

ORIGINAL ARTICLE

Prevalence of HIV, HSV-2 and pregnancy among high school students in rural KwaZulu-Natal, South Africa: a bio-behavioural cross-sectional survey

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ABSTRACT

Objective Adolescents in southern African high schools are a key population for HIV prevention interventions. We report on the prevalence of HIV, HSV-2 and pregnancy as indicators of high-risk sexual behaviour among high school students in rural KwaZulu-Natal.

Design Bio-behavioural cross-sectional survey.

Methods Students completed a self-administered structured, standardised demographic and sexual behavioural questionnaire. Dried blood spot specimens were collected for HIV and HSV-2 testing. Urine specimens were used for pregnancy testing in female students.

Results A total of 2675 (1423 females, 1252 males) consenting students were enrolled from 14 high schools between September and November 2010. The median age of students was 16 years (IQR 15–18). HIV prevalence was 1.4% (95% CI 0.9 to 1.9) in males and 6.4% (95% CI 4.6 to 8.3) in females ($p<0.001$). HSV-2 prevalence was 2.6% (95% CI 1.6 to 3.7) in males and 10.7% (95% CI 8.8 to 12.6) in females ($p<0.001$). Pregnancy prevalence was 3.6% (95% CI 2.6 to 4.5). Risk factors for prevalent HIV infection in female students included being over 18 years of age (adjusted OR (aOR)=2.67, 95% CI 1.67 to 4.27; $p<0.001$), prevalent HSV-2 infection (aOR=4.35, 95% CI 2.61 to 7.24; $p<0.001$), previous pregnancy (aOR=1.66, 95% CI 1.10 to 2.51; $p=0.016$) and experience of two or more deaths in the household in the previous year (aOR=1.97, 95% CI 1.13 to 3.44; $p=0.016$).

Conclusions The high prevalence of HIV, HSV-2 and pregnancy underscore the need for school-based sexual and reproductive health services, and provide further impetus for the inclusion of adolescents in behavioural and biomedical trials with HIV incidence endpoints.

INTRODUCTION

The South African province of KwaZulu-Natal is at the global epicentre of the HIV epidemic, with an estimated 1.7 million people in the province living with HIV.^{1–3} Such high population prevalence is fuelled by unprecedentedly high incidence rates, particularly in young people aged 15–24 years in whom HIV prevalence in KwaZulu-Natal was estimated at 12% in 2012.^{1–3} Moreover, in South Africa, nearly a third of all new HIV infections occur in 15–24 year olds,¹ with young women in

this age group being five to six times more likely to be infected than their male peers,^{4–5} underscoring the importance of adolescents—particularly adolescent girls—as a priority group for evidence-based HIV prevention interventions.⁶

High-risk behaviour during adolescence is generally associated with unfavourable health outcomes, including HIV acquisition.⁷ Priority adolescent-targeted HIV prevention efforts should therefore include risk reduction information to increase young people's awareness and knowledge of HIV/AIDS during the early formative years. Numerous HIV prevention initiatives and campaigns for young people with these aims are being implemented.^{8–13} While these programmes are active in many schools and communities and have contributed to increasing awareness of HIV/AIDS, evidence-based behaviour change interventions that prevent HIV infection in adolescents remain rare.^{8–14–16} Nonetheless, given almost three quarters of South Africans aged 7–24 years attend schools,¹⁷ schools have the potential to be important and convenient venues for HIV prevention interventions.

In this paper, we describe the demographic and biological characteristics of high school students in rural KwaZulu-Natal, with the aim of quantifying the magnitude of HIV infection and sexual risk in high schools to inform the development of school-based HIV prevention interventions.

