced in childhood and adulthood, on the severity of symptoms experienced by patients diagnosed with schizophrenia.

The regression models were all adjusted for potential confounders as recorded in previous literature: sex, education level, study site and age. Co-morbidity variables including lifetime depression and HIV prevalence were also assessed in the models. The appropriate regression diagnostic tests were carried out to ensure that the underlying assumptions of the respective regression models were not violated. A key diagnostic test employed was the Brant test for the proportional odds assumption in the ordinal logistic regression model.

Lastly, explanatory variables that were identified as perfect predictors were omitted from the analysis. Any perfect predictors found were reported in the respective analyses.

Perfect prediction occurs if there is a level of a categorical explanatory variable for which the observed values of the outcome are identical and thus results in biased estimates (White *et al.,* 2010).

Chapter 4: Results

4.1. Demographic and clinical data

4.1.1. Demographic data

The socio-demographic and clinical characteristics of the study sample are summarized in Tables 2 and 3 below.

Table 2. Socio-demographic characteristics of patients diagnosed with schizophrenia

	%	n
Study site		
Masaka	22.61	71
Butabika	77.39	243
Age		
18 – 28	18.15	57
28 – 38	30.25	95
38 – 48	27.71	87
48 – 58	17.20	54
58 – 72	6.37	20
Missing data	0.32	1
Sex		
Males	49.36	155
Females	50.32	158
Missing data	0.32	1
Employment status		
Fisherman/Farmer	21.66	68
Professional	9.87	31
Informal	13.06	41
Unemployed	55.10	173
Missing data	0.32	1
Marital status		
Married	25.48	80
Widowed	4.46	14
Separated/divorced	27.07	85
Single	42.99	135

4.1.2. Clinical data

Table 3. Clinical characteristics of patients diagnosed with schizophrenia		
	%	N
Taking psychiatric medication		
Yes	98.09	308
No	1.27	4
Missing data	0.64	2
Adherence to medication		
Yes	71.34	224
No	26.43	83
Missing data	2.23	7
Cannabis use		
Yes	0	0
No	99.68	313
Missing	0.32	1
HIV status		
Positive	5.10	16
Negative	82.80	260
Missing data	12.10	38
Ever experienced depression		
Yes	50.64	159
No	49.36	155
Lifetime number of depressive episodes		
0	21.97	69
1– 5	48.73	153
6 – 10	2.87	9
Missing data	26.43	83
BMI		
Less than 18	1.27	4
18 – 25	66.56	209
25 – 30	19.11	60
Greater than 30	10.83	34
Missing data	2.23	7
BP (systolic)		
Normal	42.68	134
Elevated	22.93	72
Hypertension stage 1	18.15	57
Hypertension stage 2	14.33	45
Hypertensive crisis	0.96	3
Missing data	0.96	3
BP (diastolic)		
Normal to elevated	37.90	119
Hypertension stage 1	35.35	111
Hypertension stage 2	24.52	77
Hypertensive crisis	1.27	4
Missing data	0.96	3

4.2. Childhood and adult trauma count data

4.2.1. Childhood trauma count data

The scores for individual childhood traumatic events are summarized in Table 4 below. Mean scores (with a standard deviation) as well as median scores are presented for each individual traumatic event. Summaries were computed after specified items on the CTQ-SF were reverse scored (*).

Table 4. Scores of the CTQ-SF items among patients diagnosed with schizophrenia

	mean ± SD	median	n
Physical neglect			
I didn't have enough to eat	1.61 ± 1.20	1	310
*I knew there was someone to take care of me and protect me	2.10 ± 1.26	2	311
My parents were too drunk or high to take care of me	1.48 ± 1.08	1	311
I had to wear dirty clothes	1.59 ± 1.02	1	311
*There was someone to take me to the doctor if I needed it	2.20 ± 1.24	2	310
Emotional neglect			
*There was someone in my family who helped me feel important or special	2.21 ± 1.23	2	309
*I felt loved	2.20 ± 1.22	2	309
*People in my family looked out for each other	2.46 ± 1.30	2	310
*People in my family felt close to each other	2.44 ± 1.28	2	310
*My family was a source of strength and support	1.99 ± 1.13	2	310
Emotional abuse			
I thought that my parents wished I had never been born	1.42 ± 1.01	1	311
People in my family called me things like 'stupid', 'lazy', or 'ugly'	1.91 ± 1.29	1	311
I felt that someone in my family hated me	1.95 ± 1.32	1	311
People in my family said hurtful or insulting things to me	1.87 ± 1.26	1	311
I believe I was emotionally abused	1.79 ± 1.26	1	310
Physical abuse			
I got hit so hard by someone in my family that I had to see a doctor	1.53 ± 1.12	1	309
People in my family hit me so hard that it left bruises or marks	1.55 ± 1.11	1	311
I was punished with a belt, a board, a cord, or some hard object	1.63 ± 1.18	1	311
I got hit or beaten so badly that it was noticed by someone like a teacher	1.55 ± 1.16	1	311
I believe that I was physically abused	1.58 ± 1.16	1	311
Sexual abuse			
Someone tried to touch me in a sexual way, or tried to make me touch Them	1.47 ± 1.01	1	311
Someone threatened to hurt me or tell lies about me unless I did something sexual with them	1.33 ± 0.92	1	310
Someone tried to make me do sexual things or make me watch sexual things	1.44 ± 1.03	1	312
Someone molested me	1.36 ± 0.93	1	311
I believe that I was sexually abused	1.36 ± 0.94	1	310

*reverse scored items

4.2.2. Prevalence of adult trauma

The number of participants and prevalence (%) experiencing individual adult traumatic events is summarized in Table 5 below.

Table 5. Prevalence of individual adult traumatic events among patients diagnosed with schizophrenia

Sexual abuse	%	n
My father or mother forced me to have sexual intercourse against my will	2.23	7
My father or mother forced me to do or endure sexual activities (other than intercourse against my will	2.23	7
My brother(s) or sister(s) forced me to have sexual intercourse against my will	3.50	11
My brother(s) or sister(s) forced me to do or endure sexual activities (other than intercourse against my will	2.89	9
My partner(s) forced me to have sexual intercourse against my will	5.41	17
My partner(s) me to do or endure sexual activities (other than intercourse against my will	4.78	15
Someone (or more than one person) who is not my parent, sibling or partner forced me to do or endure sexual activities (other than intercourse against my will	11.78	37
Someone (or more than one person) who is not my parent, sibling or partner forced me to do or endure sexual activities (other than intercourse against my will	7.64	24
Someone forced me to prostitute myself	2.55	8
As a result of war, I experienced rape (single or multiple) or/and attempted rape	2.24	7
Physical abuse		
I was seriously beaten up or otherwise physically mistreated by those responsible for my upbringing	14.01	44
I was severely beaten up or otherwise physically mistreated by one of my brother(s) or sister(s)	14.65	46
My partner(s) beat me up or physically mistreated me	8.63	27
A non-partner or non-relative beat me up or physically mistreated me	15.61	49
I experienced any of the following as a result of war: beating and kicking, bayonet injuries, gunshot wounds, cutting off of body parts, forced hard labour, severe body tying (Kandoya), deprivation of food/water/medication	4.79	15

4.3. Symptom severity among patients with schizophrenia

A summary of the symptom severity experienced by patients with schizophrenia is presented in Figure 2.

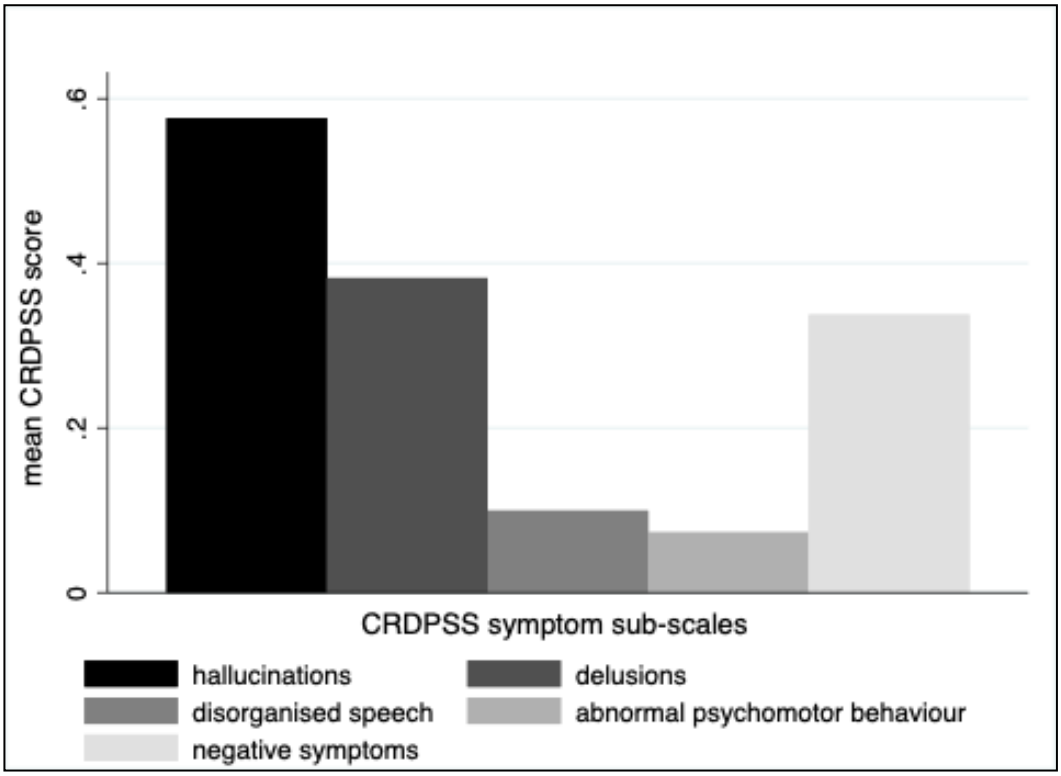


Figure 2. Histograms depicting mean scores for CRDPSS symptom sub-scale

A similar pattern of symptom severity across the five symptom sub-scales was evident among both males and females as shown in Figure 3 below.

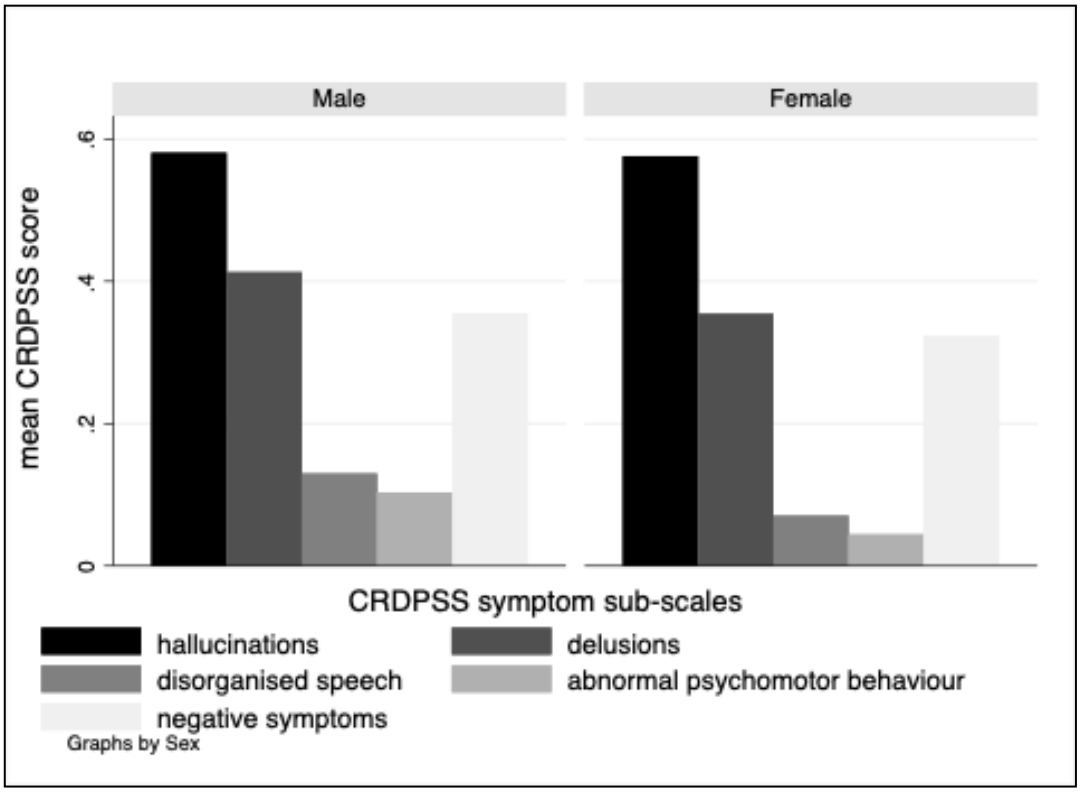


Figure 3. Histograms depicting mean scores for CRDPSS symptom sub-scales

Hallucinations, delusions and negative symptoms (restricted emotional/expression and avolition) appeared to be the symptoms experienced with greater severity among patients with schizophrenia as shown by their respective mean scores of 0.58 (SD = 1.155), 0.38 (SD = 0.93) and 0.34 (SD = 0.78). Disorganised speech had a higher mean score of 0.10 (SD = 0.45) compared to that of abnormal psychomotor issues which had a mean of 0.07 (SD = 0.33).

Detailed summary statistics suggested that 99 percent of the sample had a score ≤ 4 (present and severe) for hallucinations and delusions, a score of ≤ 3 (present and moderate) for negative symptoms (restricted emotional expression/avolition) and a score of ≤ 2 (present and mild) for abnormal psychomotor behaviour and disorganized speech. Over 75 percent of the sample experienced none of the five symptoms. A Wilcoxon rank-sum (Mann-Whitney) test showed that there was insufficient evidence of a difference in overall CRDPSS score between males and females ($p = 0.669$).

4.3.1. Effect of childhood trauma on symptom severity

4.3.1.1. Effect of overall childhood trauma on overall symptom severity

Initially, a scatter plot was used to explore if the overall symptom severity score, as measured by the CRDPSS, was linearly related to the overall CTQ score.

As presented in Figure 4 below, there is some evidence to support the existence of a linear relationship where an increase in the overall childhood trauma score resulted in an increase in the overall symptom severity score. It can be noted that many participants obtained a CRDPSS score of zero.

