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RESEARCH ARTICLE

REVISED Prevalence and correlates of neurocognitive

impairment and psychiatric disorders among schoolchildren

in Wakiso District, Uganda: a cross-sectional study [version 3;

peer review: 2 approved]

Margaret Nampijja^{1,2}, Wilber Sembajjwe¹, Harriet Mpairwe^{1,3}, Richard Mpango^{1,4}, Eugene Kinyanda^{1,5}

¹MRC/UVRI and LSHTM Uganda Research Unit, Entebbe, Uganda

²Maternal and Child Wellbeing Unit, African Population and Health Research Center, Nairobi, Kenya

³London School of Hygiene and Tropical Medicine, Keppel Street, Bloomsbury, London, London, WC1E 7HT, UK., UK

⁴Department of Mental Health, School of Health Sciences, Soroti University, Soroti, Uganda

⁵Department of Psychiatry, College of Health Sciences, Makerere University, Kampala,, Kampala, P.O. Box 7072, Kampala, Uganda

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Abstract

Background: There is limited data on the burden of mental disorders among children in the general population in Africa. We examined the prevalence and correlates of neurocognitive and psychiatric disorders among schoolchildren in Uganda.

Methods: This cross-sectional study enrolled 322 schoolchildren aged 5-17years in Wakiso, Uganda. We assessed for neurocognitive impairment using the Kaufmann-Assessment-Battery, and psychiatric disorders (major-depressive-disorder (MDD), attention-deficit-hyperactivity-disorder (ADHD), generalised-anxiety-disorder (GAD), and substance-use-disorder (SUD)) using the parent version of the Child and Adolescent Symptom Inventory-5, and Youth Inventory-4R Self Report. Prevalence and risk factors were determined using respectively descriptive statistics, and univariable and multivariable logistic regression.

Results: Twenty-five participants (8%) had neurocognitive impairment. Nineteen (5.9%) participants had MDD, nine (2.8%) had ADHD, seven (2.2%) had GAD, 14 (8.6%) had SUD; and 30 (9.3%) had any psychiatric disorder. Among the exposure variables examined in this study, including asthma, age, sex, grade of schooling, type of school and maternal and father's education and family socio-

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- 1. Joanna Martin (D), Cardiff University, Cardiff, UK
- 2. Rahul Shidhaye (D), Pravara Institute of Medical Sciences, Loni, India

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economic status, only asthma was associated with the disorders (MDD).

Conclusions: The relatively high burden of mental disorders in this general population of children warrants targeted screening of those at risk, and treatment of those affected. Further, future studies should extensively investigate the factors that underlie the identified psychiatric disorders in this and similar general populations.

Keywords

neurocognitive, psychiatric, disorders, children, adolescents, nonclinical

Corresponding author: Margaret Nampijja (maggie.nampijja@gmail.com)

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REVISED Amendments from Version 2

What is new in this version that was not in the previous version of the paper is that this version includes a description of the prevalence of the four psychiatric disorders by asthma status. There was a higher rate of major depressive disorder (MDD) among the asthmatic sub-sample than the non-asthmatic sub-sample. However, the rate of substance abuse disorder was higher in the non-asthmatic sub-sample but none in the asthmatic group. The rates of generalized anxiety disorder and ADHD were similar between the two groups. Therefore asthma seems to drive the prevalence of MDD in the sample but not the other disorders.

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Introduction

Globally, there is a significant burden of mental health problems among children and adolescents with a worldwide prevalence of approximately 20%¹⁻⁴. The problem is higher in low-income countries where poverty, diseases, and conflict increase the risk for these disorders, and yet access to mental health services is limited^{1,5}. In Uganda, for instance, studies have shown a high (about 18%) prevalence of neurocognitive impairment and psychiatric disorders among children and adolescents living with HIV/AIDS and in areas affected by civil war (northern Uganda)5-10. About 17% of children perinatally infected with HIV are reported to suffer neurological disorders¹¹ and around the same proportion (18%) have psychiatric disorders9. Among adolescents in northern Uganda and particularly those that were abducted during the war, there was a high prevalence of specific psychiatric disorders including post-traumatic stress disorder (26.8%), major depression (19.5%), and generalized anxiety disorder $(13.4\%)^5$.

Thus, a lot is known with regards to the burden of neurocognitive and psychiatric problems in children with HIV or exposed to conflict. However, there is limited data on the prevalence and risk factors of these disorders in the non-clinical and non-vulnerable (general) populations. Such populations are assumed to be healthy since they are not exposed to any known overt risk factors for neurocognitive and psychiatric disorders, yet they may carry genetic and perinatal vulnerabilities to these disorders^{12–16} or may have been exposed to traumatising events within their families¹⁷. Research carried out in the UK that examined risky behaviour among young people revealed that there is a shared risk for mental disorders regardless of whether one is vulnerable or not¹⁸. It is possible that effects of disease, conflict and other adverse exposures are superimposed upon this essential vulnerability^{2,18}.

Research and intervention programs have focused on children at risk of mental health problems because of a major exposure such as a serious medical condition (e.g. HIV), or adverse social circumstances (e.g. war, violence)^{19,20}. Absence of data on the mental disorders in the general population means that many children may be battling with mental health problems that are not recognised¹⁸. The child and adolescent mental health policy in Uganda recommends screening for mental, neurological and substance problems among school-going children and adolescents¹, however this has not been implemented implying that any children suffering from these disorders are not identified and therefore do not get treated^{1,21}. Failure to address neurocognitive and psychiatric challenges among children and adolescents may derail attainment of Sustainable Development Goal (SDG) targets including universal access to quality education (Goal 4) and minimising child abuse and neglect (Goal 16)²². This may consequently hold back the potential of this generation and in turn lock them in a vicious cycle of poverty. Epidemiological data on mental disorders among children in the general population are therefore critical. They will generate reference data for clinical populations, but also for monitoring trends in the burden of the disorders over time. Such data will inform the planning of appropriate interventions to respond to the problem in a timely manner and ultimately promote the mental wellbeing and productivity of affected individuals. The current study examined the prevalence of neurocognitive impairment and psychiatric disorders in a sample of non-clinical schoolchildren and adolescents living in a peri-urban setting in Wakiso, Uganda.

Methods

Design and setting

This work was nested within a case-control study that was investigating risk factors for asthma among schoolchildren in Uganda (SONA)²³. SONA was conducted among schoolchildren in Entebbe Municipality and Katabi zone in Wakiso District, central Uganda, a predominantly peri-urban area. All schools, primary and secondary, in this pre-determined study area were approached for SONA study between May 2015 to July 2017, and 96% of these participated²³. We nested the mental health sub-study in SONA, as a cross-sectional study to estimate the prevalence and risk factors of neurocognitive and psychiatric disorders among schoolchildren in a peri-urban setting.

Participants

For this mental health study, we recruited schoolchildren enrolled into the SONA study between March and August 2016, from a total of 41 primary and secondary schools. The mental health sub-study was done in 41 schools. The number of students enrolled per school varied between 1 and 35. Ten of the 41 schools were government-supported, while 31 were privately owned.