METHODS

Study setting and population

The study was conducted in Vulindlela, a rural sub-district of KwaZulu-Natal characterised by limited infrastructure, poverty and high rates of HIV infection.¹⁸ In total, 14 out of a total of 42 high schools in the district were included in this study. Selection of schools was based on criteria that included a minimum of 150 enrolled students, grade 12 exam pass rates, ease of physical access to schools and school principal acceptance of the survey. All students in grades 9 and 10 of selected schools, regardless of age, gender or HIV status, were eligible for inclusion. Students were recruited following extensive community consultation. First person consent was obtained from students ≥ 18 years following a literacy and comprehension assessment. For students < 18 years, assent was obtained from the student and consent from the parent/guardian.

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If a parent or guardian was unavailable (due to migrant labour, illness or death), the participation of the relevant student was assessed by a representative of the School Research Support Group (SRS) who provided proxy parental consent.

Study design and methods

This cross-sectional bio-behavioural study was undertaken between September and November 2010. Demographic and behavioural characteristics of participants were assessed using self-reported, standardised, structured questionnaires. Names of participants were collected as identifying information to facilitate follow-up care if later required. Field staff maintained a secure database that had the unique study number and name, school and grade of enrolled students. A delinked database using the unique study number was used for data analysis purposes. Students completed self-administered questionnaires facilitated by study staff; students were able to choose between English or *isiZulu* for the preferred language of this questionnaire.

HIV testing was performed using HIV ELISA from Vironostika Uniform 11 plus O Assay, Biomerieux, (Netherlands). All samples testing HIV-positive were further confirmed with the SD Bioline HIV-1/2 ELISA V3.0 kit (SD Standard Diagnostics, INC, Korea). HSV-2 testing was performed using HerpeSelect HSV-2 ELISA Kits (Focus Diagnostics, California, USA) for the qualitative detection of human IgG class antibodies to HSV-2 based on recombinant gG2; this method for detection has been validated for use on dried blood spots.^{8 16 19} Urine pregnancy testing was performed using the QuickVue One-Step hCG Urine Test (Quidel Corporation, San Diego, USA). Group pretest counselling was provided to all learners prior to specimen collection.

Follow-up care

On completion of laboratory testing, students were invited to attend their local primary healthcare clinic to access results from study staff in the context of individual pretest and post-test counselling. Students found to be HIV-positive, pregnant or requiring additional care, were referred for further care within the clinic, or had the option of referral to the adolescent-friendly services at the Centre for the AIDS Programme of Research in South Africa (CAPRISA) Vulindlela Clinic for free care and treatment, including provision of antiretrovirals. Students in need of psychosocial support were referred to a local experienced non-government organisation, *Zimnande Zonke*.

In the case that a student was found to be HIV-positive or pregnant and failed to collect their results, they were proactively followed up through a process designed to ensure confidentiality and minimise stigma and discrimination by including HIV-negative and non-pregnant learners in interviews with the stated aim of validation of biological and behavioural assessments. This process excluded learners who tested HSV-2 positive because the South African Department of Health Guidelines for management of sexually transmitted diseases was used, which is based on syndromic management rather than diagnostic testing. Throughout the follow-up process, confidentiality and minimisation of stigma and discrimination was respected to the extent permitted by Section 13(1)(d) of the Children's Act of 2005.²⁰

Data management

All self-reported data were collected on standardised case report forms (CRFs) using the student's unique study number and

faxed using DataFax (Clinical DataFax Systems Inc, Hamilton, Canada). All laboratory data were linked to the questionnaire data using the student's unique identification number.

Statistical analysis

The demographic, behavioural and biological characteristics were summarised using descriptive summary measures, expressed as means (\pm SD) and/or medians (with IQR) for continuous variables and percentages for categorical variables. In order to adjust for cluster effects inherent in school-based sampling, cluster-level summaries were computed. In the adjusted analysis, prevalence was calculated in each cluster and these cluster level prevalence estimates were then averaged by gender. The unadjusted analysis ignored the clustering and merely calculated the prevalence by combining all clusters. The estimates of prevalence calculated from each of the 14 clusters were compared by gender using t tests for two independent samples as described in Hayes and Moulton.²¹ A multivariate analysis was performed to explore risk factors for HIV and HSV-2 infection in female students and overall. Univariate and multivariate adjusted ORs (aOR) were calculated with 95% CIs using generalised linear mixed models with a logit link modelling the probability of being infected and including a random effect for school. The SAS statistical package (V9.3; Statistical Analysis Software, North Carolina, USA) was used for the analysis.

