

## Original Article

**Cite this article:** Mall S, Platt JM, Temmingh H, Musenge E, Campbell M, Susser E, Stein DJ (2020). The relationship between childhood trauma and schizophrenia in the Genomics of Schizophrenia in the Xhosa people (SAX) study in South Africa. *Psychological Medicine* 50, 1570–1577. <https://doi.org/10.1017/S0033291719001703>

Received: 2 October 2018  
Revised: 19 June 2019  
Accepted: 24 June 2019  
First published online: 7 August 2019

**Key words:**  
Case-control; childhood trauma; psychosis; South Africa

**Author for correspondence:**  
Sumaya Mall,  
E-mail: [Sumaya.mall@wits.ac.za](mailto:Sumaya.mall@wits.ac.za)

# The relationship between childhood trauma and schizophrenia in the Genomics of Schizophrenia in the Xhosa people (SAX) study in South Africa

Sumaya Mall<sup>1,2</sup>, Jonathan M. Platt<sup>3</sup>, Henk Temmingh<sup>1</sup>, Eustasius Musenge<sup>2</sup>, Megan Campbell<sup>1</sup>, Ezra Susser<sup>3,4</sup> and Dan J. Stein<sup>1,5</sup>

<sup>1</sup>Department of Psychiatry and Mental Health, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa; <sup>2</sup>Division of Epidemiology and Biostatistics, School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; <sup>3</sup>Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, USA; <sup>4</sup>New York State Psychiatric Institute, New York, USA and <sup>5</sup>SU/UCT Medical Research Council Unit on Risk & Resilience in Mental Disorders, South Africa

## Abstract

**Background.** Evidence from high-income countries suggests that childhood trauma is associated with schizophrenia. Studies of childhood trauma and schizophrenia in low and middle income (LMIC) countries are limited. This study examined the prevalence of childhood traumatic experiences among cases and controls and the relationship between specific and cumulative childhood traumatic experiences and schizophrenia in a sample in South Africa.

**Methods.** Data were from the Genomics of Schizophrenia in the South African Xhosa people study. Cases with schizophrenia and matched controls were recruited from provincial hospitals and clinics in the Western and Eastern Cape regions in South Africa. Childhood traumatic experiences were measured using the Childhood Trauma Questionnaire (CTQ). Adjusted logistic regression models estimated associations between individual and cumulative childhood traumatic experiences and schizophrenia.

**Results.** Traumatic experiences were more prevalent among cases than controls. The odds of schizophrenia were 2.44 times higher among those who experienced any trauma than those who reported no traumatic experiences (95% CI 1.77–3.37). The odds of schizophrenia were elevated among those who experienced physical/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 who did not. Cumulative physical/emotional abuse and neglect experiences increased the odds of schizophrenia as a dose–response relationship.

**Conclusion.** Childhood trauma is common in this population. Among many other benefits, interventions to prevent childhood trauma may contribute to a decreasing occurrence of schizophrenia.

## Introduction

Childhood trauma refers to adverse experiences and conditions during childhood and includes emotional, physical and sexual abuse as well as emotional and physical neglect (Morgan and Fisher, 2007). Research suggests that childhood trauma has enduring neurobiological effects (Gunnar and Quevedo, 2007; McCrory *et al.*, 2011) and is associated with a range of physical and mental illnesses in adolescence and adulthood (Kraan *et al.*, 2015; Mandelli *et al.*, 2015; Baumeister *et al.*, 2016). These include both clinical and subclinical levels of schizophrenia (Matheson *et al.*, 2012). Further, childhood trauma may impact the course of schizophrenia and affect symptom severity and prognosis (Matheson *et al.*, 2012; van Dam *et al.*, 2012; Trotta *et al.*, 2015).

Two recent meta-analyses of observational studies found that experiences of childhood adversity were significantly higher among schizophrenia cases compared with controls (Matheson *et al.*, 2012) (Varese *et al.*, 2012). These analyses found an increased risk of psychosis or schizophrenia due to childhood trauma, irrespective of study designs or trauma measure.

Nearly all studies to date have examined these relationships using samples from high-income countries (Trotta *et al.*, 2013; Fisher *et al.*, 2014; Dantchev *et al.*, 2018; Sideli *et al.*, 2018). Among the few studies conducted in low- and middle-income countries, South African studies found that childhood trauma was associated with premorbid adjustment and schizophrenia outcomes (Kilian *et al.*, 2017a, 2017b; Asmal *et al.*, 2018). Further, studies in LMICs have rarely considered the type of event or the number of cumulative traumas. It is

important to study these relationships in LMICs in order to understand the context-specific schizophrenia risk and morbidity associated with childhood trauma, and to potentially inform appropriate interventions and policies to improve social and mental health outcomes for children. South Africa has a high prevalence of childhood trauma in the general population and more evidence is needed to understand the experience of trauma among people with severe mental illness (Jewkes *et al.*, 2010; Denckla *et al.*, 2017).

The current paper seeks to contribute to the literature on childhood trauma and schizophrenia in LMICs through the following aims: (1) to describe the prevalence of an array of childhood traumas in cases and controls; (2) to examine how types of childhood trauma are associated with schizophrenia; and (3) to examine the associations between the cumulative number of traumas and schizophrenia.

## Methods

### Sample

This study utilized data from the Genomics of Schizophrenia in the South African Xhosa people (SAX) project. SAX is a case-control study designed to identify genetic variations and social exposures related to schizophrenia risk in a sample of the Xhosa population. Xhosa speaking people are one of the largest indigenous groups in South Africa and live mainly in the Eastern and Western Cape regions of South Africa (Koen *et al.*, 2012; Campbell *et al.*, 2017a).