Eligibility (inclusion and exclusion criteria)

For the SONA study, all children with asthma symptoms were eligible and twice the number of children without asthma were randomly selected from the class register, using the random numbers generator programme in STATA (StataCorp, Texas, USA). A total of 1702 participants were recruited in the SONA study. For the mental health sub-study, all SONA participants enrolled between March and August 2016 and

interested in participating in the sub-study were eligible. This included schoolchildren with and without asthma. Children were excluded if the parent/guardian was not available to provide written informed consent and to answer the additional questionnaires for this sub-study. This is represented in the recruitment flow chart diagram (Figure 1).

Sociodemographic and health data collection. Sociodemographic data including children's age, sex, schooling information (including the status of the school based on the amount of school fees paid), and mothers' and fathers' highest education level were collected using a questionnaire which was administered to the children. Asthma was doctor-diagnosed as per the SONA protocol²³.

Assessing for psychiatric disorders. The psychiatric diagnoses were determined using the parent version (5–17 years) of the Child and Adolescent Symptom Inventory-5 (CASI-5)²⁴. This structured diagnostic interview was used to elicit the

following DSM V disorders: attention-deficit hyperactivity disorder of the inattentive type (ADHD-I), attention-deficit hyperactivity disorder of the hyperactivity-impulsive type (ADHD-HI), attention-deficit hyperactivity disorder-Combined (ADHD-C), generalised anxiety disorder (GAD), major depressive disorder (MDD), and substance use disorder (SUD). The CASI-5 also provides a global psychological assessment score for the children. The Youth Inventory-4R (YI-4R)-Self Report²⁵ was also used. The criteria for assessing the disorders looked at both CASI-5 and/or YI-4R. The whole spectrum of psychiatric disorders assessed by both tools were examined, however for the analysis we focused on four psychiatric disorders i.e. ADHD (all forms), GAD, MDD, and SUD (tobacco, marijuana, or illegal drugs) as only these were present in the study population; the rest were absent.

The CASI-5 (Parent version) was administered to parents/ guardians of children (5–11 years of age) at the schools of their children over the weekends. The YI-4 R was self-administered

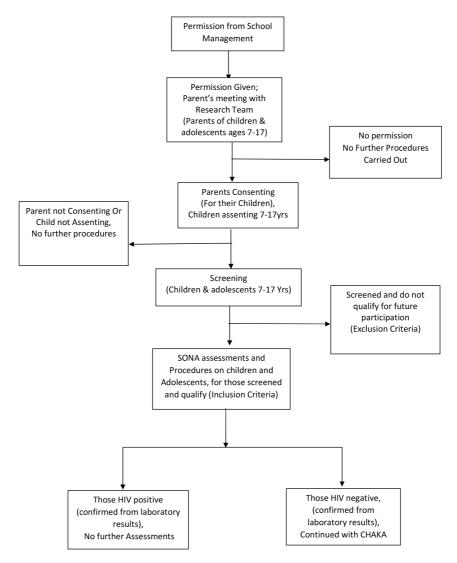


Figure 1. Recruitment flow chart for SONA /CHAKA.

to youths (12-18 years). Younger children did not complete this measure.

The disorders considered under the CASI-5 and YI-4-R were MDD, ADHD, GAD, separation anxiety disorders, social phobia, eating disorders (Anorexia and Bulimia Nervosa), Post Traumatic Stress Disorder (PTSD). Bipolar affective disorders, conduct disorders, oppositional defiant disorders, psychosis, Tics, somatic symptom disorder (SSD) and substance use disorder(SUD) (one item on the CASI-5, category O was used to screen for SUDs). Additionally, the CASI-5 also screened for autism spectrum disorder (ASD), Enuresis, Encopresis and excoriation disorder. The tool was culturally adapted and translated to Luganda the predominant language in the study setting.

Assessments were conducted at school by two psychiatric clinical officers (PCOs) who had training and experience in administering the different tools. Assessments were conducted for about 45 minutes. Children/adolescents identified to have emotional and behavioural disorders were given initial attention by the PCO but those with persistent symptoms were referred to Entebbe Hospital or Butabika Hospital for further management.

Assessing neurocognitive functioning. Neurocognitive functioning was assessed using the Kaufmann Assessment Battery (KABC-II) which has previously been validated in Uganda by Bangirana and colleagues²⁶. The KABC-II was used to measure performance of participants on Sequential Processing, Simultaneous Processing and Planning domains of intellectual ability. Assessments were conducted at school by two PCOs who had training and experience in administering these tools. These were supervised by a senior clinical psychologist. Individual assessment lasted about 40 minutes. Data collection was done using pre-coded questionnaires which were double entered into OpenClinica open source software version 3.1.4 (OpenClinica LLC and collaborators, Waltham, MA, USA).

Ethical approval and consent to participate

This study was approved by the Uganda Virus Research Institute Research and Ethics Committee (reference number GC/127/14109/481), and the Uganda National Council for Science and Technology (reference number HS 1707). The ethical approvals and consent were obtained for the overall SONA study, which contained information about this sub-study. All participants' parents or guardians provided written informed consent (or witnessed thumb print). In addition, children aged eight years and above provided written informed assent to participate in the study. In addition, we obtained permission from the head teachers and education officials from Wakiso district and Entebbe Municipality to conduct the study within the schools.

Statistical considerations

Sample size calculation. The mental health sub-study was observational and exploratory to measure the prevalence of neurocognitive impairment and psychiatric disorders among

schoolchildren; hence the sample size was not powered on any specific exposure or outcome. We used convenient sampling of SONA participants that were enrolled between March and August 2016, when the mental health sub-study was conducted. We aimed to recruit as many participants as possible from those enrolled into SONA therefore sampling was entirely based on convenience.

Data analysis. Statistical analyses were conducted using STATA version 15 (StataCorp, College Station, Texas, USA). Participants' characteristics were described using means and standard deviations for continuous variables, and proportions for categorical variables. Raw scores on neurocognitive tests were first described using means and standard deviations before the data were categorised into a binary variable. We compared neurocognitive scores based on each of the sociodemographic variables using group means. For each neurocognitive domain and for each age group, raw scores were converted into z-scores by dividing individual scores by the standard deviations in the respective domain. Neurocognitive impairment was defined as having a z-score of less than -2 in any of the domains, or a z-score of -1 in at least two domains. For the psychiatric disorders, binary diagnosis for each disorder was derived using a symptom count and other criteria as given by the CASI-5 and YI-4R scoring instructions.

Associations between neurocognitive impairment, with sociodemographic variables and psychiatric disorders were examined using crude and adjusted logistic regression (adjusting for each variable). Similarly, associations between psychiatric disorder and sociodemographic exposures were examined using crude and adjusted logistic regression analysis to generate odds ratios. For all analyses, the 95% confidence interval was determined.

Results

Participant sociodemographic characteristics

Of the 515 SONA participants seen, 322 participants (130 boys, 40.3%)²⁷ were enrolled and assessed for neurocognitive and psychiatric disorders, including children aged 5–11 years (n=158; 40.4%) and adolescents aged 12 to 17 years (n=164, 50.8%) (Table 1). The sociodemographic characteristics are summarised in Table 1. 193(37.5%) SONA participants were excluded because they did not meet the eligibility criteria.