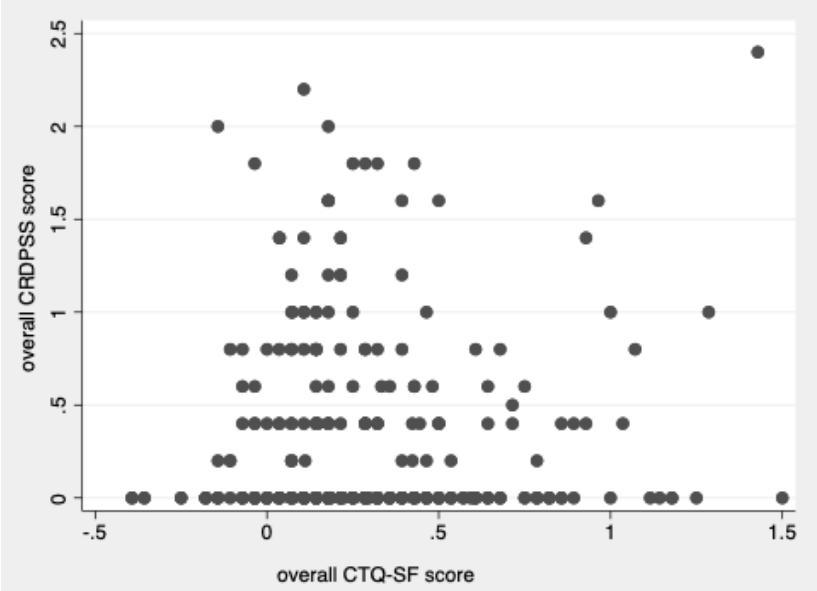


Figure 4. Scatterplot of overall symptom severity and childhood trauma scores

After examining the relationship between the overall symptom severity and CTQ scores in both male and female patients, a possible linear trend was observed in Figure 5 below. As was the case in figure 4, a large number of participants obtained a score of zero on the CRDPSS.

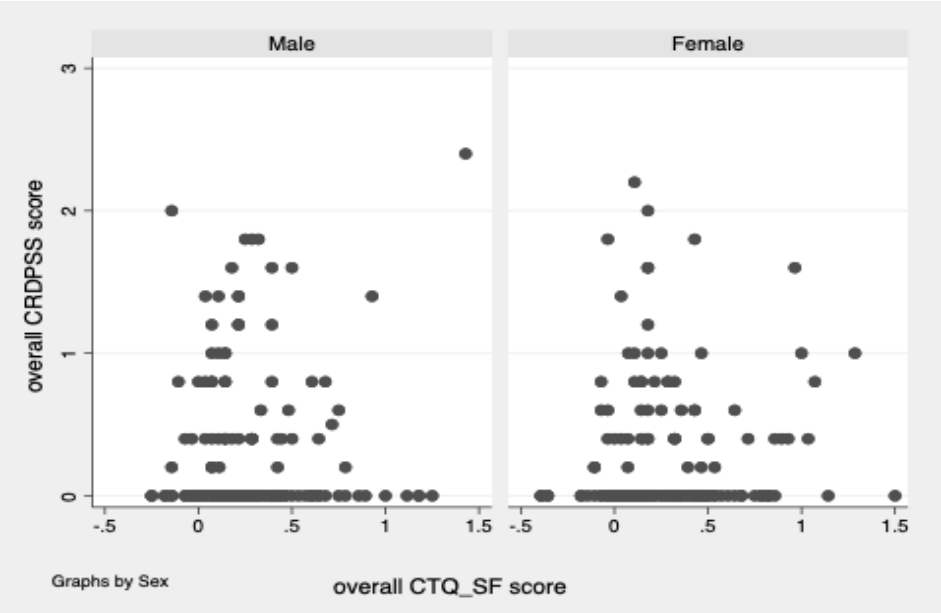


Figure 5. Scatterplot of the overall symptom severity and childhood trauma scores by sex

The explanatory variable of primary interest (i.e. overall CTQ score) as well as potential confounders (age, sex, education level and study site) were fixed in the regression model regardless of significance level as is standard practice in etiologic modelling (Dunkler *et al.,* 2014).

While the presence of heteroskedasticity is a common feature of cross-sectional studies, it results in biased standard errors which increase the likelihood of making a type I error at the 5 percent level of significance i.e. rejecting the null hypothesis when it is in fact true. To correct for the presence of heteroskedasticity, tobit regression with robust standard errors was conducted so that more accurate inference could be made from the coefficients presented in the final regression model.

Table 6 below shows the final tobit regression model which best explains the relationship between overall childhood trauma and overall symptom severity in patients suffering from schizophrenia.

Table 6. Final tobit regression model of overall CRDPSS and CTQ scores					
Factor	**Level**	**Coefficient**	**Robust Standard Error**	**95% Confidence Intervals**	**p value**
Overall CTQ Score	Per one-point increase	0.212	0.148	[- 0.079; 0.503]	0.153
Minimisation/ Denial	Per one-point increase	- 0.068	0.082	[- 0.229; 0.093]	0.407
Sex	Male (reference)				
	Female	0.018	0.149	[- 0.274;0.311]	0.902
Age	Per 1-year increase	- 0.0005	0.006	[- 0.012; 0.012]	0.994
Study site	Butabika (reference)				
	Masaka	0.523	0.161	[0.207; 0.839]	0.001
Education	None (reference)				
	Primary	0.769	0.547	[- 0.309; 1.846]	0.161
	Secondary	0.682	0.546	[- 0.391; 1.757]	0.212
	Tertiary	0.995	0.570	[- 0.127; 2.117]	0.082
BMI	Per 1kg/m^2 increase	- 0.031	0.016	[- 0.062; 0.0001]	0.051
Ever depressed	Yes	0.267	0.143	[- 0.014; 0.547]	0.062
	No (reference)				
Constant	-	- 0.361	0.740	[- 1.817; 1.095]	0.626

The effect of overall childhood trauma on overall symptom severity was not found to be statistically significant (p = 0.153).

The effect of study site on overall symptom severity score was found to be statistically significant. The overall symptom severity score was higher by 0.523 units in patients who were recruited from the Masaka Regional Referral Hospital compared to those recruited from the Butabika National Psychiatric Referral Hospital (p = 0.001).

The effect of BMI was found to be marginally significant. A one-unit increase in BMI appears to be associated with a decrease in the patient's overall symptom severity score by 0.031 points (p = 0.051).

Having been depressed at least once in a patient's lifetime was also found to be marginally significant (0.062), increasing their overall symptom severity score by 0.267 points compared to those who had never been depressed in their lifetime.

An association between the amount of childhood trauma and the overall symptom severity score was not evident and thus warranted an investigation into the association between each of the childhood trauma sub-types and the symptom sub-scales.

The distribution of the data was evaluated using a normal probability plot. Figure 6 below suggested that the data were not normally distributed. This is a common occurrence with Likert scale data. Additionally, tobit regression was carried out due to the presence of a large number of zeros in the CRDPSS score.

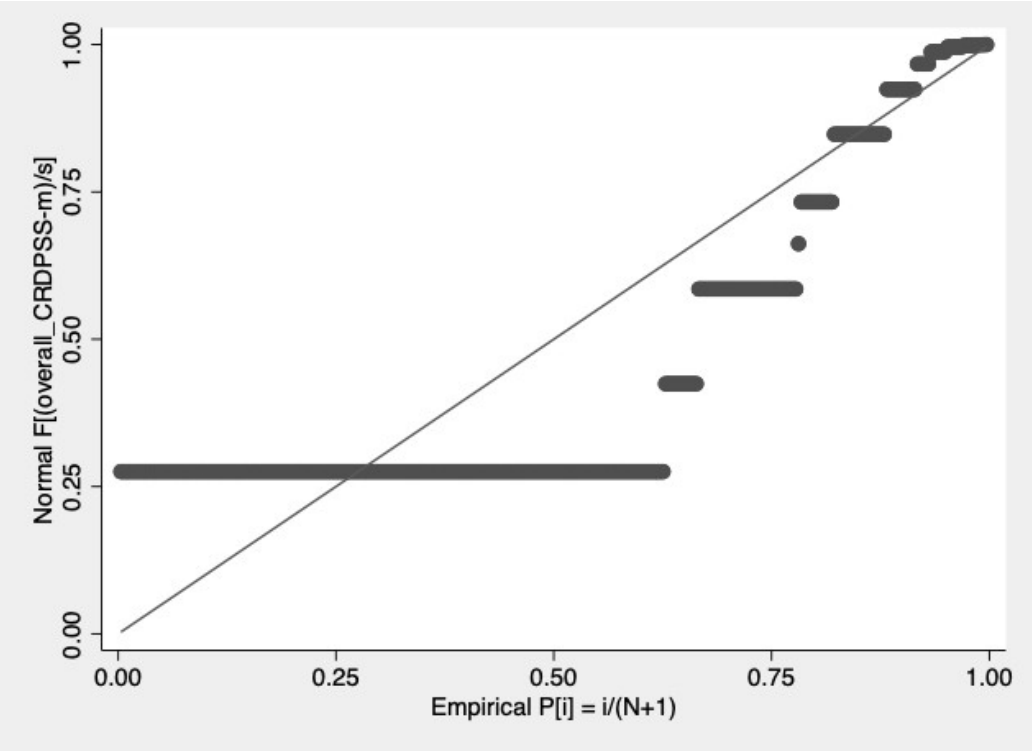


Figure 6. Normal probability plot shows the data does not follow a normal distribution

4.3.1.2. Effect of childhood trauma sub-types on severity of symptom sub-scales

4.3.1.2.1. Effect of childhood trauma sub-types on severity of hallucinations

None of the CTQ sub-types were found to statistically significantly affect the severity of hallucinations. The study site and whether or not the patients had been depressed in the 2 weeks prior to the commencement of the primary SMILE study, were the only statistically significant explanatory variables in the overall model.

Patients who had been admitted to the Masaka Regional Referral Hospital had 2.115 times the odds of experiencing more severe hallucinations compared to those patients who had been admitted to the Butabika National Psychiatric Referral Hospital.

Additionally, those patients who had been depressed 2 weeks prior to the commencement of the primary SMILE study had 2.662 the odds of experiencing more severe hallucinations compared to those who had not been depressed.

The bivariate analysis, final ordinal logistic regression model as well as model diagnostic tests have been appended to this research report (Appendix Six).

4.3.1.2.2. Effect of childhood trauma sub-types on severity of disorganized speech

According to the PCA results, one dimension of childhood physical neglect was found to be statistically significantly associated with the severity of disorganized speech ($p = 0.046$). Those patients who experienced physical neglect during childhood had 0.605 times the odds of experiencing more severe disorganized speech compared to those patients who did not experience physical neglect. Thus, childhood physical neglect appeared to have a protective effect against experiencing more severe disorganized speech.

The bivariate analysis, final ordinal logistic regression model as well as model diagnostic tests have been appended to this research report (Appendix Seven).

4.3.1.2.3. Effect of childhood trauma sub-types on severity of delusions

Emotional and physical abuse during childhood were found to be statistically significant in their association with the severity of delusions. Patients who experienced emotional abuse during childhood had 1.801 times the odds of experiencing more severe delusions compared to patients who did not experience emotional abuse during childhood ($p = 0.045$).

Patients who experienced physical abuse during childhood had 0.523 times the odds of experiencing more severe delusions compared to patients who did not experience physical abuse during childhood ($p = 0.024$). Thus, physical abuse appeared to have a protective effect against severe delusions.

Additionally, the association between BMI and the severity of delusions was statistically significant ($p = 0.034$). Those patients with higher BMIs had 0.918 times the odds of experiencing more severe delusions compared to those whose BMIs were lower.

The bivariate analysis, final ordinal logistic regression model as well as model diagnostic tests have been appended to this research report (Appendix Eight).

4.3.1.2.4. Effect of childhood trauma sub-types on severity of negative symptoms (restricted emotional expression or avolition)

According to the PCA results, one component of physical neglect which specifically encompassed not having enough to eat, there having been someone to take the individual to the doctor if they needed it and their parents having been too drunk to take care of them, was found to be significantly associated with the severity of negative symptoms (restricted emotional expression or avolition). For every one-point increase in the physical neglect score, the odds of experiencing more severe negative symptoms were 0.605 times likely. For a one-point increase in the physical neglect score, the odds ratio was 0.605, i.e. for every one-point increase in the physical neglect score, the odds of experiencing more severe negative symptoms decreased by 39.5 percent.

The association between patients who had been depressed 2 weeks prior to the commencement of the primary SMILE study and symptom severity was marginally significant (p = 0.089). Patients who had been depressed had 2.092 times the odds of experiencing more severe negative symptoms compared to those who had not been depressed.

The bivariate analysis, final ordinal logistic regression model as well as model diagnostic tests have been appended to this research report (Appendix Nine).

4.3.1.2.5. Effect of childhood trauma sub-types on severity of abnormal psychomotor behaviour

None of the CTQ sub-types were found to be significantly associated with symptom severity. However, female patients had 0.342 times the odds of experiencing more severe abnormal psychomotor behaviour compared to their male counterparts. The association was, however, only marginally significant (p = 0.062).

The bivariate analysis, final ordinal logistic regression model as well as model diagnostic tests have been appended to this research report (Appendix Ten).

4.4. Effect of adult trauma on symptom severity

4.4.1. Effect of overall adult trauma on overall symptom severity

Initially, a scatter plot was used to graphically evaluate if the overall symptom severity score as shown by the CRDPSS was linearly related to the overall adult trauma score. As shown in Figure 6 below, there was some evidence to support the existence of a linear relationship where an increase in the overall adult trauma score resulted in an increase in the overall symptom severity score.

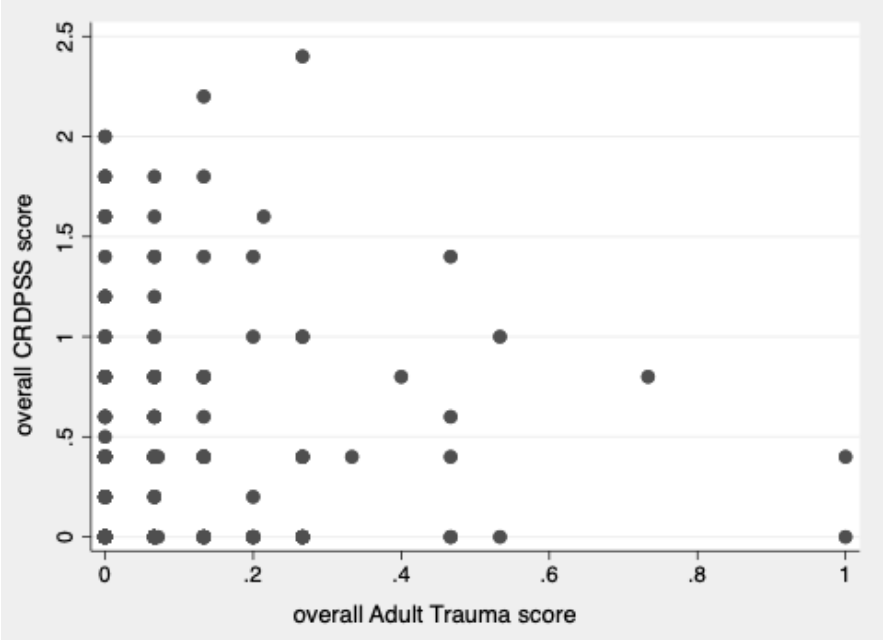


Figure 7. Scatterplot of overall symptom severity and adult trauma scores

After examining the relationship between the overall symptom severity score and overall adult trauma score in both male and female patients, a possible linear trend was observed in Figure 8 and found to be similar to that in Figure 7 presented above.