The recruitment strategies of the study have been described in previous publications (Campbell *et al.*, 2017a, 2017b). Initiated in January 2013, participants were Xhosa speaking people recruited from provincial hospitals and clinics in the Western and Eastern Cape regions of South Africa over a 5-year period. Xhosa language and ethnicity were self-reported.

Cases were defined using the following criteria: respondents who received a clinical diagnosis of schizophrenia or schizoaffective disorder for at least 2 years duration, and could give informed consent. Controls were defined as respondents who presented for treatment of non-psychiatric medical conditions at university-affiliated general medical hospitals and community health centers (CHC) that draw from similar catchment areas to the psychiatric hospitals and clinics where cases were recruited, matched by age group (e.g. 21–25) and gender.

The complete sample consists of 1420 cases (50.77%) and 1377 controls (49.23%) ( $n = 2797$ ). Within the study sample, exposure data were completely missing for 326 respondents (11.6% of the total sample), and partially missing for 374 respondents (13.3% of the full sample). We attribute this to the inconsistent administering of the CTQ when the study began in 2013. To maximize the sample size, the main analysis imputed missing items for respondents with partial exposure data, using multiple imputations with 15 combined datasets, with corrected standard errors (Rubin, 1987). Imputation models included schizophrenia status, age, education, and all traumatic experience items. Those with missing responses for all traumatic experiences were excluded. Imputed model estimates were compared to unimputed estimates to examine the robustness of the analytic models to the degree of missing data. The final analytic sample comprised 2471 individuals (49.5% cases). Compared with the analytic sample, respondents with completely missing data were younger (age 34.9 *v.* 36.2,  $p = 0.0195$ ) and more likely to be cases (60.7% *v.* 49.5%,  $p =$

0.0002). There were no differences in education and gender between included and excluded samples.

### Measures

The Structured Clinical Interview for Diagnosis for axis I disorders (DSM IV-TR version) (SCID-I), a widely used semi-structured interview tool (Spitzer *et al.*, 1992; First *et al.*, 1997) was administered to participants in Xhosa by one of the trained psychiatric nurses. The SCID-I has been found to have acceptable internal consistency, test-retest reliability as well as concurrent and predictive reliability (Spitzer *et al.*, 1992). The SCID-I collects data on psychopathology and physical illnesses including cardiovascular disease, diabetes, Tuberculosis and HIV/AIDS. For this study, interrater reliability for the translated Xhosa version of the SCID-I was obtained on a smaller sample of participants ( $N = 22$ ). Reliability was good for the principle psychotic disorder diagnosis ( $\kappa = 0.74$ ,  $p < 0.001$ ). In addition to the patient interview, information was considered in the diagnostic process from referral notes, past and current clinical records, interviews with other members of the multidisciplinary teams and information from family members or other acquaintances of the patients. SCID-I interviews typically lasted 1.5–4.5 h.

The Childhood Trauma Questionnaire (CTQ) was administered to measure participants' childhood trauma experiences. The CTQ has been employed in several contexts, including in South Africa (Martin *et al.*, 2014; Kilian *et al.*, 2017b). The CTQ consists of 25 items designed for retrospective self-report of childhood trauma (Fink *et al.*, 1995), and was originally designed to capture five broad trauma domains: emotional abuse, sexual abuse, physical abuse, emotional and physical neglect. In order to consider the cumulative effects of experiencing multiple traumas, each item was dichotomized as ever versus never experienced, consistent in several previous studies employing the CTQ to examine the onset of various psychopathologies (Gil *et al.*, 2009; Tucci *et al.*, 2010; Powers *et al.*, 2016). A full list of CTQ items can be found in online Supplementary Appendix 1. Respondents were asked to self-report how often a traumatic event occurred, from 1 (never) to 5 (often). Six items that refer to positive childhood experiences were reverse-coded so that a higher total score reflected a greater level of childhood trauma.

In addition, the CTQ includes a three-item minimization or denial scale used to assess respondents' potential for extreme reporting bias (Fink *et al.*, 1995; Bernstein *et al.*, 2003; McGrath *et al.*, 2010). However, there is disagreement regarding the validity of the scale as a measure of response bias (MacDonald *et al.*, 2014), and it has been inconsistently used, including in several previous studies of South African samples (Kenny *et al.*, 2007; Gerdner and Allgulander, 2009; Lochner *et al.*, 2010; Spies and Seedat, 2014; Spies *et al.*, 2016). Therefore we did not remove respondents who met minimization/denial criteria.

Several covariates were considered to control for unmeasured confounding, based on previous studies of childhood trauma and schizophrenia (Powers *et al.*, 2016) as well as to remove the bias introduced by our matching strategy (Pearce, 2016). These included sex, continuous age (range: 21–54), education level (0–8th grade versus more than 8th grade), urbanicity (rural, urban, township), and region (Western Cape, Eastern Cape). A second set of models were run adjusting for additional covariates that represent potential comorbidities with schizophrenia, including lifetime depression (any *v.* none); lifetime alcohol use disorder (none *v.* abuse or dependence), and lifetime cannabis disorder (none *v.* abuse or dependence).

Those who were visually impaired or unable to read were assisted in completing the questionnaire by a nurse. All survey items were translated and back-translated into Xhosa in line with World Health Organization translation procedures (Menon *et al.*, 2012).