Description of neurocognitive abilities among the participants

A total of 321 participants had complete data on the Simultaneous Processing scale, the group mean score was 13.2 (s.d, 5.9), range 2–41. All 322 participants completed the Sequential Processing scale, their mean score was 14.4 (s.d, 4.4), range 3–26. Planning scale was completed by only 130 children, since we did not assess the adolescents on this scale. Mean score on this scale was 5.3 (s.d, 2.9) and range 1–13. Medians and interquartile ranges of these scores were also explored. These results are summarised in Table 2. Performance data on each of the scales had a nearly normal distribution (Supplementary Figure 1, *Extended data*²⁷)

Mean neurocognitive scores were compared based on sex, age, school type, school status, school grade and found differences between the groups. Boys performed better than girls in Simultaneous Processing (mean diff=2.5, p<0.001); and Sequential Processing (mean diff=1.3, p<0.001), but in Planning they (boys) had a lower mean score than girls (mean diff=-0.8, p<0.001).

Participants attending privately owned schools had higher scores than those in government-supported schools, and

Table 1. Sociodemographic characteristics of participants (N=322).

Factor	Level	N (%)
Age (categorised)	Child (5–11 years) Adolescent(12–17yrs)	158(48.9) 164(50.8)
Sex	Boys Girls	130(40.3) 193(59.7)
Type of school funding	Government funded Privately owned	144(44.9) 177(55.1)
Economic status of school	Low High	158(49.2) 163(50.8)
*Grade	P1 – P4 P5 – P7 S1 – S4 S5 – S6	121(37.5) 69(21.4) 113(35) 6(1.9)
Father's education	None Primary Secondary Tertiary	9(2.8) 92(28.7) 126(39.4) 93(29.1)
Mother's education	None Primary Secondary Tertiary	3(1.0) 124(38.9) 118(36.9) 74(23.2)
Asthma status	Yes No	61(19.1) 258(80.9)

*Grades P1-P4 correspond with 6–9 years of age; P5-P7 with age 10–12 years; S1-S with age 13–16 years; S5-S6 with 17–18 years.

the differences were significant for all the domains: Simultaneous Processing (mean diff=1.5; p<0.001); Sequential Processing domains (mean diff=1.2; p<0.001), and Planning (mean diff=1.1; p<0.001) (Table 3). Similarly, higher scores were observed in participants attending high economic status schools than those in lower status schools, and the differences were significant for Simultaneous Processing (mean diff=3.0; p<0.001); Sequential Processing domains (mean diff=2.4; p<0.001), and Planning (mean diff=1.5; p<0.001) (Table 3).

Unexpectedly, children had higher scores than adolescents on Simultaneous Processing (mean diff=2.3, p<0.001) and Sequential Processing (mean diff=2.6, p <0.001) (Table 3). In the same way, participants in lower classes (academic level) tended to have higher scores than those in higher classes and this was significant for Simultaneous Processing (p<0.001), and Sequential Processing (p<0.001). Children whose parents (father or mother) had tertiary education tended to have the highest scores. The differences in means were significant for Simultaneous Processing, Sequential Processing and Planning (Table 3). We purposed to assess both the children and adolescents on all the subscales, however, the planning scale was erroneously missed for the adolescents.

Prevalence of neurocognitive impairment among participants

The z-scores on each neurocognitive domain showed a normal distribution (Figure 2). Categorising performance data based on z-scores showed that, six participants had z-score of less than -2 in any domain, and 19 participants had z-score -1 in two or more domains. Hence, 25 participants (8%); 95% CI (5.5% -11.6%) were categorised as having neurocognitive impairment.

Associations between sociodemographic factors and neurocognitive impairment

Academic level (grade) of the participant had a borderline significant association with neurocognitive impairment [adjusted odds ratio (aOR)=0.18; confidence interval (CI)= (0.03; 0.89); P=0.047]; the rest of the exposure variables were not significantly associated with neurocognitive impairment (p>0.05) (Table 4).

Prevalence of and risk factors for psychiatric disorders Four psychiatric disorders MDD, ADHD, GAD, and SUD (tobacco, alcohol, marijuana) were found in this study population;

Neurocognitive domain	N =322	Mean(SD)	Median (Interquartile range)	(Min, max)	skewness	kurtosis
Simultaneous processing scale	321	13.2(5.9)	12(4,31)	(2,41)	1.27	5.70
Sequential processing scale	322	14.2(4.4)	14(6,24)	(3,26)	0.29	2.48
Planning	130	5.3(2.9)	5(3,7)	(1,13)	0.67	2.91

		Simultaneous Processing scale	p-value	Sequential Processing scale	p-value	*Planning	p-value
Sex	Male Female	14.7 12.2	<0.001	14.6 13.9	<0.001	5.0 5.8	<0.001
Age category	Children Adolescents	14.4 12.1	<0.001	15.5 12.9	<0.001		
Type of school	Private Government	13.9 12.4	<0.001	14.7 13.5	<0.001	5.9 4.8	<0.001
Economic status of school	Low status High status	11.7 14.7	<0.001	12.9 15.3	<0.001	4.5 6.0	<0.001
Grade	P1 – P4 P5 – P7 S1 – S4 S5 – S6	14.3 13.3 12.0 12.1	<0.001	15.3 14.2 12.8 13.1	<0.001	5.4 5.4 -	0.591
Father's education	None Primary Secondary Tertiary	14.5 12.8 12.8 14.1	<0.001	15.1 14.0 13.8 14.8	<0.001	3 5.1 4.6 6.7	0.006
Mother's education	None Primary Secondary Tertiary	12.8 13.1 12.8 14.1	<0.001	14.3 14.2 13.8 14.7	0.006	5.6 5.4 5.4 5.6	0.518
Asthma status	Yes No	12.9 13.3	0.281	13.8 14.3	0.102	5.2 5.5	0.142

Table 3. Comparison of neurocognitive scores base	d on sociodemographic variables.
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*Planning was done only among children

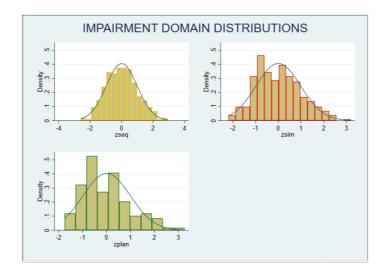


Figure 2. Distribution of neurocognitive impairment (z-scores). Zseq – Sequential Processing scale; Zsim – Simultaneous Processing scale; Zplan – Planning scale.