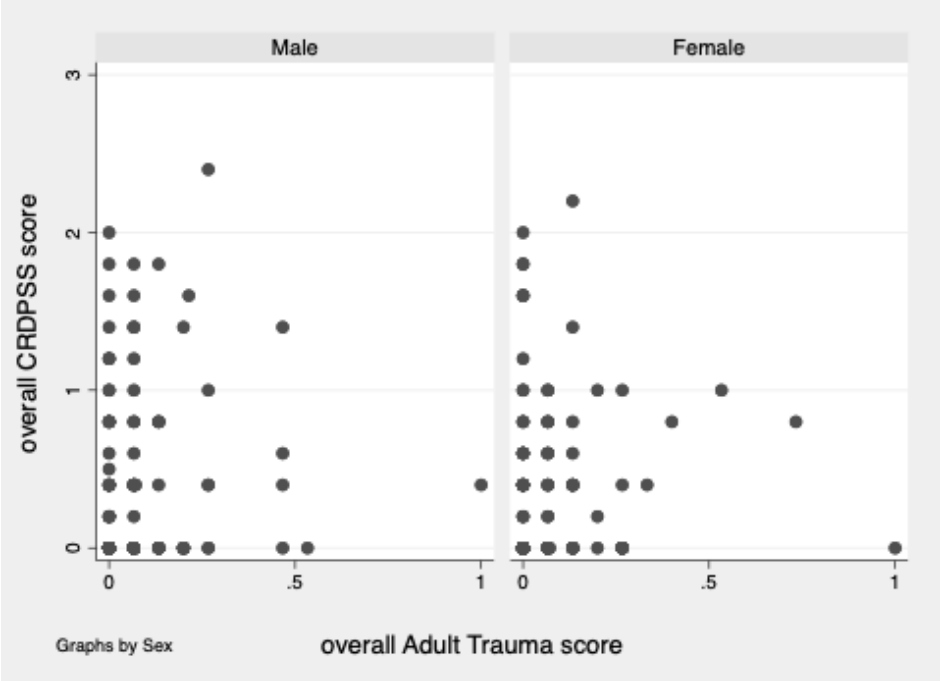


Figure 8. Scatterplot of overall symptom severity and adult trauma scores by sex

As with childhood trauma, tobit regression was carried out to investigate the association between the overall adult trauma and symptom severity scores. The bivariate analyses conducted previously were used to inform which explanatory variables would be eligible for backward elimination. The final tobit regression model is presented in Table 7.

Table 7. Final tobit regression model of overall symptom severity and adult trauma scores

Factor	**Level**	**Coefficient**	**Robust Standard Error**	**95% Confidence Intervals**	**p value**
Overall Adult Trauma Score	Per one-point increase	1.234	0.470	[0.310; 2.159]	0.009
Sex	Male (reference) Female	0.032	0.147	[- 0.258; 0.322]	0.828
Age	Per one-year increase	- 0.002	0.006	[- 0.014; 0.009]	0.692
Study site	Butabika (reference) Masaka	0.527	0.158	[0.217; 0.838]	0.001
Education	None (reference) Primary Secondary Tertiary	 0.771 0.636 0.998	 0.571 0.571 0.591	 [-0.353; 1.895] [-0.488; 1.760] [-0.164; 2.161]	 0.178 0.267 0.092
BMI	Per 1kg/m^2 increase	- 0.033	0.016	[- 0.063; - 0.002]	0.039
Ever depressed	Yes No (reference)	0.266	0.142	[- 0.014; 0.545]	0.062
Constant	-	- 0.512	0.700	[- 1.885; 0.861]	0.464

To allow for the presence of heteroskedasticity, robust standard errors were computed for the tobit regression models to ensure that more accurate inference could be made from the coefficients presented in the final model.

There was very strong evidence that overall adult trauma was associated with overall symptom severity. A one-point increase in the overall adult trauma score resulted in the increase of the overall symptom severity scale by 1.234 points ($p = 0.009$).

Additionally, the patient's BMI was found to be significantly associated with the symptom severity score. For every one-unit increase in the patient's BMI, the overall symptom severity score decreased by 0.033 points (p = 0.039).

Study site was found to be statistically significantly associated with overall symptom severity. The symptom severity score of patients admitted to the Masaka Regional Referral Hospital was, on average, 0.527 points higher (p = 0.001) compared to those patients admitted to the Butabika National Psychiatric Referral Hospital.

Interestingly, the symptom severity score of patients who had a tertiary level of education was, on average, 0.998 points higher than patients without education entirely. The association was, however, only marginally significant (p = 0.092).

Similarly, the symptom severity score of patients who had experienced depression at least once in their lifetime was, on average, 0.266 points higher compared to those who had never experienced depression. The association was however only marginally significant (p = 0.062).

4.4.2. Effect of adult trauma sub-types on severity of symptom sub-scales

4.4.2.1. Effect of adult trauma sub-types on severity of hallucinations

Sexual abuse experienced during adulthood was found to be significantly associated with the severity of hallucinations (p = 0.012). For every one-point increase in the adult sexual abuse score, the odds of more severe hallucinations increased 18.524 times (p = 0.012).

Patients who had been admitted to the Masaka Regional Referral Hospital had 1.960 times (p = 0.037) the odds of experiencing more severe hallucinations compared to those patients who had been admitted to the Butabika National Psychiatric Referral Hospital.

Additionally, patients who had been depressed in the 2 weeks prior to the commencement of the primary SMILE study had 2.303 times the odds of experiencing more severe hallucinations compared to those who had not been depressed (p = 0.035).

The bivariate analysis, final ordinal logistic regression model as well as model diagnostic tests have been appended to this research report (Appendix Eleven).

4.4.2.2. Effect of adult trauma sub-types on severity of delusions

Neither sexual abuse nor physical abuse experienced during adulthood was significantly associated with the severity of delusions.

Study site was, however, significantly associated with symptom severity. Patients who were admitted to the Masaka Regional Referral Hospital had 3.936 times ($p < 0.001$) the odds of experiencing more severe delusions compared to those who were admitted to the Butabika National Psychiatric Referral Hospital.

The bivariate analysis, final ordinal logistic regression model as well as model diagnostic tests have been appended to this research report (Appendix Twelve).

4.4.2.3. Effect of adult trauma sub-types on severity of negative symptoms (restricted emotional expression or avolition)

Neither physical abuse nor sexual abuse were found to be significantly associated with the severity of negative symptoms. In this particular case, no variable was found to be significantly associated with the severity of negative symptoms.

The bivariate analysis and final ordinal logistic regression model have been appended to this research report (Appendix Thirteen).

4.4.2.4. Effect of adult trauma sub-types on severity of abnormal psychomotor behaviour

The association between physical abuse experienced during adulthood and the severity of abnormal psychomotor behaviour, was marginally significant (0.077). The odds of experiencing more severe abnormal psychomotor behaviour among those patients who had experienced physical abuse during adulthood were 8.158 times the odds of those patients who had not experienced physical abuse.

Study site was found to be significantly associated with symptom severity. Those patients who were admitted to the Masaka Regional Referral Hospital had 9.408 times ($p < 0.001$) the odds of experiencing more severe abnormal psychomotor behaviour compared to patients admitted to the Butabika National Psychiatric Referral Hospital instead.

The final ordinal logistic regression model and diagnostic test have been appended to this research report (Appendix Fourteen).

4.4.2.5. Effect of adult trauma sub-types on severity of disorganised speech

Neither adult physical abuse nor sexual abuse were found to be significantly associated with the severity of disorganised speech.

Patients' adherence to taking their oral psychiatric medication, however, was significantly associated with the severity of disorganised speech. Interestingly, patients who had a high level of adherence had 3.507 times ($p = 0.017$) the odds of experiencing more severe disorganised speech compared to patients whose level of adherence was lower.

The final ordinal logistic regression model has been appended to this research report (Appendix Fifteen).

4.5. Cumulative effect of childhood and adult traumatic events on overall symptom severity

A tobit regression model with robust estimation of variance was fitted to determine whether there was a dose-response relationship between the cumulative number of individual childhood and adult traumatic events and overall symptom severity. Bivariate analyses conducted previously were used to inform the selection of explanatory variables that were eligible for backward elimination. The final tobit regression model is presented in Table 8.

Table 8. Final tobit regression model for cumulative adult and childhood traumatic events and overall symptom severity					
Factor	**Level**	**Coefficient**	**Robust Standard Error**	**95% Confidence Intervals**	**p value**
Adult trauma	Per one-point increase	0.071	0.031	[0.011; 0.132]	0.021
Childhood Trauma	Per one-point increase	0.007	0.016	[- 0.026; 0.039]	0.690
Minimisation/ Denial	Per one-point increase	- 0.103	0.071	[- 0.242; 0.037]	0.148
Sex	Male (reference)				
	Female	0.032	0.149	[- 0.261; 0.324]	0.831
Age	Per one-year increase	- 0.00005	0.006	[- 0.012; 0.012]	0.993
Education	None (reference)				
	Primary	0.776	0.544	[- 0.293; 1.846]	0.154
	Secondary	0.645	0.544	[- 0.425; 1.715]	0.236
	Tertiary	1.005	0.566	[- 0.110; 2.119]	0.077
Study site	Butabika (reference)				
	Masaka	0.530	0.159	[0.217; 0.843]	0.001
Ever depressed	No (reference)				
	Yes	0.237	0.148	[- 0.054, 0.528]	0.110
BMI	Per 1kg/m^2 increase	- 0.032	0.016	[- 0.063; - 0.001]	0.043
Constant	-	- 0.332	0.760	[- 1.828; 1.165]	0.663

The total number of individual adult traumatic events exhibited a dose-response relationship with overall symptom severity. For every additional traumatic event the patient had endured during adulthood, their overall symptom severity score increased by 0.071 points (p = 0.021). The total number of childhood traumatic events was not significantly associated with overall symptom severity.

The symptom severity score for those patients who were admitted to the Masaka Regional Referral Hospital was, on average, 0.530 points higher compared to those patients who were admitted to the Butabika National Psychiatric Referral Hospital instead (p = 0.001). Additionally, a patient's BMI was also found to be significantly associated with the overall symptom severity score. A one-unit increase in BMI resulted in the decrease of the overall symptom severity score by 0.032 points (p = 0.043).

The symptom severity score of patients with a tertiary level of education, was on average, 1.005 points (p = 0.077) higher than that of patients who did not have any education. The association was, however, only marginally statistically significant.

4.5.1. Cumulative effect of childhood traumatic and adult traumatic events on symptom sub-scale severity

4.5.1.1. Cumulative effect of childhood traumatic and adult traumatic events on severity of hallucinations

The total number of adult traumatic events exhibited a dose-response relationship with the severity of hallucinations. For every additional traumatic event the patient had endured during adulthood, the odds of experiencing more severe hallucinations were 1.156 times greater (p = 0.043). The total number of childhood traumatic events was not significantly associated with the severity of hallucinations.

Having experienced depression 2 weeks prior to the commencement of the primary SMILE study was significantly associated with the severity of hallucinations. The odds of experiencing more severe hallucinations in patients who had been depressed were 2.275 times (p = 0.037) the odds of those patients who had not been depressed.

Study site was also found to be significantly associated with symptom severity. Patients who were admitted to the Masaka Regional Referral Hospital had 2.025 times the odds of experiencing more severe hallucinations compared to patients who had been admitted to the Butabika National Psychiatric Referral Hospital instead (p = 0.029).

The final ordinal logistic regression model and diagnostic test have been appended to this research report (Appendix Sixteen).

4.5.1.2. Cumulative effect of childhood traumatic and adult traumatic events on severity of delusions

For each additional traumatic event, the odds of experiencing more severe delusions were 1.148 times more likely. However, the association was only marginally significant ($p = 0.055$. The total number of childhood traumatic events was not significantly associated with the severity of delusions.

Additionally, the study site was found to be significantly associated with symptom severity. The odds of experiencing more severe delusions among those patients who were admitted to the Masaka Regional Referral Hospital, were 4.059 times ($p < 0.001$) the odds of those patients who had been admitted to the Butabika National Psychiatric Referral Hospital instead.

The final ordinal logistic regression model and diagnostic test have been appended to this research report (Appendix Seventeen).

4.5.1.3. Cumulative effect of childhood traumatic and adult traumatic events on severity of negative symptoms (restricted emotional expression or avolition)

Neither the total number of adult events nor the total number of childhood traumatic events were statistically significantly associated with the severity of negative symptoms. This was also the case for all other potential determinants of the severity of negative symptoms that were included in the regression analysis.

The final ordinal logistic regression model has been appended to this research report (Appendix Eighteen).

4.5.1.4. Cumulative effect of childhood traumatic and adult traumatic events on severity of abnormal psychomotor behaviour

The total number of adult traumatic events was significantly associated with the severity of abnormal psychomotor behaviour. For every additional traumatic event that the patient had endured during adulthood, the odds of experiencing more severe abnormal psychomotor behaviour were 1.246 times likely ($p = 0.043$).

Female patients had 0.350 times ($p = 0.059$) the odds of experiencing more severe abnormal psychomotor behaviour compared to their male counterparts. Female patients were thus 65 percent less likely to experience more severe abnormal psychomotor behaviour compared to male patients. The association was however only marginally significant.

The final ordinal logistic regression model and diagnostic test have been appended to this research report (Appendix Nineteen).

4.5.1.5. Cumulative effect of childhood traumatic and adult traumatic events on severity of disorganized speech

Neither the total number of adult traumatic events nor the childhood traumatic events were found to be significantly associated with the severity of disorganised speech. This was the case for all other potential determinants that were included in the regression analysis.

The final ordinal logistic regression model was appended to this research report (Appendix Twenty).

4.6. Summary of key findings

The overall symptom severity was significantly associated with adult traumatic events, showing a dose-response relationship while the childhood trauma score was not associated with the overall symptom severity score. None of the CTQ sub-types were significantly associated with the severity of hallucinations and abnormal psychomotor behaviour while physical neglect was significantly associated with the severity of disorganised speech and negative symptoms. Furthermore, emotional and physical abuse during childhood were both

significantly associated with the severity of hallucinations. Overall adult trauma was significantly associated with overall symptom severity while sexual abuse experienced during adulthood was significantly associated with the severity of hallucinations. Additionally, the association between physical abuse experienced during adulthood and the severity of abnormal psychomotor behaviour was found to be marginally significant. The total number of adult traumatic events exhibited a significant dose-response relationship with overall symptom severity, the severity of hallucinations and abnormal psychomotor behaviour while the association with the severity of delusions was only marginally significant.

Chapter 5: Discussion & Conclusion

5.1. Discussion

The purpose of this secondary analysis was to examine the relationship between childhood and adult traumatic events and the severity of symptoms experienced by patients diagnosed with schizophrenia. Additionally, the study aimed to examine whether or not there was a dose-response relationship between cumulative childhood and adult traumas and symptom severity. There were several potential confounders including medication-related psychosis, psychosis as a result of HIV and comorbid medical conditions resulting in psychosis. Furthermore, the effects of sex, education level, BMI, comorbid psychiatric conditions such as depression as well as oral psychiatric medication were discussed at length coupled with the impact of the findings of low CRDPSS scores that were observed in the study population.