RESULTS

The total grade 9 and 10 school student population in the 14 schools sampled was 3781. A total of 2675 (70.7%) students provided consent or assent with parent or guardian consent and were enrolled in the study. Of these, 1423 (53.2%) were females and 1252 (46.8%) were males. The most common reason for non-enrolment was parental refusal of consent (653/1106, 59.0%); a small proportion of students had insufficient cognitive ability to provide consent/assent (2/1106, 0.2%).

Demographic and behavioural characteristics

The demographic and selected behavioural characteristics of students are presented in [table 1](#). The overall median age of students was 16 years (IQR 15–18), with a median age of 17 years (IQR 16–18) for males and 16 years (IQR 15–17) for females ($p < 0.001$). Substantial proportions (18.2% of males, 11.0% of females) of students were over 18 years of age. The age range of students was wide at 12–28 years for males, and 13–24 years for females. A significant proportion of students (43.0% of males, 47% of females) had experienced at least one death in the household in the last year, potentially contributing to the low percentages of students in households headed by both parents (16.9% of males, 20.1% of females). Moreover, in this setting, as marriage is rare, it is common for students to be living in female-headed households (33.1% of males, 32.1% of females).

The median age of coital debut for those students that had ever had sex was 15 (IQR 14–17) years for males compared to 16 (IQR 15–17) years for females ($p < 0.001$), and compared with females more males reported ever being sexually active (33.1% males vs 21.6% females; $p = 0.01$). Self-reported experience or threat of violence to have sex was 6.7% for males and 6.9% for females ($p = 0.92$). Males were significantly more likely to have a sexual partner of their own age or younger compared with females ($p < 0.001$). More than one in three sexually active females reported having a sexual partner at least 4 years their senior.

Table 1 Demographics and behavioural characteristics of students in rural KwaZulu-Natal, South Africa

Characteristic	Males (N=1252)		Females (N=1423)		Adjusted* p Value
	Unadjusted % (n/N)	Adjusted* %	Unadjusted % (n/N)	Adjusted* %	
Demographic characteristics					
Age median (IQR)	17 (16–18) years	–	16 (15–17) years	–	<0.001
Age range	12–28 years	–	13–24 years	–	
Age category (years)					
<15	23.7 (297)	25.6	41.5 (591)	41.6	0.002
16–17	40.3 (505)	40.4	37.7 (537)	37.5	0.383
18–19	27.5 (344)	26.0	14.9 (212)	14.8	0.005
>20	8.5 (106)	8.0	5.8 (83)	6.1	0.518
Head of household					
Both parents	16.9 (210/1240)	16.9	20.1 (283/1411)	20.1	0.210
Father only	16.9 (210/1240)	17.2	15.7 (222/1411)	15.6	0.241
Mother only	33.1 (410/1240)	33.2	32.4 (457/1411)	32.1	0.613
Other	33.1 (410/1240)	32.7	31.8 (449/1411)	32.1	0.838
Adult deaths in household in last year					
0	57.5 (709/1234)	57.0	53.4 (751/1406)	53.0	0.137
1	18.3 (226/1234)	18.6	20.3 (285/1406)	20.2	0.311
>1	24.2 (299/1234)	24.4	26.3 (370/1406)	26.9	0.399
Grade					
9	45.9 (572)	45.6	49.2 (699)	47.9	0.575
10	54.1 (675)	54.4	50.8 (722)	52.1	0.575
Behavioural characteristics					
Experience of penovaginal sex	34.8 (429/1232)	33.1	21.9 (307/1399)	21.6	0.009
Age at coital debut (Median, IQR); (N)	15 (14–17) years; (423)	–	16 (15–17) years; (293)	–	<0.001
Threat of violence for sex	6.7 (83/1234)	6.7	6.8 (95/1406)	6.9	0.924
Partner characteristics					
Younger partner	24.4 (119/487)	26.8	9.0 (28/311)	10.8	<0.001
Same age partner	22.2 (108/487)	22.4	9.0 (28/311)	9.7	<0.001
<4 years older	39.2 (191/487)	38.0	43.4 (135/311)	43.1	0.177
4–7 years older	11.3 (55/487)	10.0	32.8 (102/311)	31.5	<0.001
≥8 years older	2.9 (14/487)	2.9	5.8 (18/311)	4.9	0.304