Factor	level	Crude OR (95%CI)	*Adjusted OR (95%CI)
Sociodemographic characteristics			Aujusteu OK (JS/Jel)
Age (categorised)	Child (5–11 years) Adolescent (12–17yrs)	1 0.58(0.25; 1.31) p=0.189	1 0.51(0.22; 1.19) p=0.120
Sex	Boys Girls	1 1.57(0.66; 3.72) p=0.307	1 1.81(0.75; 4.39) p=0.187
Type of school funding	Government Private	1 0.80(0.36; 1.78) p=0.583	1 0.74(0.33; 1.66) p=0.466
Economic status of school	Low High	1 0.58(0.25; 1.32) p=0.194	1 0.48(0.20; 1.13) P=0.156
Grade	P1 – P4 P5 – P7 S1 – S4 S5 – S6	1 0.32(0.09; 1.15) 0.40(0.15; 1.06) 1 p=0.061	1 0.18(0.03; 0.89) 0.14(0.03; 0.75) 1 p=0.047
Mother's highest education level attained	None Primary Secondary Tertiary	1 9.9(1.28; 76.6) 5.2(0.64; 42.7) 1 P=0.056	1 7.5(0.95; 59.6) 4.7(0.56; 40.35) 1 P=0.133
Father's highest education level attained	None Primary Secondary Tertiary	1 0.37(0.07; 2.11) 0.27(0.05; 1.49) 0.20(0.03; 1.23) P=0.318	1 0.22(0.03; 1.43) 0.20(0.03; 1.29) 0.13(0.02; 0.91) P=0.237
Psychiatric illness factors			
Major depressive disorder	Yes	0.62(0.08; 4.84) p=0.648	0.58(0.07; 4.58) P=0.606
Attention deficit hyperactive disorder	Yes	1.45(0.17; 12.02) P=0.733	1.15(0.13; 9.96) P=0.897
Generalised anxiety disorder	Yes	1.94(0.22; 16.74) P=0.547	1.44(0.16; 12.98) P=0.741
At least one psychiatric disorder	Yes	0.80(0.18; 3.57) P=0.770	0.92(0.19; 4.26) P=0.913
Substance use			
Use of at least one substance	Yes	2.94(0.56; 15.41) P=0.203	2.93(0.54; 15.69) P=0.210

Table 4. Factors associated with neurocognitive impairment among school children.

OR=odds ratio, CI=confidence interval, P=primary, S=secondary; *association with each sociodemographic variable was adjusted for all the other sociodemographic variables in this table

the other disorders were not present. The prevalence of the four disorders was as follows: MDD was 5.9% (n=19); ADHD 2.8% (n=9); GAD 2.2% (n=7); and SUD 8.6% (n=14). Of the nine participants found to have ADHD, seven presented with the inattentive type while two had hyperactive-impulsive type. Prevalence of any psychiatric disorder was 9.3% (n=30), and was more common among children (12.0%) than adolescents (6.7%). There were no significant differences in the prevalence

of psychiatric disorders between boys (8.5%) and girls (9.8%) (p=0.675).

We conducted crude and adjusted logistic regressions between having any psychiatric disorder and the sociodemographic variables. Asthma was found to be associated with MDD (AOR, 95%CI 2.71 1.02; 7.20) but not with the other disorders. None of the sociodemographic characteristics were significantly associated with having any psychiatric disorder (p>0.05) both in the crude and adjusted logistic regressions (Table 5).

Prevalence of psychiatric disorders by asthmatic status Subgroup analysis for the prevalence of the four psychiatric disorders among children with and without asthma revealed a higher rate of MDD in the asthmatic sub-sample than the non-asthma sub-sample (11.7% versus 4.6%), and a higher prevalence of substance abuse among non-asthmatic sub-sample, with none in the asthmatic sub-sample. The rates of ADHD and Generalised anxiety disorder were similar between the two groups. These data are shown in Table 6.

Table 5. Associations between psychiatric disorders and soci	o demographic characteristics (*Adjusted OR; 95%CI).
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		Major depressive disorder Adjusted OR; 95%CI*	Attention deficit hyperactive disorder Adjusted OR; 95%CI*	Generalized anxiety disorder Adjusted OR; 95%CI*	Substance abuse disorder	At least one psychiatric disorder (MDD,ADHD,GAD) Adjusted OR; 95%CIv
Age (categorised)	Child Adolescent	1 0.74(0.12;4.39) P=0.740	-	-	-	1 0.37(0.08;1.79) P=0.218
Sex	Male Female	1 2.10(0.64;6.83) P=0.215	1 0.62(0.14;2.72) P=0.533	1 1.42(0.30;6.58) P=0.655	1 1.01(0.29; 3.49) P=0.984	1 1.18(0.52;2.71) P=0.687
Type of school funding	Government Private	1 0.34(0.11;1.02) P=0.049	1 0.73(0.17;3.08) P=0.673	1 4.99(0.58;42.71) P=0.142	1 1.61(0.50; 5.20) P=0.422	1 0.71(0.32;1.59) P=0.411
Economic status of school	Low High	1 0.37(0.12;1.13) P=0.083	1 0.36(0.08;1.56) P=0.172	1 4.13(0.48;35.33) P=0.195	1 0.63(0.19; 2.27) P=0.511	1 0.59(0.26;1.34) P=0.210
Grade	P1 – P4 P5 – P7 S1 – S4 S5 – S6	1 1.57(0.33;7.38) 1.49(0.19;11.84) 12.60(0.96;164.8) P=0.1443	1 0.49(0.06;4.14) - - P=0.512	1 1.40(0.26;7.59) - - P=0.655	1 1 0.66(0.07; 6.17) 1 P=0.719	1 1.06(0.35;3.25) 1.05(0.17;6.35) 9.34(0.88;98.55) P=0.145
Mother's highest education level attained	None Primary Secondary Tertiary	1 1.38(0.31;6.05) 1.62(0.39;6.72) - P=0.799	1 0.37(0.06;2.40) 1.12(0.21;6.07) - P=0.458	1 0.53(0.07;4.02) 1.60(0.25;10.39) - P=0.495	1 2.42(0.26; 22.76) 2.74(0.31; 23.69) 1 P=0.401	1 0.67(0.24;1.89) 1.01(0.37;2.78) - P=0.655
Father's highest education level attained	None Primary Secondary Tertiary	1 0.46(0.04;4.72) 0.34(0.03;3.50) 0.21(0.02;2.50) P=0.582	1 0.39(0.03;4.53) 0.30(0.02;3.92) 0.29(0.02;3.82) P=0.794	1 0.80(0.11;6.05) 1.45(0.23;9.20) - P=0.810	1 1.28(0.30; 5.47) 0.56(0.14; 2.29) 1 P=0.541	1 1.14(0.12;10.35) 0.89(0.10;8.23) 0.80(0.08;7.53) P=0.919
Asthma	Non-asthmatic Asthmatic	1 2.71 (1.02; 7.20) P= 0.046	1 1.24(0.25;6.11) P=0.795	1 0.71(0.08; 6.03) P=0.755	1 -	1 2.01(1.05;3.11) P<0.001

OR=odds ratio, CI=confidence interval. P=primary. *Adjusted for other sociodemographic variables.

Psychiatric Disorder	Asthmatic N=61 Prevalence (95%CI)	Non-asthmatic N=258 Prevalence (95%CI)
Major Depressive Disorder	n=7 11.7%(5.6% - 22.8%)	n=12 4.6%(2.7% - 8.0%)
Attention Deficit Hyperactive Disorder	n=2 3.3%(0.8% - 12.7%)	n=7 2.7%(1.2% - 5.5%)
Generalised Anxiety Disorder	n=1 1.7%(0.2% - 11.3%)	n=6 2.3%(1.0% - 5.1%)
Substance Abuse	n=0	n=14 10.9%(6.5% - 17.7%)
Any psychiatric disorder	n=8 13.1(6.6% - 14.4%)	n=22 8.5%(5.7% - 12.6%)

Table 6. Prevalence of psychiatric disorders by asthma.