Overall childhood trauma

Our findings did not find an association between the overall childhood trauma score and the overall symptom severity score whereas there was very strong evidence of an association between the overall adult trauma score and the overall symptom severity score. A 2018 meta-analysis conducted by Bailey and colleagues, which consisted of 29 studies, failed to find a significant association between overall childhood trauma and negative symptoms of psychosis (Bailey *et al.,* 2018). However, the meta-analysis did find a significant association between overall childhood trauma and positive symptoms of psychosis (Bailey *et al.,* 2018). Thus, it is possible that our finding may have been the result of underreporting of childhood trauma on the whole as retrospective recall of childhood trauma has been shown to be less reliable (Widom *et al.,* 2015).

Childhood trauma subtypes

The finding that specific childhood traumas namely, physical neglect, emotional and physical abuse were related to the severity of both positive and negative symptoms, has emerged in several previous studies (Mørkved *et al.,* 2017; Asmal *et al.,* 2018; Kilian *et al.,* 2017). While the methodologies employed by these studies were different, their findings were similar in that patients who were exposed to childhood trauma were more likely to have worse health outcomes compared to the controls. For example, Asmal and colleagues investigated the effect of childhood trauma on white matter abnormalities in patients with first-episode schizophrenia (FES) and found that emotional neglect and sexual abuse had a differential effect on white matter in patients with first-episode schizophrenia (Asmal *et al.,* 2018). Additionally, Kilian and colleagues investigated the factors moderating the relationship between childhood trauma and premorbid adjustment in patients with FES and found a general, rather than specific, association between childhood traumas and premorbid adjustment (Kilian *et al.,* 2017). Furthermore, a meta-analysis conducted by Bailey and colleagues, which included 41 cross-sectional studies and 5 longitudinal studies, suggested that childhood trauma was significantly correlated with the severity of both hallucinations ($r = 0.199$, $p < 0.001$) and delusions ($r = 0.172$, $p < 0.001$) but not with negative symptoms (Bailey *et al.,* 2018).

Additionally, the CTQ yielded results with low means with items being scored in the “never or rarely” range. While the CTQ has previously been used in Sub-Saharan Africa including Uganda and Nigeria, the retrospective recall of childhood trauma remains a challenge and thus may have contributed to the low means reported (Aloba *et al.,* 2020; Kinyanda *et al.,* 2017). In terms of the clinical significance of such low means, it is not an easy task to comment on given that the study is a secondary analysis of baseline data from the SMILE study.

Cumulative childhood traumas

Surprisingly, we did not find a relationship between cumulative childhood traumas and symptom severity. Previous several studies have, however, shown the existence of a dose-response relationship between childhood traumas and schizophrenia (Mall *et al.,* 2019; Carbone *et al.,* 2019; Li *et al.,* 2015). In the case-control study conducted by Mall and colleagues, they found a dose-response relationship between childhood trauma and schizophrenia where no previous study had compared the relationship between childhood

trauma and schizophrenia as outcome (Mall *et al.,* 2019). Our finding may have been the result of the underreporting of childhood trauma due to either social desirability bias or the psychological burden that comes with disclosing trauma (Widom *et al.,* 2015). However, the minimisation/denial scale was included in the analyses and was not found to be significant.

Overall adult trauma

Overall symptom severity was found to be significantly associated with the overall adult trauma score. The finding that there was a dose-response relationship between cumulative adult traumas, overall symptom severity and the severity of hallucinations, abnormal psychomotor behaviour and delusions, is again not widely corroborated by previous studies. This may suggest that when adult traumas are experienced infrequently, hallucinations, delusions and abnormal psychomotor behaviour specifically, may not be affected.

Adult trauma subtypes

The finding that sexual abuse during adulthood is significantly associated with severe hallucinations is a finding that, to the best of our knowledge, has not been investigated with regards to symptom severity in previous studies. The few studies that have focused on adult trauma in relation to psychosis in general were conducted in high-income countries suggesting that there is a need for studies on the African continent. The few studies examining adult trauma in relation to psychosis have focused on investigating the effects of recent adverse life events, stressful life events and threatening life events, on the onset of psychosis (Beards *et al.,* 2020; Beards *et al.,* 2013; Mayo *et al.,* 2017). A previous study investigated the interplay between childhood and adult victimisation on the onset of psychosis (Honings *et al.,* 2017). The findings of that study showed that adult victimisation was bidirectionally associated with psychosis in that it remained unclear whether psychosis predicts incident adult victimisation, or whether adult victimisation predicts incident psychosis. There was no interaction found between adult victimisation and childhood victimisation (Honings *et al.,* 2017). Patients with severe psychiatric disorders including schizophrenia are more likely to experience stigma from broader society (Razali & Ismail, 2014; Mak *et al.,* 2015). As a result, patients often internalise this stigma which adversely affects prognosis and in turn leads to poor recovery (Mak *et al.,* 2015; Assefa *et al.,* 2012; Yılmaz & Okanlı, 2015). While our particular finding was considerable in its magnitude, the fairly wide confidence intervals (1.925; 178.276) indicated, however, that a larger sample size was

required to make more definitive conclusions.

Childhood and adult trauma under the neural diathesis-stress model

Childhood trauma was not found have a significant effect on symptom severity in this study despite several other studies which have found otherwise (McCabe *et al.,* 2012; Bailey *et al.,* 2018; Pruessner *et al.,* 2019). However, given that adult trauma was found to generally increase symptom severity in patients with schizophrenia, the neural diathesis-stress model provides a framework upon which to explain the findings of this study. According to the model, stressors trigger an existing genetic disposition or vulnerability to psychosis through the HPA axis which releases glucocorticoids in response to stress (Preussner *et al.,* 2017). These glucocorticoids have been known to alter neurotransmitter systems and neuronal functioning in the brain which collectively underlies the pathophysiology of psychosis including schizophrenia (Frodl & O'Keane, 2013). It is possible that exposure to childhood trauma alone is not sufficient to affect symptomology in patients with schizophrenia and that additional exposure to adult trauma is what subsequently results in patients experiencing more severe schizophrenia symptoms. Long term effects of stressors, in this case both childhood trauma followed by adult trauma, have been implicated in the onset and symptomology of schizophrenia (Sinclair *et al.,* 2012).

Significance of low CRDPSS scores

The CRDPSS scores were much lower than expected from the power calculation conducted in the methodology of the study. Both issues are addressed extensively below.

In order to allow for simpler power calculations, we hypothetically regarded the exposures (childhood and adult trauma) as being dichotomous, although the intention was always to treat the exposures as being continuous in the analyses. The reason for treating the exposures as continuous is that treating an exposure as dichotomous results in a loss of power (Royston *et al.,* 2006). The actual power of the study required to detect an association would thus be greater than the nominal power found in the power calculations. Nevertheless, the lower-than-expected CRDPSS scores would result in decreased power to detect a significant association with traumas. The fact that we found very strong evidence of an association between the overall CRDPSS score and adult trauma suggests that the sample size (which we were not in a position to influence since this was a secondary analysis) was in fact sufficient. The very low CTQ

scores also mitigated against finding an association between childhood trauma and the overall CRDPSS score.

The power calculation depended on the assumed standard deviation and the assumed mean difference. In the power calculation, we assumed a standard deviation (for the hallucination scale) of 1.3 and a mean difference of 0.5 (Park *et al.,* 2016). In our data, we found a standard deviation of 1.16 which was observably lower than the assumed 1.30. Using the concept of "effect size", however, the assumed effect size was 2.60. Thus, for a standard deviation of 1.16, we were instead able to detect a difference of 0.44, rather than the assumed 0.50.

Since the study found that the CRDPSS sub-scales were significantly related to adult trauma, this suggests that the study was in fact sufficiently powered as we were able to subsequently detect the moderate effects of one of our exposures.

Furthermore, very little work has been carried out on these CRDPSS sub-scales in sub-Saharan Africa. Therefore, the finding that the CRDPSS sub-scale scores are low is useful and could serve to reconsider and adjust the use of the CRDPSS in sub-Saharan Africa. Particular items could also be evaluated for cultural relevance in addition to evaluating the translations into Luganda. The results of this secondary analysis can be used by the principal investigators of the SMILE study and other researchers to further explore the association between the CRDPSS sub-scale scores and the clinical progression of the patients diagnosed with schizophrenia.

Induced psychotic symptoms

The finding of a significant association between patients who adhered to taking their oral psychiatric medication and severe disorganized speech was not unexpected. A study by Park and colleagues found that the adjunctive use of mood stabilisers in the treatment of patients diagnosed with schizophrenia was directly associated with the presence of disorganized speech (Park *et al.,* 2018; Sim *et al.,* 2011). Given that approximately 99 percent of the sample was taking oral psychiatric medication, the possible adjunctive use of mood stabilisers could account for the experiencing of more severe disorganized speech among such patients. Several studies have investigated the effects of certain medications on psychosis. For instance, efavirenz, one of the most widely used antiretroviral drugs on the market, has been known to have a range of neuropsychiatric effects including mania and psychosis among patients with a

history of mental illness (Kenedi & Goforth, 2011). Another example is intrathecal ziconotide, an analgesic which is used for the management of severe and chronic pain. While it has been known to cause neuropsychiatric adverse effects including auditory hallucinations and paranoia, there is limited information available with regards to characterising the presentation of these neuropsychiatric effects (Phan & Waldfogel, 2015).

Aside from medication-induced psychosis, there are several comorbid medical conditions that can result in psychosis. These conditions include, but are not limited to, brain diseases such as Parkinson's and Huntington's as well as brain tumours and cysts. It must be noted that Huntington's is quite rare and will thus not be expounded upon. On the other hand, a review outlining the presentation, diagnosis and management of Parkinson's, a neurodegenerative disorder characterised by motor and non-motor symptoms, states psychosis as being common feature of the disease (Schneider *et al.,* 2017). Additionally, Parkinson's psychosis disease is also known to encompass both visual and non-visual hallucinations as well as delusions with efforts among healthcare workers to reduce or discontinue medications being administered to patients which may either induce or exacerbate psychosis (Schneider *et al.,* 2017).

Furthermore, HIV-associated neurocognitive disorders are also established causes of psychosis. These neurocognitive disorders begin in the early stages of HIV infection and commonly result in subcortical dementia and affect memory, concentration and attention (Eggers *et al.,* 2017). HIV infection targets the central nervous system in the subcortical brain areas and subsequently results in higher rates of delirium and dementia (Watkins & Treisman, 2015). The course of the neurocognitive disorders is significantly altered, however, following the administering of combination antiretroviral therapy (Eggers *et al.,* 2017). HIV-associated neurocognitive disorders are important to highlight as HIV prevalence is generally higher among patients with severe mental illnesses including schizophrenia, major depressive disorder and bipolar disorder, compared to the general population (Maling *et al.,* 2011; Mugisha *et al.,* 2015). However, the effect of HIV-associated neurocognitive disorders in this particular study sample is admittedly negligible as the HIV prevalence was only 5.10 percent—much lower than the general population.

Substance abuse-related psychosis is perhaps the most common. The abuse of alcohol and illicit substances such as cannabis has been found to increase the risk of developing psychosis in a number of studies (Barnett *et al.,* 2007, Kavanagh *et al.,* 2004, Weaver *et al.,* 2003). A nationwide population-based register study conducted in Denmark found that the abuse of

cannabis, hallucinogens and sedatives significantly increased the risk of developing schizophrenia (Nielsen *et al.,* 2017). Furthermore, the study found that the risk was still significant even 10 to 15 years after having been diagnosed for substance abuse (Nielsen *et al.,* 2017). A more recent systematic review on novel psychoactive substances found that they had a severe effect on patients with psychotic disorders and caused exacerbated symptoms such as aggression, violence and agitation (Gray *et al.,* 2016). On the other hand, a 10-year cohort study found that the incident use of cannabis increased the development of incident psychotic symptoms from baseline to 3.5 years into the study (Kuepper *et al.,* 2011). Additionally, continued use of cannabis increased the risk of developing persistent psychotic symptoms between 3.5 and 8.4 years into the study (Kuepper *et al.,* 2011). While the use of cannabis, alcohol and other substances could not be analysed in the models due to missing data, it is important to highlight the documented effect of these substances on psychosis.

Comorbid psychiatric conditions

The finding that depression was significantly associated with overall symptom severity and that of hallucinations, is again corroborated by previous studies which have investigated the effects of comorbid depressive symptoms and a number of health outcomes, including quality of life and global functioning in schizophrenia (Hou *et al.,* 2016; Upthegrove *et al.,* 2017; Lee *et al.,* 2003). It has become well-established that depression mediates the relationship between trauma (childhood and otherwise) and psychotic symptoms (Bebbington *et al.,* 2011; Hardy *et al.,* 2016; Gracie *et al.,* 2007).

Sex

The initial finding that showed that female patients experienced more severe abnormal psychomotor behaviour compared to males, is consistent with the findings of some studies while others have failed to show an association entirely (Canuso and Pandina, 2007; Eranti *et al.,* 2013; Cutajar *et al.,* 2010; Shevlin *et al.,* 2015). However, upon closer inspection of our initial finding, the respective confidence intervals were all inclusive of 1 suggesting that the differences between males and females should be interpreted with caution. Sex was not found to be statistically significant in the models evaluating overall symptom severity score.

BMI

The finding that a higher BMI was associated with overall symptom severity and delusions, is consistent with findings from previous studies which have investigated the effects of BMI as it pertains to quality of life, obesity and cognition in schizophrenia (Faulkner *et al.,* 2007; Subramaniam *et al.,* 2014; Friedman *et al.,* 2010). Obesity is common among patients diagnosed with schizophrenia (Gurpegui *et al.,* 2012). Aside from dietary patterns and genetic predisposition, the use of second-generation (atypical) antipsychotics (SGAs) remains the first-line treatment for schizophrenia (Patel *et al.,* 2014). However, one of the primary metabolic side-effects of these drugs includes weight gain (Raedler, 2010).

Education level

Interestingly, tertiary education was found to be marginally significant in its association with symptom severity in patients with schizophrenia. This could indicate that tertiary education, and the general university or higher-education environment, may act as a recent life stressor which subsequently contributes to worse outcomes in psychosis. This is further supported by increasing rates of mental illness and mental distress among university students in countries such as the UK, the US, Egypt and several others (Thorley, 2017; Lipson *et al.,* 2019; Wahed & Hassan, 2017; Pedrelli *et al.,* 2014). This association warrants further investigation and may point towards the potential benefits in increasing access to mental health facilities and counselling in order to mitigate the effects of the university environment.

Differences were observed between the two study sites, Masaka and Butabika, as has been the case in previous studies (Kinyanda *et al.,* 2017). However, no sufficient explanation has thus far been provided.