### CTQ validation

There has been limited use of the CTQ in Xhosa-speaking samples and previous studies have not translated the instrument (Spies *et al.*, 2016). Therefore, in a preliminary analysis, we examined validity and internal consistency of the translated instrument in our sample using factor analysis and  $\omega$  coefficients (Dunn *et al.*, 2014). In the validation, an initial confirmatory factor analysis (CFA) was run to attempt to replicate the factor structure as originally designed. In the event of a poor CFA fit, we allowed for a newly derived factor structure, using exploratory factor analysis (EFA) in order to identify the best-fitting factor model of latent trauma domains. This exploratory approach was chosen over the use of CFA modification indices, to derive the most interpretable factor solution from the instrument. Factor loadings were estimated using weighted least squares means and variances, in order to handle categorical variables with non-normally distributed errors (Costello and Osborne, 2005). Goodness-of-fit was evaluated using the Root Mean Square Error of Approximation (RMSEA) and its 95% confidence interval (CI), and the Comparative Fit Index (CFI). Based on previous recommendations, we set cutoffs for acceptable fit at RMSEA < 0.10 and CFI > 0.90, and good fit at RMSEA < 0.05 and CFI > 0.95 (Hu and Bentler, 1999; Wall and Amemiya, 2000). Additionally, in order to obtain an interpretable factor solution, we excluded items with low (<0.3) loadings on all factors, as well as statistically significant cross-loadings on multiple factors. Factor correlation was estimated using Pearson's  $r$  coefficient. Using the best-fitting factor solution, we then examined the internal consistency of each factor and the total CTQ scale with  $\omega$  coefficients. Subsequent analyses were based on the best-fitting interpretable factor solution.

### Data analysis

First, to better understand the degree of co-occurring traumatic events, we estimated the correlations between individual childhood trauma experiences. Second, we estimated the prevalence of individual traumas in the total sample, and compared the prevalence of each item among cases and controls using  $\chi^2$  tests. Third, we estimated the prevalence of each trauma domain, dichotomized as ever versus never experienced, in the total sample and among cases and controls. Fourth, we estimated the odds ratios (ORs) of schizophrenia among those who experienced each trauma domain, compared with those who did not, in adjusted logistic regression models. Fifth, to examine the total burden of childhood traumatic experiences, we calculated the prevalence of experiencing cumulative individual traumas and estimated the odds of schizophrenia among those who experienced 1, 2, or 3 or more cumulative trauma domains compared with no trauma. Data were analyzed using SAS version 9.4 and Mplus version 7.

### Ethical considerations

Ethical approval was granted by the Human Ethics Committee of the Faculty of Health Sciences, University of Cape Town, South

Africa (HREC number: 049/2013) to conduct the study. Prior to data collection, our fieldworkers carefully explained in Xhosa the purpose and procedures of the study emphasizing that participation is entirely voluntary. He or she also explained that withdrawing from the study at any time is the participant's right and that data will be kept confidential by the study team. Individuals with schizophrenia may experience cognitive decline (Keefe and Harvey, 2012; Bora, 2015) so to ensure that informed consent was fully understood, all participants were screened for decisional capacity using the University of California, San Diego Brief Assessment of Capacity to Consent (UBACC) questionnaire (Seaman *et al.*, 2015; Campbell *et al.*, 2017b). This is a well validated tool for screening for decisional capacity in participants with cognitive impairment.

### Results

The initial EFA included the entire 25-item instrument. The model fit of a five-factor solution was good, however, there were several items with significant cross-loadings onto multiple factors. After removing four items, we identified a three-factor model with 21 items that evidenced good fit (CFI = 0.98; TLI = 0.97; RMSEA = 0.054), was interpretable, and was consistent with the original CTQ design. The  $\omega$  coefficients for each factor domain indicated acceptable to excellent internal consistency. The three-factors included: (1) physical/emotional abuse (12 items;  $\omega = 0.94$ ); (2) neglect which comprises the lack of protective factors during childhood (4 items;  $\omega = 0.85$ ); and (3) sexual abuse (5 items;  $\omega = 0.93$ ). The total scale  $\omega$  coefficient was 0.96 and the factor correlation coefficients ranged from 0.45 to 0.71. The final factor model is presented in online Supplementary Table S1. Together these findings suggest that the 21-item modified version of the CTQ has acceptable reliability and validity in this population.

The analytic sample comprised 88.1% men. The mean age of the sample was 36.1 years (s.d. = 9.13, range 21–54 years) and 71.9% had a minimum of primary school education. Overall, correlations between CTQ items were greater than 0.05 ranging from 0.16 to 0.70. The factor correlations were moderate, ranging from 0.21 to 0.42. All correlations are presented in online Supplementary Table S2.

The prevalence of individual childhood traumatic experiences overall and among cases and controls is presented in Table 1. Notably, the prevalence of experiencing any trauma was very high among cases (94.4%) as well as among controls (87.1%). All individual traumatic events were more prevalent among cases than controls. The prevalence of experiencing each trauma domain is presented in Table 2. Cases were significantly more likely to have experienced all trauma domains compared with controls. In the fully adjusted logistic regression models, the odds of schizophrenia was higher among those who experienced physical/emotional abuse (OR 1.63, 95% CI 1.28–2.1), neglect (OR 1.23, 95% CI 1.0–1.52) and sexual abuse (OR 1.22, 95% CI 1.0–1.48), compared with those who did not have these experiences. The odds of schizophrenia were 2.05 times higher among those who experienced any trauma than those who did not (95% CI 1.45–2.91). All model estimates are presented in Table 3.