Discussion

The main aim of the current study was to measure the prevalence of neurocognitive and psychiatric disorders in schoolchildren in Uganda using a sample of children drawn from the general population. The prevalence of neurocognitive impairment and any psychiatric disorder was 8% and 9.3%, respectively. Among the many psychiatric disorders examined in the sample, four were found to be prevalent, these were ADHD (all forms), GAD, MDD, and SUD (tobacco, marijuana, or illegal drugs). The burden of specific disorders varied, with substance use disorder presenting the highest burden at 8.6% followed by MDD (5.9%), ADHD (2.8%) and lowest for general anxiety (2.2%). The overall prevalence of psychiatric disorders in this sample of schoolchildren is less than the 20% reported globally, and as would be expected, less than the rates reported in children affected by HIV and war, however, it represents a significant burden of mental disorder in a general population that is assumed to be healthy. These results indicate that ideally in this population children and adolescents would benefit from routine screening for neurocognitive and psychiatric disorders, and provision of treatment for those found to be affected in line with the existing policy on routine screening. The government, through the Ministry of Health, could ensure that this policy is implemented. That said, routine screening for mental disorders in the entire (general) child and adolescent population would be expensive and maybe not feasible given the limited funds within which the Ministry of Health operates. It would perhaps be more practical and possibly more cost-effective to conduct targeted screening for psychiatric and neurocognitive disorders among those at risk and those showing signs of dysfunction in the identified mental health areas such as poor academic performance, social isolation, depressed mood, fear and anxiety, and conduct behaviour.

We explored associations between neurocognitive impairment, psychiatric disorders and sociodemographic and health

factors to identify possible risk factors. Mean differences in neurocognitive scores (as a continuous variable) based on the different characteristics were observed and all were in the expected direction except the differences between children and adolescents, and between lower and higher academic class which were in the opposite direction. This finding was unexpected since developmentally adolescents should exhibit more mature cognitive skills including planning and inhibitory control than younger children. The surprising finding could be due to the tendency of some adolescents to take on deviant behaviour as they go through the self-identification that characterises the adolescent stage²⁸ and hence appearing to be more impulsive than young children.

We noted gender differences in the cognitive scores particularly where males performed better than females on sequential and simultaneous processing scales, while in planning, females performed better than the males. Gender differences in cognitive abilities have been widely studied using various tests, and have revealed differences in performance between males and females (girls and boys) with many showing a consistent pattern where females outscore males on the planning ability^{29,30}. It is possible that females naturally have an advantage in planning over the males, therefore not surprising that these differences were observed in this study population.

However, adjusted logistic regressions analysis showed that among the factors examined, only having history of asthma was significantly associated with the mental disorders, and this was only with MDD. The recruitment for this study was originally for a case-control study of asthma and the sample was over-represented for asthma (19.1% of the sample). The over-representation of asthma in the sample appears to have increased the prevalence of major depressive disorder but not substance abuse which was absent among asthmatics or generalised anxiety disorder and ADHD which were relatively similar between the asthmatic and non-asthmatic subgroups. Absence of associations with other factors might be because of the small number of participants with neurocognitive impairment and psychiatric disorder in the sample. Hence we are not able to identify other factors that underlie the burden of mental health disorders in this sample of children. We recommend larger studies to explore this topic further.

We acknowledge the following limitations. First, the study was conducted within a larger study and was limited to the few sociodemographic items that were assessed in the main study. In as much as the risk factors included in the analysis were based on previous literature, the availability of information on those variables in the SONA study also determined what exposure variable was included in the analyses. Apart from asthma which was the main exposure in the SONA study, other risk factors for the neurocognitive and psychiatric outcomes used i.e. age, sex, grade of schooling, type of school and maternal and father's education and family socio-economic status were included both based on the theoretical grounds but also because data on these had been collected within the main study. Hence, as such, mother's and father's highest education level attained, the school type and school status (determined based on amount of school fees) that the child was attending were used as a proxy for socioeconomic status (SES). A more exhaustive measure of SES might have provided better discrimination with regards to the risk for neurocognitive impairment and psychiatric disorder and probably shown associations that have been reported in previous studies³¹. Secondly, household exposures such as domestic violence, single parenthood and other family characteristics have been reported to be associated with mental health problems in children³¹⁻³⁵; however, as explained above, there was limited collateral information regarding the family environment hence it was not possible to examine the role of household characteristics in this study. Thirdly, the modest sample size and cross-sectional design of the study further limited the capacity of the study to effectively examine risk factors associated with neurocognitive and psychiatric disorders. Of note, it was surprising that ADHD was not associated with neurocognitive impairment; this could have been due to the few cases of ADHD (n=9) and of neurocognitive impairment (n=25) that were found in the study population. Out of the 1702 participants who took part in SONA, 322 (18.9%) were included in the neurocognitive study, by convenient sampling. Ideally, a predetermined and randomly selected sample size would have provided a more representative sample. Although the decision to undertake the neurocognitive study was made from the beginning of the SONA study, actual data collection began much later (due to logistical reasons), therefore it was not possible to apply a systematic sample size calculation and random sampling. We opted for convenient sampling through which 37.5% of the SONA participants who were seen during the period were not included in neurocognitive assessments because their parents did not send back the consents or other exclusion criteria. There was therefore a risk for a selection and response bias since individuals who need help or who perceive themselves to have a health problem tend to volunteer to participate in studies of this nature. On the other hand, their interest in participating was probably out of a general curiosity

to know about their children's mental health status since such opportunities are not common in this setting. Lastly, the SONA study in which our study was nested was conducted in schools and within a peri-urban setting and hence there was no opportunity to examine the neurocognitive and psychiatric disorders in children and adolescents out of school and from rural settings. This may limit the generalisability of our findings to the general population.

Nonetheless, this study provided important data, and an epidemiological picture on the prevalence of neurocognitive and psychiatric disorders of these conditions among children and adolescents in the general population in Uganda, and filled an important gap in the literature, particularly for tropical Africa. Future studies that recruit a much larger and random sample of participants are recommended.

Chronic diseases including HIV have been associated with poor neurodevelopmental outcomes in children^{19,20,36}. As part of the SONA study, all participants in this sub-study were tested for HIV and all were negative. The prevalence of asymptomatic malaria (thick smear) and worm infection was very low²³ and all children reported to be in good health (no complaints) at the time of assessments. A fifth of the participants reported history of asthma, and even though they were clinically in good health at the time of neurocognitive and psychiatric assessments, the data showed significant association between being asthmatic and major depressive disorder. Therefore, apart from those that reported history of asthma, the rest of this sample of children and adolescents were considered to be in good health status and hence would represent a general population.

Conclusion

This study provides epidemiological data on the prevalence of neurocognitive and psychiatric disorders in the general population of children and adolescents in Uganda. The high prevalence of neurocognitive and mental disorders calls for investigation of risk factors using an epidemiological study, and for operationalisation of the child and adolescent mental health policy in Uganda through targeted screening of children and adolescents at risk¹. These data also provide very useful reference figures from the general population to compare with clinical populations including HIV, and to track trends in the burden of mental health problems over time. Having accurate data on the true burden of disease is vital for necessary interventions to be instituted in order to promote the mental wellbeing of children and adolescents. Larger epidemiological studies should be undertaken to generate more evidence on the burden and risk factors for mental health problems in children and adolescents in the general population, including exploring the role of the family and community environment.

Data availability

Underlying data

LSHTM Data Compass: CHAKA-SONA Normative dataset, https://doi.org/10.17037/DATA.00002434²⁷.