The findings discussed above must be interpreted in light of the limitations outlined below.

5.2. Limitations of the secondary study

Given the cross-sectional design of the secondary study, antecedent-consequent bias was a limitation. Seeing as the exposure and outcome were measured simultaneously, it was not possible to determine causality. However, because the CTQ measures trauma prior to the age of 18 years old, we do have some sense of temporality i.e. that the childhood trauma occurred before the onset of schizophrenia symptoms. The onset of schizophrenia during childhood or pre-adolescence is remarkably rare with several studies having established the age of onset to be either during late adolescence or early adulthood (Jablensky, 1997; Miettunen *et al.,* 2018; Chen *et al.,* 2018). Given the established influence of cannabis on schizophrenia, our inability to evaluate the effect of cannabis use in the regression analyses was a limitation. Similarly, our inability to evaluate the effect of alcohol use due to considerable missing data, was an additional limitation.

Missing data, due to item non-response within any one of the questionnaires, was another limitation of the secondary data analysis. As a result, the effect of alcohol and cannabis use, as well as the use of other substances including heroin, cocaine, khat and kubab, could not be evaluated.

Furthermore, while the statistical approaches used were appropriate for the type of data collected for use in the secondary analysis, there were limitations with regards to the types of inference that could be made.

Recall bias may have been introduced into the study through participants' inability to accurately recall the different types of trauma as well as the degree of severity they may have experienced during childhood. While recall bias was less likely with the measurement of adult trauma, Frissa and colleagues found that a number of factors including mental disorder status, sex and experience of childhood traumas influenced the likelihood of a patient accurately recalling an adult trauma (Frissa *et al.,* 2016)

5.3. Recommendations for future studies

The findings from this study that adult traumas (and to a lesser extent, early life traumas) are associated with the severity of schizophrenia, have implications for the management of this disorder. These results suggest that addressing these traumas at clinical management may have positive prognostic dividends. There are several studies which have been conducted whose findings suggest that management of traumas in schizophrenia has a positive impact on prognosis (Fuller, 2010; Lysaker *et al.,* 2010; Lysaker *et al.,* 2011, Silverstein & Bellack, 2008).

A common criticism of studies which have investigated the effect of especially childhood trauma on psychosis, is that of the cross-sectional study design which has often limited the ability of researchers to establish true cause and effect. However, the cross-sectional study design remains the most convenient. The findings of this particular study were part of a longitudinal study (SMILE) where some of the significant associations will be explored further. The World Mental Health (WMH) surveys, which make use of cross-sectional studies, have been of tremendous value in their elucidation of the prevalence of psychiatric disorders, disorder-specific abilities and treatment options (Kessler, 2007). Kessler, in his evaluation of the challenges and opportunities facing psychiatric epidemiology, suggests that current epidemiological research in psychiatry move towards including more analytical or experimental studies as opposed to just descriptive studies (Kessler, 2007). Similarly, the findings of this study could be used to inform randomised controlled trials (RCTs) to treat victims of childhood trauma who may then have better schizophrenia prognosis. The use of control groups is essential. Additionally, future work could also look into other recent adverse life events other than just physical and sexual abuse during adulthood. Studies investigating the differential effect of childhood and adult trauma among patients with comorbid psychiatric disorders will be of tremendous value.

Lastly, re-analysing the data from this study using structural equation modelling may prove more beneficial than multivariate analyses using regression modelling. Given the paucity of data in Africa on childhood and adult trauma and their relationship with schizophrenia, we also advocate for more studies in LMICs. Understanding the mechanisms involved between childhood trauma and schizophrenia among specific populations will allow for an improved understanding of the aetiology of the psychiatric disorder and subsequently better inform targeted strategies in the treatment of the disorder.

5.4. Conclusion

The study has yielded important findings which are summarized as follows:

i) The overall symptom severity was significantly associated with adult traumatic events, showing a dose-response relationship.
ii) Physical neglect, emotional and physical abuse during childhood contributed to the severity of specific positive symptoms namely delusions, disorganized speech and negative symptoms (restricted emotional expression or avolition).
iii) Sexual abuse experienced during adulthood contributed to the severity of hallucinations while physical abuse experienced during childhood was marginally associated with abnormal psychomotor behaviour.
iv) Cumulative adult traumas were found to have a dose-response relationship with both the overall symptom severity and the severity of hallucinations, delusions and abnormal psychomotor behaviour.
v) Patients who adhered to taking their oral psychiatric medication were more likely to develop severe disorganized speech.
vi) The sex of patients was found to be significantly associated with the severity of abnormal psychomotor behaviour.
vii) Comorbid depression was found to be related to hallucinations.
viii) Higher BMI was found to be related with overall symptom severity and the severity of delusions.
ix) The study site and tertiary education were both found to be significantly associated with symptom severity.

This secondary study makes a meaningful contribution to the existing body of literature examining the effects of childhood and adult trauma particularly in LMICs. The findings further support claims that adult trauma, more so than childhood trauma, affects the prognosis of psychiatric disorders such as schizophrenia in this instance. This knowledge is useful in providing holistic care to patients with severe mental illness where both early-life and recent life adversities should be screened for and managed for better treatment outcomes.

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APPENDIX ONE: Plagiarism Declaration

SENATE PLAGIARISM POLICY

I **Rufaro Catherine Samanga** (Student number: **719121**) am a student registered for the degree of **MSc. Epidemiology & Biostatistics** in the academic year **2020**.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature:  Date: 20 April 2020

APPENDIX TWO: Ethics Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Rufaro Samanga

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL) CLEARANCE CERTIFICATE NO. M191072

NAME: Rufaro Samanga

(Principal Investigator) DEPARTMENT: Epidemiology & Biostatistics

PROJECT TITLE: The relationship between childhood and adult trauma and the severity of psychiatric symptoms in adults with schizophrenia in Uganda

DATECONSIDERED: 25/10/2019

DECISION: Approved

unconditionally CONDITIONS:

SUPERVISOR: Dr S Mall, Prof E Kinyanda and Prof J Levin

APPROVED BY: Dr. C Penny, Chairperson, HREC (Medical)

DATE OF APPROVAL: 11/11/2019

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for. DECLARATION OF INVESTIGATORS

To be completed in duplicate and ONE COPY returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. I aqree to submit a yearly proqress report. The date for annual re- certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in October and will therefore be due in the month of October each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

15/11/2019
Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX THREE: Childhood Trauma Questionnaire-Short Form

These questions ask about some of your experiences growing up **as a child and a teenager**. For each question, circle the number that best describes how you feel. Although some of these questions are of a personal nature, please try to answer as honestly as you can.

	QUESTION **When I was growing up, …** **Bwennali nkula, ……..**	**RESPONSE**	**DATA-ENTRY**
10.1	I didn't have enough to eat. *Ssaafunanga byakulya bimala/binzikusa.*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	CHILDEAT1
10.2	I knew there was someone to take care of me and protect me. *Nnamanya nti waaliwo ow'okundabirira n'okunkuuma.*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true	CHILDCARE 1

		1= Sibwekyali *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	
10.3	People in my family called me things like “stupid”, ”lazy”, or “ugly”. *Abeeka benvumanga nti ndi “musirusiru”, “munafu”, oba “mubi”.*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	CHILDLAZY 1
10.4	My parents were too drunk or high to take care of me. *Bazadde bange baali batamiivu nnyo era nga balujuju nga tebasobola kundabirira.*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali*	CHILDRUNK 1

		2=Kyalwangawo okuntuukako *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	
10.5	There was someone in my family who helped me feel important or special. *Mub'eka mwabeerangamu eyannyambanga nenneewulira nga ndi wa mugaso oba ow'enjawulo.*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	CHILDFEEL 1
10.6	I had to wear dirty clothes. *Nalinanga okwambala engoye enkyaafu*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo*	CHILDDIRT Y1

		okuntuukako *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	
10.7	I felt loved. *Nnali muganzi (Nnayagalwanga nnyo).*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	CHILDLOVE 1
10.8	I thought that my parents wished I had never been born. *Nnalowoozanga nti bazadde bange banneevumanga nti ssinga ssaazaalibwa*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako*	CHILDWISH 1

		3= Kyambangako emirundi egimu *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	
10.9	I got hit so hard by someone in my family that I had to see a doctor or go to the hospital. *Nnawuttulwanga nnyo omu kubeeka ekyantuusa n'okugenda muddwaliro oba okulaba omusawo.*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	CHILDHIT1
10.10	There was nothing I wanted to change about my family. *Tewaaliwo kyennayagala kikyuukemu mu beeka.*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako*	CHILDNOT1

		emirundi egimu *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	
10.11	People in my family hit me so hard that it left bruises or marks. *Abeeka bankubanga nnyo, ekyandekeranga n'ebinnuubule oba enkovu ku mubiri..*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	CHILDMARK 1
10.12	I was punished with a belt, a board, a cord, or some hard object. *Nnabonerezebwanga nga bakozesa omusipi, akabaawo, oluwaya oba ekintu kyonna ekikaluba.*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu*	CHILDBELT 1

		4= Kyateranga okubaawo *5= Kyambeerangako nnyo*	
10.13	People in my family looked out for each other. *Bulyomu eka yafangayo kumunne..*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	CHILDOUT1
10.14	People in my family said hurtful or insulting things to me. *Abeeka banjogereranga ebintu ebiruma oba ebikosa*.	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga*	CHILDINSUL1

		okubaawo *5= Kyambeerangako nnyo*	
10.15	I believe that I was physically abused. *Nkakasa banteekako obukosefu ku mubiri gwange.*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	CHILDABUSE1
10.16	I had the perfect childhood. *Obuto bwange bwaali bulungi ddala.*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo*	CHILDPERFE1

		5= Kyambeerangako nnyo	
10.17	I got hit or beaten so badly that it was noticed by someone like a teacher, neighbour, or doctor. *Nnakubwa bubi nnyo nga kyarabwa n'abalala ng'abasomesa bange, ab'okumuliraano oba abasawo.*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	CHILDBEAT 1
10.18	I felt that someone in my family hated me. *Nnalowoozanga nti mubeeka mwalimu atanjagalirako ddala.*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako*	CHILDFELT 1

		nnyo	
10.19	People in my family felt close to each other. *Abbeka balowooza nga nti buli omu yali akolagana bulungi ne munne/banne.*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	CHILDCLOSE1
10.20	Someone tried to touch me in a sexual way, or tried to make me touch them. *Waliwo eyagezaako okunkwatakwata mungeri y'okunkabawaza oba okunkwata mubifo bye ekyama.*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	CHILDSEX1

10.21	Someone threatened to hurt me or tell lies about me unless I did something sexual with them. *Waliwo eyantiisatiisanga nti ajjakuntuusaako obulabe oba okumpaayiriza nti nze nnakoze ebikyamu okujjako nga nzikirizza okukola eby'obukaba naye.*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	CHILDLIES1
10.22	I had the best family in the world. *Nnalina abeeka abasingayo obulungi munsi yonna.*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	CHILDWOR1

10.23	Someone tried to make me do sexual things or make me watch sexual things. *Waliwo eyagezaako okunkozesa eby'obukaba oba okubitunuulira nga bikolebwa*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	CHILDWAT1
10.24	Someone molested me. *Waliwo eyankabawaza.*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	CHILDMOL1
10.25	I believe that I was emotionally abused.	1= Never true	CHILDEMOT

	Nkakasa nti ebirowoozo byange oba ennewuulira yange yakosebwa.	2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	1
10.26	There was someone to take me to the doctor if I needed it. *Waaliwo omuntu ow'okuntwalanga eri omusawo buli lwennabanga nkyetaaze.*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	CHILDSICK1
10.27	I believe that I was sexually abused.	1= Never true 2= Rarely true	CHILDBEL1

	Nkakasa nti nakabawazibwa.	3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	
10.28	My family was a source of strength and support. *Abeeka be baali ensibuko yamaanyi wamu n'obuyambi.*	1= Never true 2= Rarely true 3= Sometimes true 4= Often true 5= Very often true *1= Sibwekyali* *2=Kyalwangawo okuntuukako* *3= Kyambangako emirundi egimu* *4= Kyateranga okubaawo* *5= Kyambeerangako nnyo*	CHILDSTRE 1

APPENDIX FOUR: European Para Suicide Interview Schedule I

ASSESSING FOR SEXUAL ABUSE IN ADULTHOOD USING THE LIFE EVENTS SCALE OF EPSIS I

	QUESTION	**RESPONSE**	**DATA ENTRY**
	From 18 years up to 12 months before this study, did you experience….. ***Okuva ku myaka 18 paka emyezi kumi n'ebiri emabega wafunako bino wamanga……***		
11.1	Your father or mother ever force you to have sexual intercourse against your will? *Taata wo oba maama wo bali bakukaseko akaboozi akekikulu nga teweyagalidde*	1= Yes *1=yee* 2= NO *2= Nedda*	FAMOSEXL1
11.2	Your father or mother ever force you to do or to endure sexual activities (other than intercourse) against your will?' *Taata wo oba maama wo yali akukaseko okukola ebikolwa ebyesittaza nga teweyagalidde*	1= Yes 1=*yee* 2= NO 2= *Nedda*	FAMOENDURL1
11.3	Your brother(s) or sister(s) force you to have sexual intercourse against your will? *Muganda wo or mwanyoko yali akukaseko akaboozi akekikulu nga teweyagalidde*	1= Yes 1=*yee* 2= NO 2= *Nedda*	BROSISSEXL1
11.4	Your brother(s) or sister(s) force you to do or endure sexual	1= Yes	BROSISENDL1

	activities (other than intercourse) against your will?' *Muganda wo oba mwanyoko yali akukaseko okukola ebikolwa ebyesittaza nga teweyagalidde*	1=*yee* 2= NO 2= *Nedda*	
11.5	Your partner(s) ever force you to have sexual intercourse against your will? *Omwagala wo yali akukaseko akaboozi nga teweyagalidde*	1= Yes 1=*yee* 2= NO 2= *Nedda*	PARTNERSEXL1
11.6	Your partner(s) ever force you to do or endure sexual activities (other than intercourse) against your will?' *Omwagalwa wo yali akukaseko okukola ebikolwa ebyesittaza nga teweyagalidde*	1= Yes 1=*yee* 2= NO 2= *Nedda*	PARTNENDL1
11.7	Someone (or more than one person) who is not your partners or parent or sibling ever force you to have sexual intercourse against your will?' *Eliyo omuntu omulala yena (Abantu) eyali mwagalwa wo , oba omwagalwa wo eyali akukaseko akaboozi kekikulu nga teweyagalidde*	1= Yes *1=yee* 2= NO *2= Nedda*	SOMEONESEXL1
11.8	Someone (or more than one person) who is not your partners or parent or sibling ever force	1= Yes *1=yee*	SOMEONENDUL1

	you to do or endure sexual activities (other than intercourse) against your will? *Eriyo omuntu omulala yena (abantu) , eyali mwagalwa wo oba muzadde wo oba ow'oluganda lwo eyali akukaseko okukola ebikolwa ebyesittaza nga toweyagalidde*	2= NO *2= Nedda*	
11.9	Someone ever force you to prostitute yourself?' *Waliwo eyali akaseko okwetunda*	1= Yes 1=*yee* 2= NO *2= Nedda*	PROSTITUTE1
11.10	As a result of war did you ever experience any rape (single or multiple) or/and attempted rape?' *Olwo lutalo ,wali okakiddwako akaboozi*	1= Yes *1=yee* 2= NO *2= Nedda*	WARRAPEL1
	QUESTION	**RESPONSE**	**DATA ENTRY**
	In the last 12 months, did… ***Mu myezi kumi n'ebiri ejiyise…..***		
11.11	Your father or mother ever force you to have sexual intercourse against your will? *Taata wo oba maama wo bali bakukaseko akaboozi akekikulu nga teweyagalidde*	1= Yes *1=yee* 2= NO *2= Nedda*	FAMOSEXD1