Figure 1 and online Supplementary Table S1 present the prevalence of cumulative traumas within each latent domain. A substantial proportion of the sample reported experiencing the maximum number of traumas within the domains of physical/emotional abuse (15.6%), neglect (26.7%), and sexual abuse (18.2%). In the fully adjusted logistic regression models, there

**Table 1.** Prevalence of childhood traumatic events among those with and without schizophrenia

	Total		Controls		Cases		<i>p</i> value
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	
<b>Physical/emotional abuse</b>							
I didn't have enough to eat	885	42.2	440	40.4	445	48.1	0.0829
People in my family called me things like 'stupid', 'lazy', or 'ugly'	934	44.5	425	39.0	509	50.5	<0.0001
My parents were too drunk or high to take care of me	723	34.5	351	32.2	372	36.9	0.025
I had to wear dirty clothes	702	33.5	326	29.9	376	37.3	0.0004
I thought that my parents wished I had never been born	784	37.4	379	34.8	405	40.2	0.011
I got hit so hard by someone in my family that I had to see a doctor	642	30.6	312	28.7	330	32.7	0.042
People in my family hit me so hard that it left bruises or marks	730	34.8	353	32.4	377	37.4	0.017
I was punished with a belt, a board, a cord, or some hard object	982	46.8	470	43.2	512	50.8	0.001
People in my family said hurtful or insulting things to me	847	40.4	398	36.6	449	44.5	0.0002
I believe that I was physically abused	825	39.3	409	37.6	416	41.3	0.082
I got hit or beaten so badly that it was noticed by someone like a teacher	618	29.5	300	27.6	318	31.6	0.045
I felt that someone in my family hated me	876	41.8	417	38.3	459	45.5	0.001
<b>Neglect</b>							
I knew there was someone to take care of me and protect me	871	41.5	427	39.2	444	44.1	0.025
There was someone in my family who helped me feel important or special	1055	50.3	519	47.7	536	53.2	0.012
I felt loved	1077	51.4	531	48.8	546	54.2	0.013
There was someone to take me to the doctor if I needed it	1099	52.4	539	49.5	560	55.6	0.006
<b>Sexual abuse</b>							
Someone tried to touch me in a sexual way, or tried to make me touch them	632	30.1	307	28.2	325	32.2	0.043
Someone threatened to hurt me or tell lies about me unless I did something	624	29.8	315	28.9	309	30.7	0.387
Someone tried to make me do sexual things or make me watch sexual things	629	30.0	306	28.1	323	32.0	0.049
Someone molested me	730	34.8	370	34.0	360	35.2	0.404
I believe that I was sexually abused	768	36.6	381	35.0	387	38.4	0.106

**Table 2.** Prevalence of childhood traumatic experiences by domain, among those with and without schizophrenia

		Controls		Cases		<i>p</i> value		
		<i>n</i>	%	<i>n</i>	%			
Total	2097	1089	51.9	1008	48.1			
Physical/emotional abuse	1671	79.7	829	76.1	842	83.5	<0.0001	
Neglect	1447	69.0	714	65.6	733	72.7	0.0004	
Sexual abuse	1126	53.7	558	51.2	568	56.4	0.0191	
Any trauma	1900	90.6	949	87.1	951	94.4	<0.0001	
Cumulative trauma domains	0	197	9.4	140	12.9	57	5.7	<0.0001
	1	493	23.5	255	23.4	238	23.6	
	2	470	22.4	236	21.7	234	23.2	
	3	937	44.7	458	42.1	479	47.5	

was evidence of a dose-response relationship in the number of physical/emotional abuse experiences, increasing from 1.23 (95% CI 0.86–1.76) to 2.44 (95% CI 1.61–3.71). Those with two

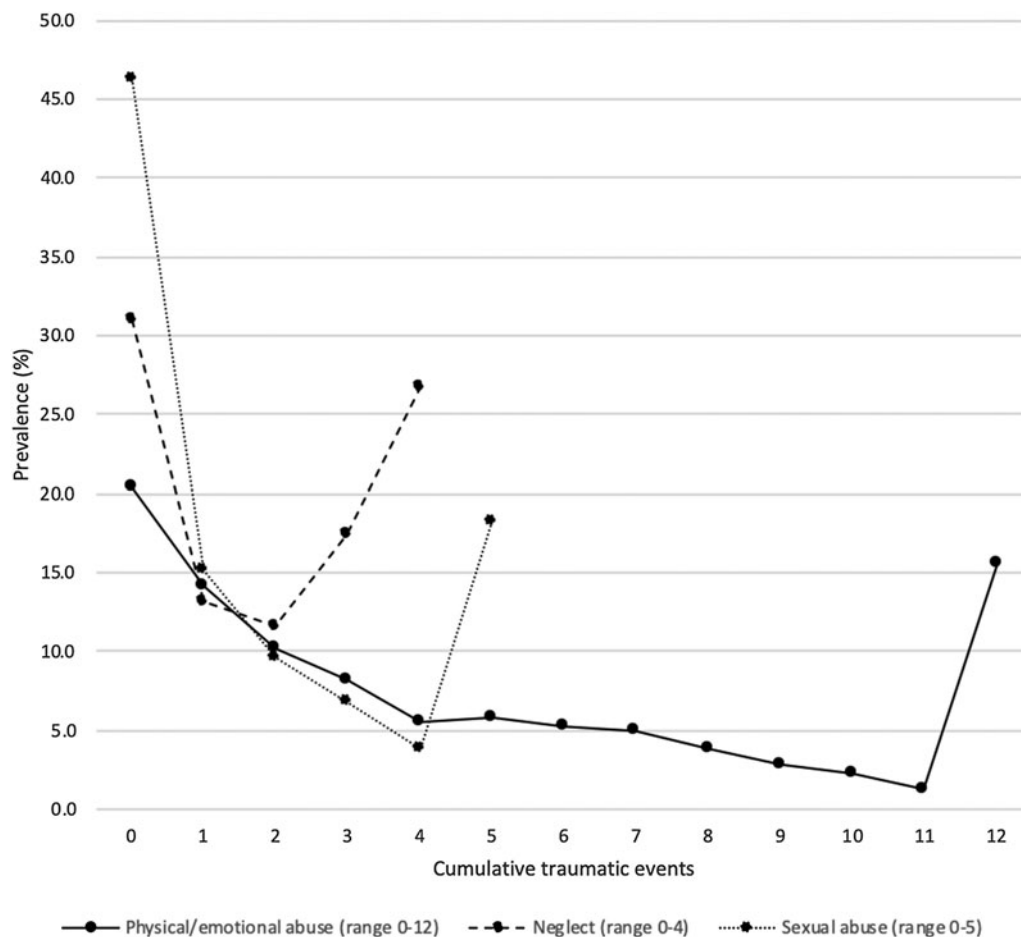
and three neglect-type traumas had 1.63 (95% CI 1.17–2.28) and 1.32 (95% CI 0.96–1.81) times the odds of schizophrenia, compared with those who experienced no neglect. There was no clear dose