This project contains the following underlying data:

- Normative_dataset.txt (sociodemographic information, health and neurocognitive and psychiatric outcomes)

Due to ethical considerations surrounding the sensitivity of the data in a vulnerable population, study consents limited the access to underlying data from this study. However, controlled access to the data posted in the above repository is permitted, subject to approval from the Uganda Virus Research Institute Research (UVRI) Ethics Committee and the Uganda National Council for Science and Technology. If access is approved, the applicant / their host institution will be asked to sign a Data Transfer Agreement, which includes conditions for the secure storage of data. Dataset use for further research will require additional ethics approval by the ethics committees that approved the original research. Access can be requested through the 'Request access' button in the above data project. The codebook (Normative_dataset_codebook.html) is available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

Extended data

Data Compass: CHAKA-SONA Normative dataset, https://doi. org/10.17037/DATA.00002434²⁷.

This project contains the following extended data:

- CHAKA-SONA_support_documents.zip (questionnaires and participant consent forms)

Data are available under the terms of the Data Sharing Agreement, as above.

- Supplementary_Figure1.pdf (Distribution of performance on neurocognitive scales – raw scores)

Supplementary Figure 1 is available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

Authors' contributions

MN led the writing of the manuscript and participated in the data collection and analysis; WS led the analysis and contributed to the writing of the manuscript; RM contributed to the design and implementation of the research, data analysis and writing of the manuscript; HM participated in the design and implementation of the research, data analysis and writing of the manuscript; EK led the study design and implementation of the research and participated in manuscript writing. All authors read and approved the final manuscript.

Acknowledgements

We thank the participants for taking part in the study. We are grateful to the school administration and teachers for their support in the recruitment and assessment of the participants. We appreciate the study team including the asthma study staff for their hard work and enthusiasm. Appreciation is extended to the research assistants (Ms Jane Edwards and Ms Teddy Ayikoru) who conducted the neurocognitive and psychiatric assessments, and other data collection procedures for this study.

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Version 3

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Joanna Martin 匝

MRC Centre for Neuropsychiatric Genetics and Genomics, Division of Psychological Medicine and Clinical Neurosciences, Cardiff University, Cardiff, UK

I have no further comments on this paper now.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Child psychiatry, neurodevelopment, mental health, epidemiology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 2

Reviewer Report 17 October 2022

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Rahul Shidhaye 匝

Department of Research, Pravara Institute of Medical Sciences, Loni, Maharashtra, India

Authors have satisfactorily addressed all my comments. I would like to thank the authors for same and congratulate them on undertaking and publishing this important work.

Competing Interests: Rahul Shidhaye is supported by DBT-WELLCOME Trust India Alliance intermediate fellowship in clinical and public health research. The review of this article is not affected by the ongoing fellowship.

Reviewer Expertise: Global Mental Health, Implementation Research, Yoga, Epidemiology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 11 October 2022

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? Joanna Martin 匝

MRC Centre for Neuropsychiatric Genetics and Genomics, Division of Psychological Medicine and Clinical Neurosciences, Cardiff University, Cardiff, UK

Thank you for responding to my previous comments. I am happy with the responses, except for the response to my comment #9, which I think has not been fully addressed yet. Although the authors noted that the only significant association between asthma and the studied disorders in this sample is MDD, the lack of significant associations with other disorders could simply be due to the small sample size, so my other suggestions could still be worthwhile to help provide additional information.

Here is my previous comment:

9. The recruitment for this study was originally for a case-control study of asthma and therefore it seems the sample is over-represented for asthma (19.1% of the sample according to Table 1). There is some evidence that asthma is associated with ADHD and therefore this over-representation of asthma in the sample may have increased the prevalence of these other problems observed in the sample. This should be mentioned in the Discussion. The authors should also check what the prevalence results for the psychiatric disorders look like in the subsample without asthma.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Child psychiatry, neurodevelopment, mental health, epidemiology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 15 Nov 2022

Margaret Nampijja, MRC/UVRI and LSHTM Uganda Research Unit, Entebbe, Uganda

We thank the reviewer for the comment raised about overrepresentation of asthma in the sample. We have checked prevalence of the psychiatric disorders among the asthmatic subsample and the non-asthmatic subsample and found a higher prevalence of major depressive disorder in the asthmatic group than the non-asthmatic group; a higher rate of substance abuse in the non-asthmatic group but none in the asthmatic group. The prevalence of generalized anxiety disorders and ADHD were similar between the two groups. Therefore asthma appears to drive the prevalence of MDD in the sample but not the other disorders.

These results are now included in the revised manuscript in (Table 6) and in the discussion.

Competing Interests: None

Version 1

Reviewer Report 30 May 2022

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了 🛛 Rahul Shidhaye 问

Department of Research, Pravara Institute of Medical Sciences, Loni, Maharashtra, India

This study aims to estimate the prevalence of neurocognitive impairment and psychiatric disorders in a sample schoolchildren and adolescents without HIV or other diagnosed health condition living in a peri-urban setting in Wakiso, Uganda. The study found that 8% participants had neurocognitive impairment, 5.9% had major depression, 2.8% had attention deficit hyperactivity disorder, 2.2% had generalized anxiety disorder, and 8.6% had substance use disorder.

- 1. In the first sentence of the abstract, it will be preferable to use the term, 'general population', or 'community sample' of schoolchildren instead of 'healthy' children.
- 2. The last sentence of the methods section of the abstract mentions, 'prevalence and risk factors were determined using percentages and logistic regression'. It will be good to say 'descriptive statistics' instead of percentages and specify simple/multiple logistic regression.
- 3. In the results section of the abstract, please mention the risk factors which were not found to be associated with the outcomes.

- 4. The term, 'unexpectedly high burden' can be modified as we don't know the expected burden of mental disorders and neurocognitive impairment in general population.
- 5. The study aimed to estimate prevalence of neurocognitive impairment and mental disorders in children in general population. If so, why only school children living in a periurban setting were selected? It is likely that these outcomes are worse in children from rural areas and not attending school. This limits the generalisability of the study findings and should be clearly mentioned in the limitations section.
- 6. The participants were selected using convenience sampling. This needs further clarification. Was there any sampling frame from which children were selected with some randomness in selection or was it entirely based on convenience?
- 7. What was the proportion of children excluded as parent was not available? This and the issue mentioned in previous comment are likely to introduce selection bias. This needs to be clearly mentioned in the limitations.
- 8. Please provide the participant flow chart in the beginning of the results section.
- 9. Is CASI-5 validated in the local language? Kindly provide the details.
- 10. Authors provide a list of disorders considered under the CASI-5 and YI-4-R. However, in the results section only four disorders are covered. Please explain.
- 11. What theoretical model/conceptual framework/DAG (Directed Acyclic Graph) guided the selection of risk factors for the outcomes studied? It is fine that only a few of the factors were included in the study and it will be good for the readers to know that the relation between the potential risk factors and the outcomes.
- 12. Why were adolescents excluded from the planning scale? This will be good for the readers to know.
- 13. It will be desirable to present median and inter-quantile range for descriptive summaries in table 2.
- 14. Figure 1 and 2 can be presented as supplementary material.