11.12	Your father or mother ever force you to do or to endure sexual activities (other than intercourse) against your will?' *Taata wo oba maama wo yali akukaseko okukola ebikolwa ebyesittaza nga teweyagalidde*	1= Yes 1=*yee* 2= NO 2= *Nedda*	FAMOENDURD1
11.13	Your brother(s) or sister(s) force you to have sexual intercourse against your will? *Muganda wo or mwanyoko yali akukaseko akaboozi akekikulu nga teweyagalidde*	1= Yes 1=yee 2= NO 2= *Nedda*	BROSISSEXD1
11.14	Your brother(s) or sister(s) force you to do or endure sexual activities (other than intercourse) against your will?' *Muganda wo oba mwanyoko yali akukaseko okukola ebikolwa ebyesittaza nga teweyagalidde*	1= Yes *1=yee* 2= NO *2= Nedda*	BROSISENDD1
11.15	Your partner(s) ever force you to have sexual intercourse against your will? *Omwagala wo yali akukaseko akaboozi nga teweyagalidde?*	1= Yes *1=yee* 2= NO 2= Nedda	PARTNERSEXD1
11.16	Your partner(s) ever force you to do or endure sexual activities (other than intercourse) against your will?'	1= Yes 1=*yee* 2= NO	PARTNENDD1

	Omwagalwa wo yali akukaseko okukola ebikolwa ebyesittaza nga teweyagalidde	*2= Nedda*	
11.17	Someone (or more than one person) who is not your partners or parent or sibling ever force you to have sexual intercourse against your will?'; *Eriyo omuntu omulala yena (Abantu) eyali mwagalwa wo , oba omwagalwa wo eyali akukaseko akaboozi kekikulu nga teweyagalidde*	1= Yes *1=yee* 2= NO 2= *Nedda*	SOMEONESEXD1
11.18	Someone (or more than one person) who is not your partners or parent or sibling ever force you to do or endure sexual activities (other than intercourse) against your will? *Eriyo omuntu omulala yena (abantu) , eyali mwagalwa wo oba muzadde wo oba ow'oluganda lwo eyali akukaseko okukola ebikolwa ebyesittaza nga toweyagalidde*	1= Yes *1=yee* 2= NO 2= *Nedda*	SOMEONENDUD1
11.19	Someone ever force you to prostitute yourself?' *Waliwo eyali akaseko okwetunda*	1= Yes *1=yee* 2= NO *2= Nedda*	PROSTITUTED1

11.20	As a result of war did you ever experience any rape (single or multiple) or/and attempted rape?' *Olwo lutalo ,wali okakiddwako akaboozi*	1= Yes *1=yee* 2= NO *2= Nedda*	WARRAPED1

ASSESSING FOR PHYSICAL ABUSE IN ADULTHOOD USING THE LIFE EVENTS SCALE OF EPSIS I

	QUESTION	**RESPONSE**	**DATA ENTRY**
	From 18 years upto 12 months before this study, did you experience…. ***Okuva ku myaka 18 paka emyezi kumi n'ebiri emabega, wafunako bino wamanga……..***		
12.1	Ever seriously beaten up or otherwise physically mistreated by those responsible for your upbringing? *Wali okubiddwako obubi enyo oba okutulugunyizibwa kuva eli abo abakukuza?*	1= Yes 1=*yee* 2= NO *2= Nedda*	PHYSICALL1
12.2	Ever severely beaten up or otherwise physically mistreated by (one of) your brother(s) or sister(s)? *Wali okubiddwako obubi enyo oba okutugulunyizibwa mwanyoko oba muganda wo?*	1= Yes 1=*yee* 2= NO 2= *Nedda*	BROSISBEATL1
12.3	Your partner(s) ever beat you up or	1= Yes	PARTNEBEATL1

	physically mistreat you? *Wali okubidwako oba okubonyabonyezebwa muganzi wo oba baganzi bo*	*1=yee* 2= NO *2= Nedda*	
12.4	A non-partner or non-relative ever beat you up or physically mistreat you? *Wali okubiddwako oba okubonyabonyezebwa omuntu atali waluganda oba atali muganzi wo*	1= Yes *1=yee* 2= NO *2= Nedda*	NONPARTNERL1
12.5	As a result of war did you ever experience any of the following: beating and kicking, bayonet injuries, gunshot wounds, cutting off of body parts, forced hard labour, severe body tying (Kandoya), deprivation of food/water/medication?'. *Olw'olutalo , wali okubiddwako oba okusambibwa sambibwa , okufumitibwa ekiso , ebiwundu eby'amasasi , okusalako ekitundu kyo mubiiri, okukaka emirimu emikakali , okutugga akandoya , okuma emeere /amazzi , oba eddagala ?*	1= Yes 1=*yee* 2= NO *2= Nedda*	WARBEATL1

APPENDIX FIVE: Clinician-Rated Dimensions of Psychosis Symptom Severity Scale

Each item asks the clinician to rate the severity of each symptom as experienced by the individual during the past 7 days.

NUMBER	QUESTION	RESPONSE	DATA-ENTRY
	Does the patient have……? ***Omulwadde alina bino*…….?**		
7.1	**Hallucinations** *Okuwulira amaloboozi abalala gebatawulira, okuwulira ebikutambula ku mubiri, kulaba ebintu abalala bye batalaba , okufuna empulira mukamwa etali yabulijjo (nga sinungi)*	**0= not present** ***0= Tekiriiwo*** **1=Equivocal**l (severityor duration not sufficient to be considered psychosis) *1= Sikakasa nti kyekyo* **2= Present, mild** (little pressure to act upon voices,not very bothered by voices) 2= *Weekiri kitono* **3= Present, moderate** some pressureto respond to voices,or is somewhat bothered by voices) 3= *Weekiri kyakigero* **4= Present, severe** (severe pressure to respond to voices,or is very bothered by voices) *4= Weekiri era ky'amanyi*	CHALLUCIN1

7.2	**Delusions** *Okukiririza mukintu nga sikituffu naye nga tekyesingamye ku diini oba obuwangwa oba ebyo kusoma kw'omuntu*	**0= not present** ***0= Tekiriiwo*** **1=Equivocal** (severityor duration not sufficient to be considered psychosis) *1= Sikakasa nti kyekyo* **2= Present, mild (** little pressure to act upon delusional beliefs, not very bothered by beliefs) *2= Weekiri kitono* **3= Present, moderate** (some pressure to act upon beliefs,or is some what bothered by beliefs) *3= Weekiri kyakigero* **4= Present, severe** (severe pressure to act upon beliefs,or is very bothered by beliefs) ***4= Weekiri kyamanyi***	CDELUSION1
7.3	**Disorganised speech** *Okwogera ebitakwatagana*	**0= not present** ***0=Tekiriiwo*** **1=Equivocal** (severity or duration not sufficient to be considered disorganization)	CSPEECHCL1

		1= Sikakasa nti kyekyo **2= Present, mild** (some difficulty following speech) 2= *Weekiri kitono* **3= Present, moderate** (speech often difficult to follow) 3= *Weekiri kyakigero* **4= Present, severe** (speech almost impossible to follow) 4= *Weekiri kyamanyi*	
7.4	**Abnormal psychomotor behavior** *Eneyiisa etali yabulijjo*	**0= not present** ***0= Tekirwo*** **1=Equivocal** (severity or duration not sufficient to be considered abnormal psychomotor behavior) *1= Sikakasa nti kyekyo* **2= Present, mild** (occasional abnormalor bizarre motor behavior or catatonia) *2= Weekiri kitono* **3= Present, moderate** (frequent abnormal or bizarre motor behaviour or catatonia)	CMOTORCL1

		3= *Weekiri kyakigero* **4= Present, severe** (abnormal or bizarre motor behavior or catatonia almost constant) *4= Weekiri kyamanyi*	
7.5	Negative symptoms (restricted emotional expressionor avolition *Obubonero obutawa manyi (tolaga oba oli musanyufu oba nti oli munyivu , butafuna manyi gakola kintu kyona)*	**0= not present** ***0= Tekiriiwo*** **1=Equivocal** (equivocal decrease in facial expressivity, prosody, gestures, or self-initiated behavior) *1= Sikakasa nti kyekyo* **2= Present, mild** (decrease in facial expressivity, prosody, gestures, or self-initiated behavior) 2= *Weekiri kitono* **3= Present, moderate** (decrease in facial expressivity, prosody, gestures,or self-initiated behavior) 3= *Weekiri kyakigero* **4= Present, severe**	CNEGATIVL1

		(decrease in facial expressivity, prosody, gestures,or self-initiated behavior) **4= *Weekiri kyamanyi***	

APPENDIX SIX: Effect of childhood trauma sub-types on severity of hallucinations

Bivariate analyses between childhood trauma sub-types and hallucinations were carried out and presented in Table 9 below.

Table 9. Bivariate analyses between childhood trauma sub-types and hallucinations

Factor	**Odds Ratio**	**95% Confidence Intervals**	**p value**
*Physical neglect_1	1.163	[0.949; 1.424]	0.145
**Physical neglect_2	1.009	[0.799; 1.273]	0.941
Emotional abuse	1.393	[1.053; 1.843]	0.020
Emotional neglect	1.360	[1.033; 1.791]	0.029
Physical abuse	1.280	[0.970; 1.689]	0.081
Sexual abuse	1.429	[1.072; 1.905]	0.015
Minimisation/denial	0.745	[0.578; 0.958]	0.022
Sex	0.953	[0.970; 1.016]	0.858
Age	0.993	[0.970; 1.016]	0.545
Education	0.970	[0.685; 1.374]	0.864
Employment	0.916	[0.744; 1.128]	0.407
Study site	1.633	[0.914; 2.918]	0.097
BMI	0.966	[0.912; 1.023]	0.233
Ever depressed	1.796	[1.050; 3.072]	0.032
Depressed in the past 2 weeks	2.835	[=1.370; 5.866]	0.005
Taking oral psychiatric medication	2.420	[- 0.866; 2.634]	0.322
Adherence to oral psychiatric medication	0.936	[0.512; 1.712]	0.831
Religion	1.160	[0.655; 2.054]	0.612
Marital status	0.968	[- 0.247; 0.182]	0.768

*The component of physical neglect which specifically encompassed not having enough to eat, there having been someone to take the individual to the doctor if they needed it and their parents having been too drunk to take care of them. **The component of physical neglect which specifically encompassed having been someone to take the individual to the doctor if they needed it, their parents having been too drunk to take care of them, wearing dirty clothes and having someone to look after them.

Thereafter, the final ordinal logistic regression of hallucinations on the childhood trauma sub-types and minimisation/denial scale was conducted and is presented in Table 10.

Table 10. Final ordinal logistic regression model of childhood trauma sub-types and hallucinations

Factor	**Level**	**Odds Ratio**	**95% Confidence Intervals**	**p value**
Physical neglect_1	Per one-point increase	0.900	[- 0.391; 0.180]	0.468
Physical neglect_2	Per one-point increase	1.187	[- 0.159; 0.502]	0.310
Emotional abuse	Per one-point increase	1.109	[0.660; 1.865]	0.695
Emotional neglect	Per one-point increase	1.304	[0.788; 2.156]	0.302
Physical abuse	Per one-point increase	2.002	[- 0.468; 0.513]	0.928
Sexual abuse	Per one-point increase	1.335	[0.869; 2.050]	0.187
Minimisation/denial	Per one-point increase	0.848	[0.598; 1.204]	0.357
Sex	Male (reference) Female	 0.892	 [0.507; 1.569]	 0.692
Age	Per one-year increase	0.994	[0.969; 1.019]	0.626
Education	None (reference) Primary Secondary Tertiary	 1.505 0.982 1.787	 [- 1.756; 2.573] [- 2.191; 2.155] [- 1.636; 2.798]	 0.711 0.987 0.608
Study site	Butabika (reference) Masaka	 2.115	 [0.099; 1.399]	 0.024
Depressed in the past 2 weeks	No (reference) Yes	 2.662	 [1.227; 5.777]	 0.013

Diagnostic tests showed that the model upheld all necessary assumptions and showed no evidence against the proportional odds assumption (p = 0.210) as shown in the STATA output below.

Brant test of parallel regression assumption

	chi2	p>chi2	df
All	42.55	0.210	36
sexual_abuse	0.63	0.889	3
physical_abuse	3.72	0.294	3
emotional_abuse	2.33	0.507	3
emotional_neglect	1.22	0.748	3
minimalism_denial	0.44	0.932	3
CT_physnegl_pca1	4.15	0.246	3
CT_physnegl_pca2	3.54	0.316	3
age	0.15	0.986	3
sex	0.87	0.832	3
educat	3.34	0.342	3
studsite1	2.25	0.521	3
depb1	11.62	0.009	3

A significant test statistic provides evidence that the parallel

APPENDIX SEVEN: Effect of childhood trauma sub-types on severity of disorganised speech

Bivariate analyses between childhood trauma sub-types and disorganized speech were carried out and presented in Table 11 below.

Table 11. Bivariate analyses between childhood trauma sub-types and disorganized speech

Factor	**Odds Ratio**	**95% Confidence Intervals**	**p value**
*Physical neglect_1	1.272	[0.899; 1.800]	0.174
**Physical neglect_2	0.673	[0.441; 1.028]	0.067
Emotional abuse	1.280	[0.777; 2.109]	0.333
Emotional neglect	1.305	[0.792; 2.150]	0.296
Physical abuse	0.966	[0.545; 1.713]	0.906
Sexual abuse	1.347	[0.829; 2.190]	0.229
Minimisation/denial	1.09347	[0 .686; 1.743]	0.707
Sex	0.521	[0.188; 1.445]	0.210
Age	1.001	[0.960; 1.043]	0.960
Education	0.850	[0.446; 1.620]	0.622
Employment	1.317	[0.832; 2.083]	0.240
Study site	1.445	[0.492; 4.248]	0.503
BMI	0.915	[0.802; 1.044]	0.186
Ever depressed	1.121	[0.421; 2.985]	0.819
Depressed in the past 2 weeks	2.536	[0.780; 0.246]	0.122
Taking oral psychiatric medication	6.215	[0.627; 61.585]	0.118
Adherence to oral psychiatric medication	3.650	[1.314; 10.136]	0.013
Religion	0.884	[0.272; 2.868]	0.837
Marital status	0.725	[0.494; 1.064]	0.100

*The component of physical neglect which specifically encompassed not having enough to eat, there having been someone to take the individual to the doctor if they needed it and their parents having been too drunk to take care of them. **The component of physical neglect which specifically encompassed having been someone to take the individual to the doctor if they needed it, their parents having been too drunk to take care of them, wearing dirty clothes and having someone to look after them.