**Table 3.** Unadjusted and adjusted ORs of schizophrenia, among those who ever experienced each traumatic event domain, compared with those who never experienced each domain

Trauma domain	Model 1			Model 2			Model 3		
	OR	95% CI		OR	95% CI		OR	95% CI	
Physical/emotional abuse	1.37	1.13	1.67	1.34	1.10	1.65	1.63	1.28	2.09
Neglect	1.37	1.15	1.64	1.35	1.13	1.61	1.23	1.00	1.52
Sexual abuse	1.16	0.99	1.36	1.15	0.97	1.35	1.22	1.00	1.48
Any trauma	2.25	1.66	3.06	2.21	1.63	2.99	2.05	1.45	2.91

CI, confidence interval.

Note: Model 2 adjusted for sex, education, age, urbanicity, locality; Model 3 adjusted for model 2 covariates + lifetime depression, lifetime alcohol use disorder, and lifetime cannabis use disorder.

**Fig. 1.** Cumulative proportion of traumatic events experienced for each domain.

response for sexual abuse events. The odds of schizophrenia increased with increases in cumulative trauma experiences (range: 1.85–2.14). Compared with unimputed models, estimates were slightly attenuated after imputation, though were not substantively different. All model estimates are presented fully in Table 4.

## Discussion

This study sought to examine the prevalence of childhood traumas, whether exposure to childhood trauma is associated with increased risk of schizophrenia, and whether that risk increased with

cumulative trauma exposure in a South African, Xhosa-speaking population. First, our findings suggest that childhood traumatic events are very common among controls as well as cases. Second, all three latent domains of physical/emotional abuse, neglect, and sexual abuse are nonetheless associated with an increased risk of schizophrenia, most evident for those who had more than one traumatic event within a domain. Third, there is some evidence of a dose-response relationship between the number of physical/emotional abuse experiences and schizophrenia. There are several strengths to the methodology of the study, including the care taken to translate instruments into Xhosa.

**Table 4.** Adjusted ORs of schizophrenia, by a number of cumulative traumatic events experienced in each domain, compared with no traumatic experiences

Number of traumatic events by domain (0 = ref)	Model 1			Model 2			Model 3			
	OR	95% CI		OR	95% CI		OR	95% CI		
Physical/emotional abuse	1	1.07	0.79	1.43	1.06	0.79	1.43	1.23	0.86	1.76
	2	1.40	1.02	1.94	1.41	1.02	1.95	1.78	1.21	2.62
	3+	1.88	1.33	2.65	1.87	1.32	2.65	2.44	1.61	3.71
Neglect	1	1.22	0.93	1.59	1.22	0.93	1.59	1.26	0.92	1.72
	2	1.60	1.21	2.11	1.58	1.20	2.08	1.63	1.17	2.28
	3+	1.52	1.19	1.94	1.51	1.18	1.92	1.32	0.96	1.81
Sexual abuse	1	1.29	1.01	1.63	1.28	1.01	1.63	1.46	1.11	1.93
	2	1.00	0.75	1.33	1.00	0.75	1.32	1.25	0.89	1.75
	3+	1.33	0.95	1.84	1.30	0.94	1.81	1.44	0.94	2.20
Any trauma domains	1	2.11	1.50	2.97	2.09	1.49	2.93	1.85	1.25	2.74
	2	2.34	1.67	3.28	2.31	1.65	3.25	2.11	1.43	3.12
	3+	2.28	1.66	3.13	2.21	1.61	3.03	2.14	1.49	3.08

CI, confidence interval.

Note: Model 2 adjusted for sex, education, age, urbanicity, locality; Model 3 adjusted for model 2 covariates + lifetime depression, lifetime alcohol use disorder, and lifetime cannabis use disorder.

Our findings that childhood traumatic events are high among cases and controls are consistent with several previous studies examining trauma and related conditions in South Africa (Jewkes *et al.*, 2016; Gibbs *et al.*, 2018). Our results of the increased risk of schizophrenia among those who have experienced cumulative traumas are generally consistent with previous studies (Anda *et al.*, 2006; van Os *et al.*, 2008) including three systematic reviews of the relationship between childhood trauma and schizophrenia (Read *et al.*, 2005; Matheson *et al.*, 2012; Varese *et al.*, 2012). We note that several studies of trauma in schizophrenia suggest that specific experiences of childhood trauma, e.g. physical or emotional neglect may have differential patterns of impact on various outcomes (i.e. premorbid adjustment, cognition and white matter abnormalities) (Kilian *et al.*, 2017a, 2017b; Asmal *et al.*, 2018). To our knowledge where previous studies have examined the relationship between childhood trauma and cognition in schizophrenia Kilian *et al.* (2017a), pre morbid adjustment (Kilian *et al.*, 2017b) and white matter abnormalities (Asmal *et al.*, 2018), no previous study has compared the relationship between childhood trauma and schizophrenia as outcome.

In modeling the exposure as cumulative traumatic events, we found evidence of potential threshold and dose–response effects. Experiencing a single physical/emotional abuse- and neglect-type event was not significantly associated with schizophrenia, and odds increased to significance among those who experienced 2 and 3+ events, in a dose–response manner for physical/emotional abuse. This may suggest that when experienced infrequently, children can overcome these forms of adversity without an increased risk of schizophrenia. In contrast, a single experience of sexual abuse was associated with elevated odds of disorder, emphasizing the severity of these particular experiences. Future research should further interrogate individual and accumulated traumas and the specific mechanisms underlying their potential differential effects.