*Adjusted measures were calculated based on cluster (school)-level summaries appropriate for school-based sampling; for those variables where there were missing observations, the total number of observations (N) is shown.

Prevalence of HIV, HSV-2 and pregnancy

The prevalence of HIV and HSV-2 students stratified by gender and age are presented in [table 2](#). The HIV prevalence was 1.4% (95% CI 0.9 to 1.9) in males and 6.4% (95% CI 4.6 to 8.3) in females ($p<0.001$). In males, HIV prevalence remained low (~1%) in those below 18 years of age and increased steadily thereafter with increasing age. In contrast, a substantial proportion of females were HIV infected by age 18 years, with risk of infection increasing rapidly from age 15 years; by age 20, one in four females were HIV infected. The overall HIV prevalence varied between 1.9% (95% CI 0.0 to 4.0) and 8.3% (95% CI 4.0 to 12.7) in the 14 schools included in the survey.

Variability was also observed in HSV-2 prevalence between schools, which ranged from 2.5% (95% CI 0.1 to 5.0) to 9.6% (95% CI 4.2 to 14.9). HSV-2 prevalence was 2.6% (95% CI 1.6 to 3.7) in males and 10.7% (95% CI 8.8 to 12.6) in females ($p<0.001$). In both sexes, prevalence of HSV-2 infection increased rapidly from age 15 years such that acquisition of HSV-2 infection was synonymous with sexual debut. Similar to the age–sex disparity in HIV prevalence, females had a consistently threefold to fourfold higher prevalence of HSV-2 across most age groups and were observed to bear a disproportionate burden of HSV-2 infection compared with males.

The overall pregnancy prevalence was 3.6% (95% CI 2.6 to 4.5). Pregnancy prevalence was highest in females aged 18–19 years (7.2%). As with HIV and HSV-2 prevalence, pregnancy prevalence varied between 0.9% (95% CI 0.0 to 2.7) and 5.7% (95% CI 2.1 to 9.4) across schools.

Risk factors associated with prevalence of HIV, HSV-2 and pregnancy

A multivariate analysis was performed to adjust for confounding and to explore risk factors associated with prevalence of HIV, HSV-2 and pregnancy in high school students (see online supplementary table S1). This analysis confirmed that compared with their male peers, female students face substantially higher burdens of both HIV (aOR=4.49, 95% CI 2.94 to 6.88; $p<0.001$) and HSV-2 (aOR=4.66, 95% CI 3.16 to 6.87; $p<0.001$). As such, a further multivariate analysis was performed on female students to avoid dilution of any associations, and to better inform future interventions targeted to this priority population by identification of female-specific risk factors of HIV, HSV-2 and pregnancy ([table 3](#)).