Thereafter, the final ordinal logistic regression of disorganized speech and the five CTQ sub-types and minimisation/denial scale was carried out and presented in Table 12.

Table 12. Final ordinal logistic regression model of childhood trauma sub-types and disorganized speech

Factor	**Level**	**Odds Ratio**	**95% Confidence Intervals**	**p value**
Physical neglect_1	Per one-point increase	1.214	[0.735; 2.006]	0.450
Physical neglect_2	Per one-point increase	0.605	[0.370; 0.992]	0.046
Emotional abuse	Per one-point increase	1.759	[0.694; 4.460]	0.234
Emotional neglect	Per one-point increase	1.119	[0.487; 2.572]	0.792
Physical abuse	Per one-point increase	0.531	[0.214;1.317]	0.172
Sexual abuse	Per one-point increase	1.495	[0.712; 3.098]	0.292
Minimisation/ denial	Per one-point increase	1.526	[0.782; 2.979]	0.215
Sex	Male (reference)			
	Female	0.415	[0.139; 1.240]	0.115
Age	Per one-year increase	1.001	[0.957; 1.046]	0.969

The model had several instances of perfect prediction. Thus, the following explanatory variables were removed from the analysis in order to resolve the issue: marital status, education and study site.

Thereafter, the Brant test for the proportional odds/parallel lines assumption did not yield a significant test statistic ($p = 0.114$) which thus indicated that the assumption had been upheld as shown by the STATA output below.

Brant test of parallel regression assumption

	chi2	p>chi2	df
All	25.40	0.114	18
CT_physnegl_pca1	1.35	0.510	2
CT_physnegl_pca2	3.50	0.174	2
emotional_abuse	1.13	0.569	2
emotional_neglect	0.14	0.931	2
physical_abuse	1.65	0.439	2
sexual_abuse	3.44	0.179	2
minimalism_denial	0.52	0.773	2
2.sex	0.13	0.937	2
age	2.25	0.324	2

A significant test statistic provides evidence that the parallel regression assumption has been violated.

APPENDIX EIGHT: Effect of childhood trauma sub-types on severity of delusions

Bivariate analyses between childhood trauma sub-types and delusions were conducted and presented in Table 13 below.

Table 13. Bivariate analyses between childhood trauma sub-types and delusions

Factor	**Odds Ratio**	**95% Confidence Intervals**	**p value**
*Physical neglect_1	0.967	[0.758; 1.233]	0.785
**Physical neglect_2	0.834	[0.644; 1.080]	0.169
Emotional abuse	1.206	[0.882; 1.649]	0.241
Emotional neglect	1.239	[0.915; 1.679]	0.166
Physical abuse	0.933	[- 0.4078; 0.2710]	0.693
Sexual abuse	1.151	[0.827; 1.603]	0.405
Minimisation/denial	0.817	[0.619; 1.079]	0.154
Sex	0.793	[0.444; 1.419]	0.435
Age	1.008	[0.983; 1.033]	0.535
Education	1.049	[0.717; 1.534]	0.807
Employment	0.832	[0.665; 1.041]	0.108
Study site	3.338	[1.815; 6.141]	0.000
BMI	0.932	[0.867; 1.002]	0.056
Ever depressed	1.769	[0.973; 3.219]	0.062
Depressed in the past 2 weeks	0.687	[0.256; 1.844]	0.456
Taking oral psychiatric medication	1.870	[0.189; 18.46]	0.592
Adherence to oral psychiatric medication	0.732	[0.366; 1.467]	0.379
Religion	1.134	[0.603; 2.133]	0.697
Marital status	1.121	[0.877; 1.432]	0.362

*The component of physical neglect which specifically encompassed not having enough to eat, there having been someone to take the individual to the doctor if they needed it and their parents having been too drunk to take care of them. **The component of physical neglect which specifically encompassed having been someone to take the individual to the doctor if they needed it, their parents having been too drunk to take care of them, wearing dirty clothes and having someone to look after them.

Thereafter, the final ordinal logistic regression of delusions on the five CTQ sub-types and minimisation/denial scale was conducted and presented in Table 14.

Table 14. Final ordinal logistic regression model for childhood trauma sub-types and delusions

Factor	**Level**	**Odds Ratio**	**95% Confidence Intervals**	**p value**
Physical neglect_1	Per one-point increase	0.830	[- 0.623; 0.088]	0.280
Physical neglect_2	Per one-point increase	0.845	[- 0.473; 0.306]	0.355
Emotional abuse	Per one-point increase	1.801	[0.160; 1.388]	0.045
Emotional neglect	Per one-point increase	1.019	[- 0.428; 0.736]	0.944
Physical abuse	Per one-point increase	0.523	[- 1.229; - 0.063]	0.024
Sexual abuse	Per one-point increase	1.298	[- 0.247; 0.787]	0.303
Minimisation/denial	Per one-point increase	0.808	[- 0.552; 0.241]	0.264
Sex	Male (reference) Female	 0.947	 [- 0.685; 0.643]	 0.868
Age	Per one-year increase	1.012	[- 0.017; 0.035]	0.348
BMI	Per 1kg/m^2 increase	0.918	[- 0.154; 0.014]	0.034

Due to issues with perfect prediction, study site and education were removed from the analysis to resolve the issue.

The Brant test did not yield a significant test statistic (p = 0.459) for the overall model which indicated that the assumption of proportional odds/parallel lines had been upheld as shown in the STATA output below.

Brant test of parallel regression assumption

	chi2	p>chi2	df
All	30.13	0.459	30
CT_physnegl_pca1	4.39	0.223	3
CT_physnegl_pca2	2.75	0.431	3
emotional_abuse	0.25	0.968	3
emotional_neglect	1.65	0.648	3
physical_abuse	3.76	0.289	3
sexual_abuse	1.33	0.721	3
minimalism_denial	2.47	0.480	3
sex	1.35	0.718	3
age	1.59	0.661	3
bmi	8.70	0.034	3

A significant test statistic provides evidence that the parallel regression assumption has been violated.

APPENDIX NINE: Effect of childhood trauma sub-types on severity of negative symptoms (restricted emotional expression or avolition)

Bivariate analyses between childhood trauma sub-types and negative symptoms (restricted emotional expression or avolition) were carried out and presented in Table 15 below.

Table 15. Bivariate analyses between childhood trauma subtypes on negative symptoms (restricted emotional expression or avolition)

Factor	**Odds Ratio**	**95% Confidence Intervals**	**p value**
*Physical neglect_1	0.806	[0.624; 1.042]	0.100
**Physical neglect_2	0.935	[0.728; 1.201]	0.598
Emotional abuse	1.032	[0.752; 1.416]	0.847
Emotional neglect	1.067	[0.787; 1.446]	0.678
Physical abuse	0.961	[0.694; 1.331]	0.813
Sexual abuse	0.918	[0.634; 1.330]	0.652
Minimisation/denial	0.944	[0.720; 1.239]	0.680
Sex	0.799	[0.452; 1.412]	0.439
Age	1.000	[0.976; 1.025]	0.976
Education	1.190	[0.823; 1.722]	0.355
Employment	0.907	[0.752; 1.134]	0.392
Study site	2.107	[1.147; 3.871]	0.016
BMI	0.960	[0.900; 1.025]	0.221
Ever depressed	1.080	[0.613; 1.905]	0.789
Depressed in the past 2 weeks	1.932	[0.877; 4.259]	0.102
Taking oral psychiatric medication	1.88	[0.130; 10.877]	0.879
Adherence to oral psychiatric medication	1.471	[0.795; 2.723]	0.219
Religion	0.750	[0.369; 1.522]	0.426
Marital status	1.240	[0.965; 1.593]	0.093

*The component of physical neglect which specifically encompassed not having enough to eat, there having been someone to take the individual to the doctor if they needed it and their parents having been too drunk to take care of them. **The component of physical neglect which specifically encompassed having been someone to take the individual to the doctor if they needed it, their parents having been too drunk to take care of them, wearing dirty clothes and having someone to look after them.

Thereafter, the final ordinal logistic regression of negative symptoms on the five CTQ sub-types and minimisation/denial scale was carried out and presented in Table 16.

Table 16. Final ordinal logistic regression model of childhood trauma sub-types and negative symptoms (restricted emotional expression or avolition)

Factor	**Level**	**Odds Ratio**	**95% Confidence Intervals**	**p value**
Physical neglect_1	Per one-point increase	0.605	[0.419; 0.875]	0.008
Physical neglect_2	Per one-point increase	1.045	[0.710; 1.536]	0.825
Emotional abuse	Per one-point increase	1.301	[0.737; 2.300]	0.364
Emotional neglect	Per one-point increase	1.378	[0.787; 2.411]	0.262
Physical abuse	Per one-point increase	1.108	[0.652; 1.882]	0.705
Sexual abuse	Per one-point increase	0.919	[0.548; 1.540]	0.748
Minimisation/denial	Per one-point increase	0.940	[0.638; 1.385]	0.754
Sex	Male (reference)			
	Female	0.814	[0.442; 1.500]	0.507
Age	Per one-year increase	0.997	[0.972; 1.024]	0.841
Depressed in the past 2 weeks	No (reference)			
	Yes	2.092	[- 0.112; 1.589]	0.089

Study site and education were removed from the analysis as they were perfect predictors.

The Brant test showed no evidence against the proportional odds assumption ($p = 0.965$) as shown by the STATA output below.

Brant test of parallel regression assumption

	chi2	p>chi2	df
All	17.57	0.965	30
CT_physnegl_pca1	2.23	0.526	3
CT_physnegl_pca2	2.16	0.540	3
emotional_abuse	1.00	0.802	3
physical_abuse	5.27	0.153	3
sexual_abuse	1.59	0.661	3
emotional_neglect	1.15	0.766	3
minimalism_denial	9.28	0.026	3
age	1.39	0.708	3
2.sex	5.65	0.130	3
1.depb1	3.05	0.384	3

A significant test statistic provides evidence that the parallel regression assumption has been violated.

APPENDIX TEN: Effect of childhood trauma sub-types on severity of abnormal psychomotor behaviour

Bivariate analyses between childhood trauma sub-types and abnormal psychomotor behaviour were carried out and presented in Table 17 below.

Table 17. Bivariate analyses between childhood trauma sub-types and abnormal psychomotor behaviour

Factor	**Odds Ratio**	**95% Confidence Intervals**	**p value**
*Physical neglect_1	1.251	[0.875; 1.789]	0.220
**Physical neglect_2	0.694	[0.455; 0.058]	0.089
Emotional abuse	1.036	[0.600; 1.789]	0.900
Emotional neglect	1.398	[0.847; 2.308]	0.190
Physical abuse	1.299	[0.819; 2.062]	0.267
Sexual abuse	1.090	[0.623; 1.908]	0.762
Minimisation/denial	0.879	[0.5534; 1.395]	0.583
Sex	0.391	[0.134; 1.137]	0.085
Age	1.013	[0.973; 1.055]	0.529
Education	0.590	[0.302; 1.153]	0.123
Employment	0.955	[0.648; 1.409	0.818
Study site	9.409	[3.194; 27.712]	0.000
BMI	0.813	[0.686; 0.964]	0.017
Ever depressed	1.848	[0.666; 5.125]	0.238
Depressed in the past 2 weeks	1.730	[0.472; 6.338	0.408
Taking oral psychiatric medication	5.365	[0.554; 51.881]	0.147
Adherence to oral psychiatric medication	0.902	[0.282; 2.880]	0.862
Religion	2.066	[0.845; 5.053]	0.112
Marital status	0.855	[0.581; 1.259]	0.427

*The component of physical neglect which specifically encompassed not having enough to eat, there having been someone to take the individual to the doctor if they needed it and their parents having been too drunk to take care of them. **The component of physical neglect which specifically encompassed having been someone to take the individual to the doctor if they needed it, their parents having been too drunk to take care of them, wearing dirty clothes and having someone to look after them.

Thereafter, the final ordinal logistic regression of abnormal psychomotor behaviour on the five CTQ sub-types and minimisation/denial scale was carried out and presented in Table 18 below.

Table 18. Final ordinal logistic regression model for childhood trauma sub-types and abnormal psychomotor behaviour

Factor	**Level**	**Odds Ratio**	**95% Confidence Intervals**	**p value**
Physical neglect_1	Per one-point increase	1.279	[0.749; 2.182]	0.367
Physical neglect_2	Per one-point increase	0.727	[0.444; 1.188]	0.203
Emotional abuse	Per one-point increase	0.667	[0.246; 1.809]	0.426
Emotional neglect	Per one-point increase	1.150	[0.525; 2.521]	0.726
Physical abuse	Per one-point increase	1.691	[0.736; 3.885]	0.216
Sexual abuse	Per one-point increase	0.934	[0.397; 2.196]	0.875
Minimisation/denial	Per one-point increase	1.161	[0.604; 2.232]	0.655
Sex	Male (reference)			
	Female	0.342	[0.111; 1.054]	0.062
Age	Per one-year increase	1.027	[0.981; 1.074]	0.254
Religion	Christian (reference)			
	Muslim	2.169	[0.630; 7.460]	0.219
	Others	5.670	[0.485; 66.919]	0.166

Education and study site were removed from the analysis as they were perfect predictors.

The Brant test showed no evidence (p = 0.530) against the proportional odds assumption as shown in the STATA output below.

Brant test of parallel regression assumption

	chi2	p>chi2	df
All	10.01	0.530	11
CT_physnegl_pca2	0.23	0.633	1
CT_physnegl_pca1	1.68	0.196	1
sexual_abuse	0.30	0.584	1
emotional_abuse	0.01	0.933	1
physical_abuse	0.08	0.777	1
emotional_neglect	0.10	0.746	1
minimalism_denial	0.52	0.469	1
age	0.07	0.785	1
2.sex	0.22	0.639	1
2.religion	0.75	0.385	1
3.religion	4.25	0.039	1

A significant test statistic provides evidence that the parallel regression assumption has been violated.

APPENDIX ELEVEN: Effect of adult trauma sub-types on severity of hallucinations

Following backward elimination, the final ordinal logistic regression model best describing the association between adult trauma sub-types and the severity of hallucinations was presented in Table 19 below.

