Full title: Prevalence of Sexually Transmitted Infections among Young People in South Africa: A Nested Survey in a Health and Demographic Surveillance Site

Short title: STI/BV among Young People in South Africa

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ABSTRACT

Background

Sexually transmitted infections (STI) and bacterial vaginosis (BV) are associated with increased transmission of HIV, and poor reproductive and sexual health. The burden of STI/BV among young people is unknown in many high HIV prevalence settings. We conducted an acceptability, feasibility and prevalence study of home-based sampling for STI/BV among young men and women aged 15–24 years old in a health and demographic surveillance site (HDSS) in rural KwaZulu-Natal, South Africa.

Methods and Findings

A total of 1342 young people, stratified by age (15–19 and 20–24 years) and sex were selected from the HDSS sampling frame. 1171/1342(87%) individuals had ≥1 attempted home visit, of whom 790(67%) were successfully contacted. Among those contacted, 447(70%) enrolled. Consenting/assenting participants were interviewed and blood, self-collected urine (men) and vaginal swabs (women) were tested for *Herpes simplex* virus type-2 (HSV-2), chlamydia, gonorrhoea, trichomoniasis, and BV. Both men and women reported that sample collection was easy. Participants disagreed that sampling was painful; more than half the participants disagreed they felt anxious or embarrassed. The weighted prevalence (95% confidence intervals) of STI/BV among men and women respectively was chlamydia: 5.3%(3.0-9.4) and 11.2%(7.5-16.4); gonorrhoea: 1.5%(0.5-4.7) and 1.8%(0.7-4.3); active syphilis: 0% and 0.4% (0.1-2.5); trichomoniasis: 0.6%(0.1-4.0) and 4.6%(2.6-7.9); HSV-2: 16.8%(11.3-24.1) and 28.7%(23.3-34.8); BV: 42.1%(35.5-49.0) (women only). 75%) who had ≥1 curable STI reported no symptoms. Factors associated with a STI/BV included older age, being female, and not being in school or working. We encountered difficulties finding men at home and high migration.

Conclusions

A high burden of STI/BV was found in this rural setting characterised by its high HIV prevalence. The majority of the STI/HIV infections were asymptomatic and would not have been identified or treated under national syndromic management guidelines. A nested STI/BV survey within a health and demographic surveillance site proved acceptable and feasible. This is a proof-of-concept for population-based STI surveillance in low and middle-income countries, which could be utilised in the evaluation of STI/HIV prevention and control programmes.

AUTHOR SUMMARY

Background

- Adolescents and young people are particularly vulnerable to sexually transmitted infections.
- The first strategic direction of the 2016-2021 WHO Global Health Sector Strategy for Sexually Transmitted Infections is to collect information on STI prevalence and incidence across representative populations.
- There is evidence that bacterial vaginosis (BV) is a risk factor for poor birth outcomes and STIs including HIV. The collection of BV prevalence may also be important

Why Was This Study Done?

- Developing new cohorts for dedicated STI/BV prevalence studies may not be realistic, particularly in sub-Saharan Africa, where the impact of STI/BV and their consequences may be greatest.
- Nesting STI/BV surveys within networks of Health and Demographic Surveillance Sites (HDSS) would be an efficient way of providing data to better understand STI epidemiology among adolescents and young people in high HIV prevalence settings.
- These data are essential to advocate, fund, plan, implement and evaluate interventions for STI prevention and control among adolescents and young people.

What Did the Researchers Do and Find?

- We carried out a nested STI/BV survey among 1342 adolescent and young people in an HDSS in KwaZulu-Natal, South Africa
- Potential participants were contacted at home and invited to participate.
- Participants were interviewed, and samples were collected for STI/BV.
- We showed that this study was feasible: 1171/1342(87%) individuals had ≥1 attempted home visit, of whom 790(67%) were successfully contacted.
- The study was also acceptable: Among those contacted, 447(70%) enrolled. Both men and women reported few problems with sample collection.
- In addition, we report a high burden of STI/BV in this population, particularly of chlamydia (5% in men and 11% in women), herpes simplex virus-2 (17% in men and 29% in women) and BV (42% in women).

What Do These Findings Mean?

- Nested STI/BV surveys in HDSS can be feasible and acceptable.
- These studies should be carried out in conjunction with studies to measure prevalence in high-risk populations to provide robust prevalence estimates for the planning and evaluation of national and local STI prevention and control.