Those female students who were aged over 18 years (aOR=2.67, 95% CI 1.67 to 4.27), were HSV-2 seropositive (aOR=4.35, 95% CI 2.61 to 7.24; $p<0.001$), had previously been pregnant (aOR=1.66, 95% CI 1.10 to 2.51; $p=0.016$)

Table 2 HIV, HSV-2 and pregnancy prevalence by age group among students in rural KwaZulu-Natal, South Africa

Characteristic	Males (n=1252)		Females (n=1423)		
	Unadjusted % (n/N)	Adjusted* %	Unadjusted % (n/N)	Adjusted* %	Adjusted* p Value
HIV prevalence†					
Overall	1.4 (18/1252)	1.4	6.2 (88/1423)	6.4	<0.001
Age category (years)					
≤15	1.4 (4/297)	1.0	2.7 (16/591)	2.6	0.063
16–17	1.2 (6/505)	1.1	5.4 (29/537)	6.1	0.006
18–19	0.9 (3/344)	1.5	11.3 (24/212)	13.6	<0.001
≥20	4.7 (5/106)	1.8	22.9 (19/83)	24.7	0.010
HSV-2 prevalence†					
Overall	3.0 (38/1252)	2.6	10.4 (148/1423)	10.7	<0.001
Age category (years)					
≤15	0.7 (2/297)	0.7	4.1 (24/590)	3.5	0.006
16–17	2.0 (10/505)	2.0	8.6 (46/537)	9.3	0.001
18–19	6.1 (21/344)	6.6	22.6 (48/212)	30.2	0.002
≥20	4.7 (5/106)	3.5	36.1 (30/83)	43.3	0.001
Pregnancy prevalence†					
Overall	Not applicable		3.5 (49/1412)	3.6	Not applicable
Age category (years)					
≤15			1.7 (10/587)	1.9	
16–17			3.8 (20/533)	4.2	
18–19			7.2 (15/209)	6.2	
≥20			4.8 (4/83)	3.6	

*Adjusted measures were calculated based on cluster (school)-level summaries appropriate for school-based sampling.

†Missing observations excluded from percentage calculations.

and had experienced more than one death in their household (aOR=1.97, 95% CI 1.13 to 3.44; $p=0.016$) were all identified to be at significantly increased risk of HIV infection. A marginal association with prevalent HIV infection was observed in those female students who were from households headed by an individual who was not a parent. No additional risk factors were identified in the multivariate analysis performed on all students.

Significant risk factors for HSV-2 in female students were identified as age greater than 18 years (aOR=3.20, 95% CI 2.33 to 4.38; $p<0.001$), HIV-positive serostatus (aOR=4.34, 95% CI 2.64 to 7.13; $p<0.001$), previous pregnancy (aOR=2.52, 95% CI 1.58 to 4.03; $p<0.001$), experience of threat of violence for sex (aOR=1.95, 95% CI 1.30 to 2.95; $p=0.001$) and living in a female-headed household (aOR=1.68, 95% CI 1.02 to 2.75; $p=0.041$). In the multivariate analysis performed on all students, experience of an adult death in the household was also identified as a risk factor for HSV-2-positive serostatus (aOR=1.36, 95% CI 1.02 to 1.81; $p=0.036$).

Experience of an adult death in the household was also identified as a risk factor for pregnancy in female students (aOR=2.27, 95% CI 1.22 to 4.23; $p=0.010$), together with being over 18 years of age (aOR=2.28, 95% CI 1.17 to 4.43; $p=0.015$).

DISCUSSION

High school students in this setting already bear a substantial burden of HIV, HSV-2 and pregnancy that correlates with self-reported high-risk sexual activity. These data provide further impetus for targeting sexual reproductive health services and evidence-based HIV prevention interventions to the adolescent population in high HIV burden settings.

This comprehensive report of such high HIV prevalence in a school-based population is novel; however, the data presented

are consistent with other smaller scale school-based surveys in the region in similar age groups,⁴ underscoring the current inadequacies of HIV prevention efforts for school-based adolescents. Similarly, this is the first description in high school students of the age–sex disparity in HIV acquisition that defines the HIV epidemic in sub-Saharan Africa.^{1–22} We found HIV acquisition to be almost synonymous with sexual debut in female students. To inform the design of appropriate interventions to address these issues, the poor internalisation of HIV risk in this setting, as well as the social factors such as threats of violence for sex and adult deaths in the household that inflate the HIV risk in this population, all need to be better understood.