Is the work clearly and accurately presented and does it cite the current literature? $\ensuremath{\mathsf{Yes}}$

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others? Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility? $\ensuremath{\mathsf{Yes}}$

Are the conclusions drawn adequately supported by the results? Yes

Competing Interests: Rahul Shidhaye is a DBT-Wellcome Trust India Alliance Intermediate Fellow in Clinical and Public Health Research. This review was completed in an impartial manner with no influence from the reviewer's affiliation.

Reviewer Expertise: Global Mental Health, Implementation Research, Yoga, Epidemiology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 08 Sep 2022

Margaret Nampijja, MRC/UVRI and LSHTM Uganda Research Unit, Entebbe, Uganda

RESPONSES TO REVIEWER 2

This study aims to estimate the prevalence of neurocognitive impairment and psychiatric disorders in a sample schoolchildren and adolescents without HIV or other diagnosed health condition living in a peri-urban setting in Wakiso, Uganda. The study found that 8% participants had neurocognitive impairment, 5.9% had major depression, 2.8% had attention deficit hyperactivity disorder, 2.2% had generalized anxiety disorder, and 8.6% had substance use disorder.

1. In the first sentence of the abstract, it will be preferable to use the term, 'general population', or 'community sample' of schoolchildren instead of 'healthy' children.

RESPONSE: Thank you for this observation, the word 'general' has been adopted replace health population in the abstract and in the main text.

2. The last sentence of the methods section of the abstract mentions, 'prevalence and risk factors were determined using percentages and logistic regression'. It will be good to say 'descriptive statistics' instead of percentages and specify simple/multiple logistic regression.

RESPONSE: Thank you for the advice. We have made the necessary modification to the sentence. We used univariable and then multivariable logistic regression to examine the risk factors. This too has now been clarified in the methods section of the abstract. [Page 3]

3. In the results section of the abstract, please mention the risk factors which were not found to be associated with the outcomes.

RESPONSE: These exposure variables including asthma, age, sex, grade of schooling, type of school and maternal and father's education and family socio-economic status) have now been inserted.[Page 3]

4. The term, 'unexpectedly high burden' can be modified as we don't know the expected burden of mental disorders and neurocognitive impairment in general population. **RESPONSE:** The word "unexpectedly" has been replaced with "relatively" [Page 3]

5.The study aimed to estimate prevalence of neurocognitive impairment and mental disorders in children in general population. If so, why only school children living in a periurban setting were selected? It is likely that these outcomes are worse in children from rural areas and not attending school. This limits the generalisability of the study findings and should be clearly mentioned in the limitations section.

RESPONSE: Thank you for highlighting this limitation. The SONA study in which our study was nested was conducted in schools and within a peri-urban setting and hence there was no opportunity to examine the neurocognitive and psychiatric disorders in children and adolescents out of school and from rural settings. This may limit the generalisability of our findings to the general population. This limitation has been acknowledged. [Page 16]

6. The participants were selected using convenience sampling. This needs further clarification. Was there any sampling frame from which children were selected with some randomness in selection or was it entirely based on convenience?

RESPONSE: We used convenient sampling of SONA participants that were enrolled between March and August 2016, when the mental health sub-study was conducted, and aimed to recruit as many participants as possible from those enrolled into SONA, therefore sampling was entirely by convenience. The 'entirely by convenience' has been highlighted under sample size section. [Page 7].

7.What was the proportion of children excluded as parent was not available? This and the issue mentioned in previous comment are likely to introduce selection bias. This needs to be clearly mentioned in the limitations.

RESPONSE: SONA study sample size (during the time of the CHAKA Normative study =515 participants)

The number of participants who met the entry criteria for the CHAKA normative study (322 participants).

Therefore, the number and proportion of children excluded (who never met entry criteria; parent was not available) was 193 (37.5%). We recognize that this could have created a selection bias and hence a bias in the findings reported. The number is clarified on page 7, and the limitation has been acknowledged in the limitation section [page 16].

8. Please provide the participant flow chart in the beginning of the results section.

RESPONSE: A flow chart (Figure 1) showing how the participants were selected from the

SONA study has been inserted in the methods section. We felt that the flow chart fits more appropriately within the description of participant selection.

9. Is CASI-5 validated in the local language? Kindly provide the details.

RESPONSE: Yes, the CASI-5 was culturally adapted and translated in the local language(Luganda) that is predominantly used in the study setting. This has been indicated in the methods section. [Page 6]

10. Authors provide a list of disorders considered under the CASI-5 and YI-4-R. However, in the results section only four disorders are covered. Please explain.

RESPONSE: We would like to clarify that the whole spectrum of disorders assessed by the CASI-5 and YI-4-R were examined in the study population. However only those that were present i.e. ADHD, MDD, GAD & SUD were included in the analysis. This has been clarified both in the methods and results section.[Page 6]

11. What theoretical model/conceptual framework/DAG (Directed Acyclic Graph) guided the selection of risk factors for the outcomes studied? It is fine that only a few of the factors were included in the study and it will be good for the readers to know that the relation between the potential risk factors and the outcomes.

RESPONSE: The rational for the selection of risk factors that were included on the analysis was based on literature but also on the availability of information on those variables in the SONA study. In addition to asthma which was the main exposure in the main study, other risk factors including age, sex, grade of schooling, type of school and maternal and father's education and family socio-economic status included based on scientific(theoretical) relevance and because the data on these were available in the main SONA study. Since the study conducted within a larger study, we were limited to the few sociodemographic variables that were assessed in the main study. This limitation has been expanded under the discussion section. [Page 15]

12.Why were adolescents excluded from the planning scale? This will be good for the readers to know.

RESPONSE: We purposed to assess both the children and adolescents on all the subscales, however, the planning scale was erroneously missed for the adolescents. This has been indicated on page 10.

13. It will be desirable to present median and inter-quantile range for descriptive summaries in table 2.

RESPONSE: We had chosen Mean(SD) because of the spread of the data. However, with your advice, we have also included the median(IQR) of the same. [Table 2]

Figure 1 and 2 can be presented as supplementary material.

RESPONSE: We have taken your advice and that of the first reviewer, and moved the two Figures (now 2 and 3) Figures to the data repository as extended data. This is the equivalent of supplementary material for the Wellcome Open Research Journal.

Competing Interests: No competing interests were disclosed.

Reviewer Report 13 September 2021

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了 🛛 Joanna Martin 匝

MRC Centre for Neuropsychiatric Genetics and Genomics, Division of Psychological Medicine and Clinical Neurosciences, Cardiff University, Cardiff, UK

This is an epidemiological study examining the prevalence of neurocognitive impairments and psychiatric disorders in 322 school children aged 5-17 years old in Uganda. The results indicate that 8% of the sample had neurocognitive impairments and 9.3% had at least one psychiatric disorder. I have the following minor suggestions for improvement:

- 1. The authors describe the sample as "healthy" or "assumed healthy" in the abstract, introduction and discussion. This should be replaced with terms such as "general population" or "reference population" or "community sample" to be more accurate as we cannot assume that a sample of school children will be completely healthy. I would also suggest replacing "normal population" (in Discussion) with one of the terms above.
- 2. In the method, the authors note that the CASI-5 and YI-4-R can be used to assess many different psychiatric conditions but they focused only on ADHD, MDD, GAD & SUD. It later appears that this was because none of the other conditions were present in the sample. Can the authors clarify in the Method that they examined each of the conditions and only mention that they then focused on the specific conditions in the Results? The Discussion and abstract should also explicitly state that other disorders were also assessed but not detected in the sample.
- 3. Please state how the binary diagnoses were derived on the basis of the CASI-5 and YI-4-R. For example, how many items were used, was impairment or other clinical features (such as duration, onset) considered? How was information from multiple informants combined?
- 4. What age were the participants who completed the YI-4-R? Presumably very young children did not complete this self-reported measure.
- 5. Also please state briefly in the Results which types of SUD problems were present in the sample and how many children had which subtype of ADHD.
- 6. Table 5 does not include SUD- why is that? Surely SUD was associated with age, as younger children were not affected?