These findings should be interpreted in light of several limitations. First, the case–control study design could be subject to recall bias where cases and controls could over or under report

traumatic experiences. Also, the design limited our ability to determine the temporal ordering between each trauma and the onset of schizophrenia. It is plausible that traumatic experiences may have been a consequence of victimization after sub-clinical symptoms of schizophrenia (Beards *et al.*, 2013; Tsigebrhan *et al.*, 2014; Kraan *et al.*, 2015), which might introduce bias due to reverse causation. Third, the psychological burden or social desirability of disclosing childhood trauma may have led to under-reporting of exposures (Susser and Widom, 2012). This type of misclassification may be non-differential, or under-reporting may have been greater among the cases, though both types of misclassification would have biased the study estimates toward a null association, as found by Widom and colleagues in their 2015 study of intergenerational childhood trauma (Widom *et al.*, 2015). Fourth, the SAX survey recorded a limited set of covariates (sex, education, and age) which could be considered confounders in this study. As such, we consider the impact of unmeasured confounding as a source of bias. Fifth, we did not collect physician verified data of physical health conditions. Finally, the CTQ does not ask explicitly about the severity or duration of individual traumatic events. These characteristics should be considered in future research. We also suggest that future studies consider comorbid psychiatric conditions in schizophrenia, e.g. depression (Rössler *et al.*, 2005; Peralta and Cuesta, 2009; Herniman *et al.*, 2017) or substance use as potential interaction variables of the relationship between childhood trauma and schizophrenia (Sideli *et al.*, 2018). Several studies suggest that childhood trauma is associated with mental disorders other than schizophrenia and further work is needed to determine whether there is specificity to these associations.

## Conclusion

This study is a meaningful contribution to the literature examining childhood trauma in schizophrenia in low- and middle-income countries. The results strengthen the claim that

childhood trauma is an important determinant for psychosis and schizophrenia and may be useful to consider when designing interventions to reduce psychosis incidence.

**Supplementary material.** The supplementary material for this article can be found at <https://doi.org/10.1017/S0033291719001703>.

**Acknowledgements.** We wish to acknowledge the support of Dr Adele Pretorius, project manager of the SAX study and the data team for their assistance with data management, quality control and access.

**Financial support.** The SAX study receives funding from the National Institute of Mental Health (NIMH: Grant number 5U01MH096754) and is a member of the Human Heredity and Health in Africa Consortium (H3 Africa) (<http://h3africa.org/>). SM has received support from the Harry Crossley and National Research Foundation of South Africa's post-doctoral research fellowships, a Claude Leon Foundation early career research award and a seed award from the School of Public Health, University of the Witwatersrand, Johannesburg, South Africa. SM has received funding from the Columbia University Southern African AIDS International Training/Research Program. JP has received support from National Institute of Mental Health (grant T32-MH1304346). DJS has received research grants and/or consultancy honoraria from Biocodex, Lundbeck, Servier, and Sun.