While high school completion rates are associated with lower HIV risk,^{23–24} teenage pregnancies too commonly lead to school drop-out and perpetuate a cycle of poverty, dependency and risk taking for survival.²⁵ The high teenage pregnancy rates reported in this study are a cause for concern—particularly concerning the identification of previous pregnancy as a risk factor for HIV and HSV-2 infection—and underscore the urgent need for targeted information sessions for these students on outcomes of sexual activity and enhancing access to sexual reproductive health services.

The wide age range of both male and female students in grades 9 and 10 in these schools result in children and adults being educated simultaneously, and potentially contributes to precocious sexual behaviours in younger students. Separation of schooling of children from adults is a simple intervention that could be easily and immediately implemented to create a supportive environment for HIV risk reduction and enhance female school completion rates.

This study highlights a huge degree of variability in HIV, HSV-2 and pregnancy prevalence between schools; while elucidating the causes for such variability will be informative, this

Table 3 Risk factors associated with prevalent HIV and HSV-2 infection in female students

Characteristic		% (n/N)	Univariate analysis		Multivariate analysis	
			OR (95% CI)	p Value	OR (95% CI)	p Value
HIV						
Age	<18 years	18.9% (252/1335)	1.00 (reference)		1.00 (reference)	
	>18 years	48.9% (43/88)	4.15 (2.93 to 5.88)	<0.001	2.67 (1.67 to 4.27)	<0.001
Pregnant	Negative	6.2% (84/1363)	1.00 (reference)		1.00 (reference)	
	Positive	6.1% (3/49)	0.97 (0.29 to 3.19)	0.959	0.64 (0.17 to 2.73)	0.551
HSV-2						
Head of household	Negative	4.3% (55/1274)	1.00 (reference)		1.00 (reference)	
	Positive	22.3% (33/148)	6.32 (3.94 to 10.14)	<0.001	4.35 (2.61 to 7.24)	<0.001
Adult deaths in household in last year	Both parents	6.8% (15/222)	1.00 (reference)		1.00 (reference)	
	Father only	5% (23/457)	1.45 (0.68 to 3.06)	0.337	1.26 (0.59 to 2.73)	0.551
	Mother only	5% (14/283)	1.04 (0.53 to 2.06)	0.905	0.82 (0.38 to 1.79)	0.621
	Other	8% (36/449)	1.73 (0.92 to 3.28)	0.091	1.80 (0.93 to 3.49)	0.082
Ever been pregnant	0	4.5% (34/751)	1.00 (reference)		1.00 (reference)	
	1	6% (17/285)	1.37 (0.75 to 2.49)	0.309	1.30 (0.65 to 2.58)	0.455
	>1	10% (37/370)	2.37 (1.46 to 3.85)	0.001	1.97 (1.13 to 3.44)	0.016
Relative partner age*	No	5% (63/1258)	1.00 (reference)		1.00 (reference)	
	Yes	17% (25/147)	3.89 (2.36 to 6.41)	<0.001	1.66 (1.10 to 2.51)	0.016
Threat of violence	Peers or younger	14.7% (28/191)	1.00 (reference)			
	>4 years older	11.7% (14/120)	0.77 (0.42 to 1.41)	0.403		