Table 19. Final ordinal logistic regression model for adult trauma sub-types and hallucinations

Factor	**Level**	**Odds Ratio**	**95% Confidence Intervals**	**p value**
Adult physical abuse	Per one-point increase	1.180	[0.267; 5.209]	0.827
Adult sexual abuse	Per one-point increase	18.524	[1.925; 178.276]	0.012
Sex	Male (reference)			
	Female	0.924	[0.527; 1.621]	0.783
Age	Per one-year increase	0.992	[0.968; 1.016]	0.507
Study site	Butabika (reference)			
	Masaka	1.960	[1.041; 3.693]	0.037
Education	None (reference)			
	Primary	1.546	[0.179; 13.347]	0.692
	Secondary	0.916	[0.106; 7.956]	0.937
	Tertiary	1.991	[0.222; 17.824]	0.538
Depressed for the past 2 weeks	Yes	2.303	[1.059; 5.007]	0.035
	No (reference)			

The Brant test showed some evidence (p = 0.070) that the proprotional odds assumption did not hold and the evidence was statistically significant in the case of depression (p = 0.003). This was not pursued further in this report.

Brant test of parallel regression assumption

	chi2	p>chi2	df
All	31.21	0.070	21
AT_physical	0.88	0.831	3
AT_sexual	6.16	0.104	3
sex	1.41	0.704	3
age	0.54	0.909	3
studsite1	2.56	0.464	3
educat	4.36	0.225	3
depb1	14.13	0.003	3

A significant test statistic provides evidence that the parallel regression assumption has been violated.

APPENDIX TWELVE: Effect of adult trauma sub-types on severity of delusions

Following backward elimination, the final ordinal logistic regression model best describing the association between adult trauma sub-types and the severity of delusions was presented in Table 20 below.

Table 20. Final ordinal logistic regression model for adult trauma sub-types and delusions

Factor	**Level**	**Odds Ratio**	**95% Confidence Intervals**	**p value**
Adult physical abuse	Per one-point increase	2.502	[0.544; 11.510]	0.239
Adult sexual abuse	Per one-point increase	4.637	[0.404; 53.267]	0.218
Sex	Male (reference)			
	Female	0.854	[0.456; 1.600	0.623
Age	Per one-year increase	1.007	[0.982; 1.032]	0.612
Study site	Butabika (reference)			
	Masaka	3.936	[2.033; 7.622]	0.000
Education	None (reference)			
	Primary	1.805	[0.198; 16.426]	0.600
	Secondary	1.976	[0.215; 18.140]	0.547
	Tertiary	2.608	[0.269; 25.324]	0.409

Lifetime depression was omitted from the analysis as it was a perfect predictor.

The Brant test showed no evidence against the proportional odds assumption (p = 0.368) as shown by the STATA output below.

Brant test of parallel regression assumption

	chi2	p>chi2	df
All	19.40	0.368	18
AT_physical	3.28	0.351	3
AT_sexual	0.72	0.869	3
sex	0.90	0.826	3
age	2.87	0.412	3
studsite1	6.08	0.108	3
educat	2.31	0.511	3

A significant test statistic provides evidence that the parallel regression assumption has been violated.

APPENDIX THIRTEEN: Effect of adult trauma sub-types on severity of negative symptoms (restricted emotional expression or avolition)

Following backward elimination, the final ordinal logistic regression model best describing the association between adult trauma sub-types and the severity of negative symptoms (restricted emotional expression or avolition) was presented in Table 21 below.

Table 21. Final ordinal logistic regression of adult trauma sub-types and negative symptoms (restricted emotional expression or avolition)

Factor	**Level**	**Odds Ratio**	**95% Confidence Intervals**	**p value**
Adult physical abuse	Per one-point increase	1.264	[0.299; 5.340]	0.750
Adult sexual abuse	Per one-point increase	1.330	[0.109; 16.252]	0.823
Sex	Male (reference)			
	Female	0.803	[0.442; 1.457]	0.470
Age	Per one-year increase	1.001	[0.976; 1.027]	0.924
Education	None (reference)			
	Primary	2.014	[0.237; 17.135]	0.522
	Secondary	1.760	[0.207; 14.971]	0.605
	Tertiary	2.869	[0.326; 25.229]	0.342

APPENDIX FOURTEEN: Effect of adult trauma sub-types on severity of abnormal psychomotor behaviour

Following backward elimination, the final ordinal logistic regression model best describing the association between adult trauma sub-types and the severity of abnormal psychomotor behaviour was presented in Table 22 below.

Table 22. Final ordinal logistic regression model describing of adult trauma sub-types and abnormal psychomotor behaviour

Factor	**Level**	**Odds Ratio**	**95% Confidence Intervals**	**p value**
Adult physical abuse	Per one-point increase	8.158	[0.799; 83.264]	0.077
Sex	Male (reference)			
	Female	0.450	[0.140; 1.447]	0.180
Age	Per one-year increase	1.0148	[0.971; 1.061]	0.519
Education	None (reference)			
	Primary	0.385	[0.031; 4.774]	0.457
	Secondary	0.228	[0.0164; 3.172]	0.271
	Tertiary	0.277	[0.017; 4.554]	0.369
Study site	Butabika (reference)			
	Masaka	9.408	[2.966; 29.846]	0.000
Religion	Christian (reference)			
	Muslim	2.115	[0.541; 8.261]	0.281
	Others	7.322	[0.484;110.68]	0.151

Adult sexual abuse was omitted from the analysis due to considerably wide confidence intervals.

The Brant test showed no evidence (p = 0.139) against the proportional odds assumption as shown in the STATA output below.

Brant test of parallel regression assumption

	chi2	p>chi2	df
All	9.67	0.139	6
AT_physical	0.22	0.636	1
sex	0.13	0.718	1
age	0.07	0.793	1
educat	1.78	0.182	1
religion	2.97	0.085	1
studsite1	3.12	0.077	1

A significant test statistic provides evidence that the parallel regression assumption has been violated.

APPENDIX FIFTEEN: Effect of adult trauma sub-types on severity of disorganised speech

Following backward elimination, the final ordinal logistic regression model best describing the association between adult trauma sub-types and the severity of disorganised speech was presented in Table 23 below.

Table 23. Final ordinal logistic regression model of adult trauma sub-types and disorganised speech

Factor	**Level**	**Odds Ratio**	**95% Confidence Intervals**	**p value**
Adult physical abuse	Per one-point increase	2.385	[0.291; 19.54]	0.418
Sex	Male (reference) Female	0.628	[0.215; 1.831]	0.394
Age	Per one-year increase	1.003	[0.960; 1.048]	0.901
Adherence to taking oral psychiatric medication	Yes No (reference)	3.507	[1.253; 9.815]	0.017

Sexual abuse experienced during childhood and study site were both omitted from the analysis as the first had wide confidence intervals while the latter was a perfect predictor.

The Brant test showed no evidence against the proportional odds/parallel lines assumption ($p = 0.866$) as shown in the STATA output below.

Brant test of parallel regression assumption

	chi2	p>chi2	df
All	3.91	0.866	8
AT_physical	0.88	0.645	2
sex	0.29	0.864	2
age	1.40	0.496	2
adherence1	1.02	0.601	2

A significant test statistic provides evidence that the parallel regression assumption has been violated.

APPENDIX SIXTEEN: Cumulative effect of childhood traumatic and adult traumatic events on severity of hallucinations

Ordinal logistic regression was carried out to determine whether there was a dose-response relationship between the cumulative number of individual childhood and adult traumatic events and the severity of hallucinations. Once again, bivariate analyses conducted previously were used to inform the selection of explanatory variables that were eligible for backward elimination. The final ordinal logistic regression model is presented in Table 24 below.

Table 24. Final ordinal logistic regression model for cumulative effect of childhood traumatic and adult traumatic events and hallucinations

Factor	**Level**	**Odds Ratio**	**95% Confidence Intervals**	**p value**
Adult trauma	Per one-point increase	1.156	[1.005; 1.330]	0.043
Childhood trauma	Per one-point increase	1.037	[0.973; 1.107]	0.263
Minimisation/denial	Per one-point increase	0.133	[0.611; 1.067]	0.133
Sex	Male (reference)			
	Female	0.952	[0.546; 1.660]	0.862
Age	Per one-year increase	0.995	[0.971; 1.020]	0.705
Education	None (reference)			
	Primary	1.579	[0.183; 13.642]	0.678
	Secondary	0.943	[0.108; 8.219]	0.958
	Tertiary	1.904	[0.211; 17.176]	0.566
Study site	Butabika (reference)			
	Masaka	2.025	[1.073; 3.820]	0.029
Depressed in the past 2 weeks	No (reference)			
	Yes	2.275	[1.052; 4.923]	0.037

The Brant test did not find evidence against the proportional odds/parallel lines (p = 0.231) as shown by the STATA output below.

Brant test of parallel regression assumption See previous comments on using Courier new for tables

	chi2	p>chi2	df
All	28.71	0.231	24
adultraumsco	3.10	0.377	3
childtraumsco	0.10	0.992	3
minimalism_denial	0.45	0.929	3
sex	1.42	0.701	3
age	0.72	0.868	3
educat	4.24	0.236	3
studsite1	2.46	0.482	3
depb1	15.83	0.001	3

A significant test statistic provides evidence that the parallel regression assumption has been violated.

APPENDIX SEVENTEEN: Cumulative effect of childhood traumatic and adult traumatic events on severity of delusions

Ordinal logistic regression was carried out to determine whether there was a dose-response relationship between the cumulative number of individual childhood and adult traumatic events and the severity of delusions. Once again, bivariate analyses conducted previously were used to inform the selection of explanatory variables that were eligible for backward elimination. The final ordinal logistic regression model is presented in Table 25 below.

Table 25. Final ordinal logistic regression model of cumulative number of individual childhood and adult traumatic events and delusions

Factor	**Level**	**Odds Ratio**	**95% Confidence Intervals**	**p value**
Adult trauma	Per one-point increase	1.148	[0.997; 1.321]	0.055
Childhood trauma	Per one-point increase	1.021	[0.948; 1.101]	0.581
Minimisation/ denial	Per one-point increase	0.832	[0.612; 1.130]	0.238
Sex	Male (reference)			
	Female	0.836	[0.454; 1.539]	0.565
Age	Per one-year increase	1.011	[0.985; 1.037]	0.400
Education	None (reference)			
	Primary	1.833	[0.199; 16.903]	0.593
	Secondary	2.020	[0.217; 18.837]	0.537
	Tertiary	2.630	[0.268; 25.827	0.407
Study site	Butabika (reference)			
	Masaka	4.059	[2.059; 8.002]	0.000

The Brant test showed no evidence overall against the proportional odds assumption (p = 0.126) as shown by the STATA output below.

```
Brant test of parallel regression assumption

                    |       chi2     p>chi2      df
--------------------+-----------------------------
                All |      28.52      0.126      21
--------------------+-----------------------------
       adultraumsco |       1.90      0.593       3
     childtraumsco  |       2.76      0.430       3
  minimalism_denial |       7.96      0.047       3
                sex |       0.58      0.900       3
                age |       1.60      0.659       3
             educat |       2.33      0.508       3
          studsite1 |       6.43      0.093       3

A significant test statistic provides evidence that the parallel
regression assumption has been violated.
```

APPENDIX EIGHTEEN: Cumulative effect of childhood traumatic and adult traumatic events on severity of negative symptoms (restricted emotional expression or avolition)

Ordinal logistic regression was carried out to determine whether there was a dose-response relationship between the cumulative number of individual childhood and adult traumatic events and the severity of negative symptoms (restricted emotional expression or avolition). Once again, bivariate analyses conducted previously were used to inform the selection of explanatory variables that were eligible for backward elimination. The final ordinal logistic regression model is presented in Table 26 below.

Table 26. Final ordinal logistic model of cumulative number of individual childhood and adult traumatic events and negative symptoms (restricted emotional expression or avolition)

Factor	**Level**	**Odds Ratio**	**95% Confidence Intervals**	**p value**
Adult trauma	Per one-point increase	1.064	[0.912; 1.241]	0.428
Childhood trauma	Per one-point increase	0.963	[0.894; 1.038]	0.321
Sex	Male (reference)			
	Female	0.823	[0.460; 1.474]	0.513
Age	Per one-year increase	1.003	[0.978; 1.029]	0.795
Education	None (reference)			
	Primary	2.020	[0.238; 17.176]	0.520
	Secondary	1.699	[0.199; 14.480]	0.628
	Tertiary	3.035	[0.345; 26.701]	0.317
Minimisation/ denial	Per one-point increase	0.912	[0.681; 1.219]	0.533

APPENDIX NINETEEN: Cumulative effect of childhood traumatic and adult traumatic events on severity of abnormal psychomotor behaviour

Ordinal logistic regression was carried out to determine whether there was a dose-response relationship between the cumulative number of individual childhood and adult traumatic events and the severity of abnormal psychomotor behaviour. Once again, bivariate analyses conducted previously were used to inform the selection of explanatory variables that were eligible for backward elimination. The final ordinal logistic regression model is presented in Table 27 below.

Table 27. Final ordinal logistic model of cumulative number of individual childhood and adult traumatic events and abnormal psychomotor behaviour

Factor	**Level**	**Odds Ratio**	**95% Confidence Intervals**	**p value**
Adult trauma	Per one-point increase	1.119	[0.912; 1.373]	0.281
Childhood trauma	Per one-point increase	1.034	[0.919; 1.163]	0.578
Minimisation/ denial	Per one-point increase	0.912	[0.560; 1.485]	0.712
Sex	Male (reference)			
	Female	0.350	[0.118; 1.040]	0.059
Age	Per one-year increase	1.024	[0.980; 1.068]	0.289

Education was omitted from the model because it was a perfect predictor. Religon and study site were omitted from the analysis due to wide confidence intervals.

The Brant test did not find evidence against the proportional odds/parallel lines assumption (p = 0.822) as shown by the STATA output below.

Brant test of parallel regression assumption

	chi2	p>chi2	df
All	2.19	0.822	5
adultraumsco	0.15	0.696	1
childtraumsco	0.39	0.534	1
minimalism_denial	0.62	0.432	1
2.sex	0.09	0.763	1
age	0.04	0.837	1

A significant test statistic provides evidence that the parallel regression assumption has been violated.

APPENDIX TWENTY: Cumulative effect of childhood traumatic and adult traumatic events on the severity of disorganised speech

Ordinal logistic regression was carried out to determine whether there was a dose-response relationship between the cumulative number of individual childhood and adult traumatic events and the severity of disorganised speech. Once again, bivariate analyses conducted previously were used to inform the selection of explanatory variables that were eligible for backward elimination. The final ordinal logistic regression model is presented in Table 28 below.

Table 28. Final ordinal logistic regression model of cumulative number of individual childhood and adult traumatic events and the severity of disorganised speech

Factor	**Level**	**Odds Ratio**	**95% Confidence Intervals**	**p value**
Adult trauma	Per one-point increase	1.114	[0.908; 1.368]	0.301
Childhood trauma	Per one-point increase	1.013	[0.893; 1.148]	0.845
Sex	Male (reference) Female	0.493	[0.1753; 1.389]	0.181
Age	Per one-year increase	1.003	[0.961; 1.047]	0.890
Minimisation/ denial	Per one-point increase	1.166	[0.707; 1.922]	0.547