## References

- Anda RF, Felitti VJ, Bremner JD, Walker JD, Whitfield C, Perry BD, Dube SR and Giles WH (2006) The enduring effects of abuse and related adverse experiences in childhood: a convergence of evidence from neurobiology and epidemiology. *European Archives of Psychiatry and Clinical Neuroscience* **256**, 174–186.
- Asmal L, Kilian S, du Plessis S, Scheffler F, Chiliza B, Fouche J-P, Seedat S, Dazzan P and Emsley R (2018) Childhood trauma associated white matter abnormalities in first-episode schizophrenia. *Schizophrenia Bulletin* **45**(2), 369–376.
- Baumeister D, Akhtar R, Ciufolini S, Pariante CM and Mondelli V (2016) Childhood trauma and adulthood inflammation: a meta-analysis of peripheral C-reactive protein, interleukin-6 and tumour necrosis factor- $\alpha$ . *Molecular Psychiatry* **21**, 642–649.
- Beards S, Gayer-Anderson C, Borges S, Dewey ME, Fisher HL and Morgan C (2013) Life events and psychosis: a review and meta-analysis. *Schizophrenia Bulletin* **39**(4), 740–747.
- Bernstein DP, Stein JA, Newcomb MD, Walker E, Pogge D, Ahluvalia T, Stokes J, Handelsman L, Medrano M, Desmond D and Zule W (2003) Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child Abuse and Neglect* **27**, 169–190.
- Bora E (2015) Neurodevelopmental origin of cognitive impairment in schizophrenia. *Psychological Medicine* **45**, 1–9.
- Campbell M, Susser E, Mall S, Mqulwana SG, Mndini MM, Ntola OA, Nagdee M, Zingela Z, Van Wyk S and Stein DJ (2017a) Using iterative learning to improve understanding during the informed consent process in a South African psychiatric genomics study. *PLoS ONE* **12**(11), e0188466. <https://doi.org/10.1371/journal.pone.0188466>.
- Campbell MM, Sibeko G, Mall S, Baldinger A, Nagdee M, Susser E and Stein DJ (2017b) The content of delusions in a sample of South African Xhosa people with schizophrenia. *BMC Psychiatry* **17**, 41.
- Costello A and Osborne J (2005) Best practices in exploratory factor analysis: four recommendations for getting the most from your analysis. *Practical Assessment, Research & Evaluation* **10**, 1–9.
- Dantchev S, Zammit S and Wolke D (2018) Sibling bullying in middle childhood and psychotic disorder at 18 years: a prospective cohort study. *Psychological Medicine* **48**, 2321–2328.
- Denckla CA, Considine NS, Spies G, Cherner M, Henderson DC, Koenen KC and Seedat S (2017) Associations between neurocognitive functioning and social and occupational resilience among South African women exposed to childhood trauma. *European Journal of Psychotraumatology* **8**, 1394146. <https://doi.org/10.1080/20008198.2017.1394146>.
- Dunn TJ, Baguley T and Brunsten V (2014) From alpha to omega: a practical solution to the pervasive problem of internal consistency estimation. *British Journal of Psychology* **105**, 399–412.
- Fink LA, Bernstein D, Handelsman L, Foote J and Lovejoy M (1995) Initial reliability and validity of the childhood trauma interview: a new multidimensional measure of childhood interpersonal trauma. *American Journal of Psychiatry* **152**, 1329–1335.
- First MB, Spitzer RL, Gibbon M and Williams JBW (1997). *Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version (SCID-CV) for DSM-IV*.
- Fisher HL, McGuffin P, Boydell J, Fearon P, Craig TK, Dazzan P, Morgan K, Doody GA, Jones PB, Leff J, Murray RM and Morgan C (2014) Interplay between childhood physical abuse and familial risk in the onset of psychotic disorders. *Schizophrenia Bulletin* **40**, 1443–1451.
- Gerdner A and Allgulander C (2009) Psychometric properties of the Swedish version of the Childhood Trauma Questionnaire-Short Form (CTQ-SF). *Nordic Journal of Psychiatry* **63**, 160–170.
- Gibbs A, Dunkle K, Washington L, Willan S, Shai N and Jewkes R (2018) Childhood traumas as a risk factor for HIV-risk behaviours amongst young women and men living in urban informal settlements in South Africa: a cross-sectional study. *PLoS ONE* **13**(4), e0195369.
- Gil A, Gama CS, de Jesus DR, Lobato MI, Zimmer M and Belmonte-de-Abreu P (2009) The association of child abuse and neglect with adult disability in schizophrenia and the prominent role of physical neglect. *Child Abuse and Neglect* **33**(9), 618–624.
- Gunnar M and Quevedo K (2007) The neurobiology of stress and development. *Annual Review of Psychology* **58**, 145–173.
- Herniman SE, Allott KA, Killackey E, Hester R and Cotton SM (2017) The psychometric validity of the Center for Epidemiological Studies-Depression Scale (CES-D) in first episode schizophrenia spectrum. *Psychiatry Research* **252**, 16–22.
- Hu L and Bentler PM (1999) Structural equation modeling: a multidisciplinary journal cutoff criteria for fit indexes in covariance structure analysis: conventional criteria versus new alternatives. *Structural Equation Modeling* **6**, 37–41.
- Jewkes RK, Dunkle K, Nduna M, Jama PN and Puren A (2010) Associations between childhood adversity and depression, substance abuse and HIV and HSV2 incident infections in rural South African youth. *Child Abuse & Neglect* **34**(11), 833–841.
- Jewkes R, Nduna M, Jama-Shai N, Chirwa E and Dunkle K (2016) Understanding the relationships between gender inequitable behaviours, childhood trauma and socio-economic status in single and multiple perpetrator rape in rural South Africa: structural equation modelling. *PLoS ONE* **11**(5), e0154903.
- Keefe RSE and Harvey PD (2012) Cognitive impairment in schizophrenia. *Handbook of Experimental Pharmacology* **213**, 11–37.
- Kenny DT, Lennings CJ and Nelson PK (2007) *The mental health of young offenders serving orders in the community: implications for rehabilitation*. *Journal of Offender Rehabilitation* **45**, 123–148.
- Kilian S, Asmal L, Chiliza B, Olivier M, Phahladira L, Scheffler F, Seedat S, Marder S, Green M and Emsley R (2017a) Childhood adversity and cognitive function in schizophrenia spectrum disorders and healthy controls: evidence for an association between neglect and social cognition. *Psychological Medicine* **48**(13), 2186–2193.
- Kilian S, Burns JK, Seedat S, Asmal L, Chiliza B, du Plessis M, Olivier R, Kidd M and Emsley R (2017b) Factors moderating the relationship between childhood trauma and premorbid adjustment in first-episode schizophrenia. *PLoS ONE* **12**(1), e0170178. <https://doi.org/10.1371/journal.pone.0170178>.
- Koen L, Niehaus DJH, Wright G, Warnich L, de Jong G, Emsley RA and Mall S (2012) Chromosome 22q11 in a Xhosa schizophrenia population. *South African Medical Journal* **102**, 165–166.
- Kraan T, Velthorst E, Smit F, de Haan L and van der Gaag M (2015) *Trauma and recent life events in individuals at ultra high risk for psychosis: review and meta-analysis*. *Schizophrenia Research* **161**, 143–149.
- Lochner C, Seedat S, Allgulander C, Kidd M, Stein D and Gerdner A (2010) Childhood trauma in adults with social anxiety disorder and panic disorder: a cross-national study. *African Journal of Psychiatry* **13**, 376–381.
- MacDonald K, Thomas ML, MacDonald TM and Sciolla AF (2014) A perfect childhood? Clinical correlates of minimization and denial on