HSV-2	No	6.0% (78/1311)	1.00 (reference)		1.00 (reference)	
	Yes	10.5% (10/95)	1.72 (0.92 to 3.22)	0.090	1.09 (0.76 to 1.57)	0.645
HIV						
Age	<18 years	17.0% (217/1274)	1.00 (reference)		1.00 (reference)	
	>18 years	52.7% (78/148)	5.39 (4.00 to 7.27)	<0.001	3.20 (2.33 to 4.38)	<0.001
Pregnant	Negative	6.2% (84/1363)	1.00 (reference)		1.00 (reference)	
	Positive	6.1% (3/49)	0.97 (0.29 to 3.19)	0.959	1.37 (0.63 to 2.97)	0.425
HSV-2						
Head of household	Negative	4.3% (55/1274)	1.00 (reference)		1.00 (reference)	
	Positive	22.3% (33/148)	6.32 (3.94 to 10.14)	<0.001	4.34 (2.64 to 7.13)	<0.001
Adult deaths in household in last year	Both parents	6.8% (15/222)	1.00 (reference)		1.00 (reference)	
	Father only	5% (23/457)	1.45 (0.68 to 3.06)	0.337	1.12 (0.59 to 2.11)	0.737
	Mother only	5% (14/283)	1.04 (0.53 to 2.06)	0.905	1.68 (1.02 to 2.75)	0.041
	Other	8% (36/449)	1.73 (0.92 to 3.28)	0.091	1.16 (0.65 to 2.10)	0.615
Ever been pregnant	0	4.5% (34/751)	1.00 (reference)		1.00 (reference)	
	1	6% (17/285)	1.37 (0.75 to 2.49)	0.309	1.41 (0.92 to 2.14)	0.112
	>1	10% (37/370)	2.37 (1.46 to 3.85)	0.001	1.13 (0.70 to 1.83)	0.618
Relative partner age*	No	5% (63/1258)	1.00 (reference)		1.00 (reference)	
	Yes	17% (25/147)	3.89 (2.36 to 6.41)	<0.001	2.52 (1.58 to 4.03)	<0.001
Threat of violence	Peers or younger	24.6 (47/191)	1.00 (reference)			
	4–7 years older	25.8 (31/120)	1.05 (0.71 to 1.55)	0.799		
Pregnancy	No	9.5 (125/1311)	1.00 (reference)		1.00 (reference)	
	Yes	22.3 (21/94)	2.34 (1.55 to 3.54)	<0.001	1.95 (1.30 to 2.95)	0.001
HSV-2						
Age	<18 years	20.0% (273/1363)	1.00 (reference)		1.00 (reference)	
	>18 years	38.8% (19/49)	2.68 (1.75 to 4.11)	<0.001	2.27 (1.22 to 4.23)	0.010
Pregnant	Negative	3.5% (46/1319)	1.00 (reference)		1.00 (reference)	
	Positive	3.5% (3/87)	1.00 (0.27 to 3.74)	0.995	0.58 (0.16 to 2.18)	0.422
HSV-2						
Head of household	Negative	3.2% (40/1258)	1.00 (reference)		1.00 (reference)	
	Positive	6.1% (9/147)	1.98 (0.88 to 4.49)	0.100	1.22 (0.52 to 2.88)	0.645
Adult deaths in household in last year	Both parents	2.9% (8/280)	1.00 (reference)		1.00 (reference)	
	Father only	3.2% (7/219)	1.17 (0.51 to 2.70)	0.714	1.08 (0.45 to 2.58)	0.863
	Mother only	4.2% (19/451)	1.56 (0.65 to 3.75)	0.316	1.37 (0.54 to 3.47)	0.513
	Other	3.4% (15/444)	1.24 (0.46 to 3.30)	0.671	1.21 (0.44 to 3.32)	0.713
Ever been pregnant	0	2.3% (17/742)	1.00 (reference)		1.00 (reference)	
	1	5.3% (15/282)	2.45 (1.20 to 5.00)	0.014	2.28 (1.17 to 4.43)	0.015
	>1	4.6% (17/366)	2.12 (1.11 to 4.05)	0.022	1.78 (0.91 to 3.48)	0.091
Threat of violence	No	3.1% (38/1242)	1.00 (reference)		1.00 (reference)	
	Yes	7.5% (11/146)	2.72 (1.59 to 4.65)	<0.001	1.61 (0.79 to 3.28)	0.187