- 7. Can you please add a note to Table 1 indicating what ages the school grades correspond to for those unfamiliar with the categories P1-P4 etc.?
- 8. Figures 1 & 2: a few changes to these figures would be helpful: Figure 1 can be moved to the supplement or removed as it is of less interest than Figure 2 presenting the z-scores. It would also be helpful if the authors could change these figures to plot frequency not density on the y-axis.
- 9. The recruitment for this study was originally for a case-control study of asthma and therefore it seems the sample is over-represented for asthma (19.1% of the sample according to Table 1). There is some evidence that asthma is associated with ADHD (e.g. https://onlinelibrary.wiley.com/doi/full/10.1111/j.1398-9995.2011.02648.x) and other mental health problems (e.g. https://www.mdpi.com/2076-328X/9/7/78) and therefore this over-representation of asthma in the sample may have increased the prevalence of these other problems observed in the sample. This should be mentioned in the Discussion. The authors should also check what the prevalence results for the psychiatric disorders look like in the subsample without asthma.
- 10. As the authors point out, one limitation is the low statistical power in the analyses. This is also relevant to the analysis examining the association between neurocognitive impairment and diagnoses. It is surprising that for example ADHD is not associated with neurocognitive impairment but the sample is quite small (only 9 children with ADHD and only 25 had neurocognitive impairment). This limitation should be expanded on so that the lack of associations between the variables assessed is not over-interpreted by readers.

Is the work clearly and accurately presented and does it cite the current literature? $\ensuremath{\mathsf{Yes}}$

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others? Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility? $\ensuremath{\mathsf{Yes}}$

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Child psychiatry, neurodevelopment, mental health, epidemiology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 08 Sep 2022

Margaret Nampijja, MRC/UVRI and LSHTM Uganda Research Unit, Entebbe, Uganda

RESPONSES TO REVIEWER 1

This is an epidemiological study examining the prevalence of neurocognitive impairments and psychiatric disorders in 322 school children aged 5-17 years old in Uganda. The results indicate that 8% of the sample had neurocognitive impairments and 9.3% had at least one psychiatric disorder. I have the following minor suggestions for improvement:

1. The authors describe the sample as "healthy" or "assumed healthy" in the abstract, introduction and discussion. This should be replaced with terms such as "general population" or "reference population" or "community sample" to be more accurate as we cannot assume that a sample of school children will be completely healthy. I would also suggest replacing "normal population" (in Discussion) with one of the terms above.

RESPONSE: We thank the reviewer for this observation; we have adopted their suggestion and used "general" instead of "healthy" population, in the abstract [Page 3]

2. In the method, the authors note that the CASI-5 and YI-4-R can be used to assess many different psychiatric conditions but they focused only on ADHD, MDD, GAD & SUD. It later appears that this was because none of the other conditions were present in the sample. Can the authors clarify in the Method that they examined each of the conditions and only mention that they then focused on the specific conditions in the Results? The Discussion and abstract should also explicitly state that other disorders were also assessed but not detected in the sample.

RESPONSE: We would like to clarify that the whole spectrum of disorders assessed by the CASI-5 and YI-4-R were examined in the study population. However only those that were present i.e. ADHD, MDD, GAD & SUD were included in the analysis. This has been clarified both in the methods and results section. [Page 6]

3. Please state how the binary diagnoses were derived on the basis of the CASI-5 and YI-4-R. For example, how many items were used, was impairment or other clinical features (such as duration, onset) considered? How was information from multiple informants combined?

RESPONSE: The binary diagnosis for each disorder was derived using a symptom count and other criteria as given by the CASI-5 and YI-4R scoring instructions. [Page 7].

4.What age were the participants who completed the YI-4-R? Presumably very young children did not complete this self-reported measure.

RESPONSE: The YI-4 R was self-administered to youths aged 12–18 years. Younger children did not complete this self-reported measure. This has been clarified in the methods in the second paragraph under *Assessing for psychiatric disorders*. [Page 6]

5. Also please state briefly in the Results which types of SUD problems were present in the sample and how many children had which subtype of ADHD.

RESPONSE: The substances looked at were tobacco, alcohol, marijuana. Of the nine participants found to have ADHD, seven presented with the inattentive type while two had hyperactive-impulsive type. This has been included in the revised manuscript [page 12].

6.Table 5 does not include SUD- why is that? Surely SUD was associated with age, as younger children were not affected? **RESPONSE:** Data on SUD has been added to Table 5.

7.Can you please add a note to Table 1 indicating what ages the school grades correspond to for those unfamiliar with the categories P1-P4 etc.?

RESPONSE: Grades P1-P4 correspond with 6-9 years of age; P5-P7 with age 10-12years; S1-S4 with age 13-16 years; S5-S6 with 17-18 years. These have now been indicated below Table 1. [Page 8]

8. Figures 1 & 2: a few changes to these figures would be helpful: Figure 1 can be moved to the supplement or removed as it is of less interest than Figure 2 presenting the z-scores. It would also be helpful if the authors could change these figures to plot frequency not density on the y-axis.

RESPONSE: We have taken your advice and that of the second reviewer, and moved Figures 1 and 2 to the data repository as extended data. This is the equivalent of supplementary material for the Wellcome Open Research Journal.

The y-axis in the normal distribution represents the "probability density", which intuitively shows the chance of obtaining values near the corresponding points on the x-axis.

9. The recruitment for this study was originally for a case-control study of asthma and therefore it seems the sample is over-represented for asthma (19.1% of the sample according to Table 1). There is some evidence that asthma is associated with ADHD (e.g. https://onlinelibrary.wiley.com/doi/full/10.1111/j.1398-9995.2011.02648.x) and other mental health problems (e.g. https://www.mdpi.com/2076-328X/9/7/78) and therefore this over-representation of asthma in the sample may have increased the prevalence of these other problems observed in the sample. This should be mentioned in the Discussion. The authors should also check what the prevalence results for the psychiatric disorders look like in the subsample without asthma.

RESPONSE: We have examined the association between asthma and the psychiatric disorders. Asthma was found to be associated with MDD (AOR, 95%CI 2.71 1.02; 7.20) but not with the other disorders. [Page 13].

10. As the authors point out, one limitation is the low statistical power in the analyses. This is also relevant to the analysis examining the association between neurocognitive impairment and diagnoses. It is surprising that for example ADHD is not associated with neurocognitive impairment but the sample is quite small (only 9 children with ADHD and only 25 had neurocognitive impairment). This limitation should be expanded on so that the lack of associations between the variables assessed is not over-interpreted by readers.

RESPONSE: We thank the reviewer for highlighting this important limitation, and as advised, we have expanded the explanation on this limitation. [Page 15]

Competing Interests: None