- the childhood trauma questionnaire. *Journal of Interpersonal Violence* **30**, 988–1009.
- Mandelli L, Petrelli C and Serretti A** (2015) *The role of specific early trauma in adult depression: a meta-analysis of published literature. Childhood trauma and adult depression. European Psychiatry* **30**, 665–680.
- Martin L, Viljoen M, Kidd M and Seedat S** (2014) Are childhood trauma exposures predictive of anxiety sensitivity in school attending youth? *Journal of Affective Disorders* **168**, 5–12.
- Matheson SL, Shepherd AM, Pinchbeck RM, Laurens KR and Carr VJ** (2012) Childhood adversity in schizophrenia: a systematic meta-analysis. *Psychological Medicine*, 1–13.
- McCroy E, De Brito SA and Viding E** (2011) *The impact of childhood maltreatment: a review of neurobiological and genetic factors. Frontiers in Psychiatry* **43**.
- McGrath RE, Mitchell M, Kim BH and Hough L** (2010) Evidence for response bias as a source of error variance in applied assessment. *Psychological Bulletin* **136**, 450–470.
- Menon B, Cherkil S, Aswathy S, Unnikrishnan A and Rajani G** (2012) *The process and challenges in the translation of World health organization quality of Life (WHOQOL-BREF) to a regional language; Malayalam. Indian Journal of Psychological Medicine* **34**, 149.
- Morgan C and Fisher H** (2007) Environmental factors in schizophrenia: childhood trauma – a critical review. *Schizophrenia Bulletin* **33**, 3–10.
- Pearce N** (2016) Analysis of matched case-control studies. *BMJ (Clinical Research Ed.)* <http://dx.doi.org/10.1136/bmj.i969>.
- Peralta V and Cuesta MJ** (2009) Characterization of affective domains within the nonaffective psychotic disorders. *Schizophrenia Research* **111**(1-3), 61–69.
- Powers A, Fani N, Cross D, Ressler KJ and Bradley B** (2016) Childhood trauma, PTSD, and psychosis: findings from a highly traumatized, minority sample. *Child Abuse and Neglect* **58**, 111–118.
- Read J, Van Os J, Morrison AP and Ross CA** (2005) Childhood trauma, psychosis and schizophrenia: a literature review with theoretical and clinical implications. *Acta Psychiatrica Scandinavica* **112**, 330–350.
- Rössler W, Joachim Salize H, Van Os J and Riecher-Rössler A** (2005) *Size of burden of schizophrenia and psychotic disorders. European Neuropsychopharmacology* **15**, 399–409.
- Rubin DB** (1987) *Multiple Imputation for Nonresponse in Surveys* Donald B. Rubin. Wiley Series in Probability and Statistics.
- Seaman JB, Terhorst L, Gentry A, Hunsaker A, Parker LS and Lingler JH** (2015) Psychometric properties of a decisional capacity screening tool for individuals contemplating participation in Alzheimer's disease research. *Journal of Alzheimer's Disease* **46**, 1–9.
- Sideli L, Fisher HL, Murray RM, Sallis H, Russo M, Stilo SA, Paparelli A, Wiffen BDR, O'Connor JA, Pintore S, Ferraro L, La Cascia C, La Barbera D, Morgan C and Di Forti M** (2018) Interaction between cannabis consumption and childhood abuse in psychotic disorders: preliminary findings on the role of different patterns of cannabis use. *Early Intervention in Psychiatry* **12**, 135–142.
- Spies G and Seedat S** (2014) Depression and resilience in women with HIV and early life stress: does trauma play a mediating role? A cross-sectional study. *BMJ Open* **4**, e004200.
- Spies G, Ahmed-Leitao F, Fennema-Notestine C, Cherner M and Seedat S** (2016) Effects of HIV and childhood trauma on brain morphometry and neurocognitive function. *Journal of NeuroVirology* **22**, 149–158.
- Spitzer RL, Williams JBW, Gibbon M and First MB** (1992) The Structured Clinical Interview for DSM-III-R (SCID): I: history, rationale, and description. *Archives of General Psychiatry* **49**, 624–629.
- Susser E and Widom CS** (2012) Still searching for lost truths about the bitter sorrows of childhood. *Schizophrenia Bulletin* **38**, 672–675.
- Trotta A, Di Forti M, Mondelli V, Dazzan P, Pariante C, David A, Mulè A, Ferraro L, Formica I, Murray RM and Fisher HL** (2013) Prevalence of bullying victimisation amongst first-episode psychosis patients and unaffected controls. *Schizophrenia Research* **150**, 169–175.
- Trotta A, Murray RM and Fisher HL** (2015) The impact of childhood adversity on the persistence of psychotic symptoms: a systematic review and meta-analysis. *Psychological Medicine* **150**, 1–18.
- Tsigebrhan R, Shibre T, Medhin G, Fekadu A and Hanlon C** (2014) Violence and violent victimization in people with severe mental illness in a rural low-income country setting: a comparative cross-sectional community study. *Schizophrenia Research* **152**, 275–282.
- Tucci AM, Kerr-Corrêa F and Souza-Formigoni MLO** (2010) Childhood trauma in substance use disorder and depression: an analysis by gender among a Brazilian clinical sample. *Child Abuse & Neglect* **34**, 95–104.
- van Dam DS, van der Ven E, Velthorst E, Selten JP, Morgan C and de Haan L** (2012) Childhood bullying and the association with psychosis in non-clinical and clinical samples: a review and meta-analysis. *Psychological Medicine* **42**, 2463–2474.
- van Os J, Rutten BP and Poulton R** (2008) Gene-environment interactions in schizophrenia: review of epidemiological findings and future directions. *Schizophrenia Bulletin* **34**, 1066–1082.
- Varese F, Smeets F, Drukker M, Lieverse R, Lataster T, Viechtbauer W, Read J, Van Os J and Bentall RP** (2012) Childhood adversities increase the risk of psychosis: a meta-analysis of patient-control, prospective- and cross-sectional cohort studies. *Schizophrenia Bulletin* **38**, 661–671.
- Wall MM and Amemiya Y** (2000) Estimation for polynomial structural equation models. *Journal of the American Statistical Association* **95**, 929–940.
- Widom CS, Czaja SJ and DuMont KA** (2015) Intergenerational transmission of child abuse and neglect: real or detection bias? *Science* **347**, 1480–1485.