Continued

Table 3 Continued

Characteristic		% (n/N)	Univariate analysis		Multivariate analysis	
			OR (95% CI)	p Value	OR (95% CI)	p Value
Relative partner* age	Peers or younger	8.4% (16/191)	1.00 (reference)			
	>4 years older	6.8% (8/118)	0.8 (0.42 to 1.51)	0.4835		
Threat of violence for sex	No	3.4% (44/1302)	1.00 (reference)		1.00 (reference)	
	Yes	5.4% (5/93)	1.61 (0.88 to 2.95)	0.1189	1.17 (0.6 to 2.27)	0.647

*Relative partner age could not be included in the multivariate analysis because of the high frequency of missing data for this variable.

variability also has important implications for the design of trials to establish the efficacy of interventions to prevent HIV infection in high HIV burden settings.

Given that positive HSV-2 serostatus is recognised as an important risk factor for HIV acquisition²⁶ and that in this setting it was found to increase the risk of HIV infection almost fourfold in female students, the high HSV-2 prevalence in both male and female students in these high school students is concerning and could be an important contributor to the already high burden of HIV in this school-based population and in the wider community. Thus, HSV-2 prevention efforts should also aim to reach adolescents, and in particular adolescent girls. The results of the CAPRISA 004 tenofovir gel trial, demonstrating an overall effectiveness of 39% for HIV acquisition prevention and 51% for HSV-2 acquisition prevention in urban and rural women over 18 years, could have relevance for this adolescent school population.^{27 28} However, tenofovir gel lacks safety assessments in this age group that will be required as a precursor to implementation of any biomedical intervention.

Our school-based data are consistent with population-level surveys in similar age groups, which may be explained by the high proportion of adolescents in high schools in South Africa in the selected grades, and suggests that school-based surveys may be an important and generalisable tool in monitoring the evolving HIV epidemic.^{1 29} Moreover, any potential bias introduced by inclusion criteria for school selection appears to have had limited impact on our findings, possibly due to the high coverage rates of schools translating to one in three schools in the area participating. In contrast, the substantially higher HIV prevalence in pregnant women under 18 years attending antenatal clinics in the region (the HIV prevalence in this population was 18.3% in 2012) highlight that out-of-school adolescent females may be particularly vulnerable to infection and, despite smaller numbers, should not be neglected if school-based prevention efforts are scaled up. Further, this comparison also highlights that maintaining young girls in school and ensuring high school completion is an important structural intervention that should not be underestimated. In the South African setting, grades 9 and 10 represent a unique point for such an intervention wherein prevention benefits could be maximised, with students in these grades demonstrating sufficient cognitive ability for autonomous decision making, the majority of students in these grades still being HIV and HSV-2 uninfected and not pregnant, and these grades having comparative numbers of male and female students suggesting relatively low rates of attrition of female students at this stage.

Notwithstanding the limitation of cross-sectional surveys, prevalence estimates and self-reported sexual behaviour data, the strong correlation between behavioural findings and the biological measurements of HIV, HSV-2 and pregnancy demonstrate unequivocally that young people in this setting are

sexually active and engaging in high-risk sexual behaviour. The high prevalence of HIV, HSV-2 and pregnancy provide compelling evidence for targeting and testing both behavioural and biomedical HIV prevention interventions in school-based adolescent populations in high HIV burden settings.

Key messages

- ▶ South African high school students already bear a substantial burden of HIV, HSV-2 and pregnancy that correlates with high-risk sexual behaviour.
- ▶ Female high school students are at significantly greater risk of HIV and HSV-2 infection compared with male high school students.
- ▶ Considerable variability in HIV, HSV-2 and pregnancy is observed between schools.
- ▶ Students from child-headed households are particularly vulnerable to HIV infection in generalised epidemic settings with high mortality rates pre-antiretroviral treatment provision.
- ▶ There is an urgent need for adolescent-targeted HIV prevention in sub-Saharan Africa.

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Prevalence of HIV, HSV-2 and pregnancy among high school students in rural KwaZulu-Natal, South Africa: a bio-behavioural cross-sectional survey

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