Introduction

In 2012, 286 million people aged 12-24 lived in Africa, accounting for 18% of the global youth population. By 2040, the number of young people in Africa is projected to increase by 60% to 466 million [1]. Health interventions targeted at this age group are important for current and future adult health and for the health of the next generation. This is particularly true for sexually transmitted infections (STI) which, when acquired in adolescence, can jeopardize sexual and reproductive health later in life, and for women, the health of their babies. In low and middle-income countries (LMIC), symptomatic STIs are treated by syndromic management (presumptive treatment for symptomatic people without the use of laboratory tests) [2]; however, most STIs are asymptomatic and go unnoticed and untreated. Both symptomatic and asymptomatic STIs can cause serious morbidity, including pregnancy complications, cancer, infertility, and enhanced HIV transmission. Many of these sequelae are preventable if STI testing and treatment is implemented. Moreover, there is growing evidence that the common reproductive tract condition, bacterial vaginosis (BV) is an independent risk factor for HIV [3,4], and BV-associated microbiota may decrease the efficacy of topical microbicides [5].

Higher STI prevalence among young people has been observed worldwide and highlights the critical need for global efforts to improve sexual and reproductive health in this population. In an individual participant data meta-analysis of 18 HIV prevention studies among women in sub-Saharan Africa, STI prevalence was higher among young women aged 15–24 years compared to older women for all STIs except herpes simplex virus, type 2(HSV-2) (Elizabeth Torrone, personal communication); in this age group, the estimated range of prevalence of STIs in South Africa among clinic/community populations was 8.0% to 20.6% for chlamydia, 1.4% to 8.9% for gonorrhoea, 3.1% to 20.0% for trichomoniasis, 31.9% to 53.7% for HSV-2, and 35.8% to 52.4% for BV. In addition, for viral STI such as HSV-2 and human papillomavirus infection incidence rapidly increases after sexual debut which usually occurs in adolescence, and high incidences of both infections have been documented among young people in

120 sub-Saharan Africa [6–9]. However, many of these prevalence studies are urban and/or conducted in
121 clinical cohorts of adolescents and young adults known to be at high risk of infection. To date, there
122 have been few population estimates of the burden of STIs among adolescent girls and young women
123 and no studies of men (Elizabeth Torrone, personal communication).

124 The WHO Global Health Sector Strategy for STI, 2016-2021 has outlined the goals and targets for global
125 STI prevention and control. The first strategic direction is to collect information on STI prevalence and
126 incidence across representative populations [10]. Understanding regional and national STI epidemics
127 is essential to advocate, fund, plan, and implement interventions for STI prevention and control. The
128 strategy also urges LMIC to move from syndromic to aetiologic surveillance of STIs, and conduct
129 routine surveillance in key populations most at risk for STI including adolescents. Yet, in resource-
130 limited settings, developing new cohorts for dedicated STI prevalence studies may not be realistic,
131 particularly in sub-Saharan Africa, where the impact of STIs and their consequences may be greatest.

132 Networks of health and demographic surveillance systems (HDSS) conducting longitudinal population-
133 based research such as the INDEPTH Network may provide opportunities to obtain representative
134 STI/BV prevalence estimates for adolescents and young people and facilitate community entry and
135 engagement with sensitive topics such as sexual health [11]. However, population-based surveys can
136 be challenging to conduct. Key requirements include acceptability of being approached at home and
137 home sampling; parental availability to consent; receipt of results while maintaining confidentiality,
138 and establishing clinical pathways for the treatment of cases. We conducted a study in the Africa
139 Health Research Institute (AHRI; formerly the Africa Centre for Health and Population Studies) HDSS,
140 a member of the INDEPTH Network, to investigate the acceptability and feasibility of home-based
141 sampling of STI/BV among young people aged 15-24 years, and to measure prevalence and factors
142 associated with STI/BV. The background HIV prevalence in women aged 15-19 years and 20-24 years
143 is 14.7% and 26.5%, respectively, and in men aged 15-19 years and 20-24 years is 7.0% and 10.2%,
144 respectively [12].

Methods

This study is reported as per the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (S1 Checklist) [13].

Setting and sampling

The AHRI HDSS is located in rural uMkhanyakude district of KwaZulu-Natal, covering an area of 438 km^2, with a 2016 population of approximately 100,000 people who are members of 12,000 households [14]. Since 2000, annual household-based surveys have been used to collect information on births, deaths and migration patterns from all household members, including non-residents. In addition, resident household members aged ≥15 years are invited to participate in an annual HIV serosurvey, and to complete a questionnaire on general health and sexual behaviour.

For the STI survey, young men and women who were resident in the HDSS, based on the data collected in the routine household surveillance, and aged 15–24 years as of 19 July 2016 were eligible for inclusion. A random sample of 1342 young people was selected to obtain a target sample size of 800, allowing for 40% non-contact/refusals. This sample size would have provided relatively precision for low prevalence STIs. Sampling was stratified by age group (15–19 years and 20–24 years) and sex. The HDSS is divided into 14 subareas; within each stratum, a fixed proportion was sampled from each subarea to reflect the population distribution across the HDSS.

Ethics, informed consent and community engagement

The University of KwaZulu-Natal Biomedical Review Ethics Committee, the London School of Hygiene and Tropical Medicine Research Ethics Committee, the Southampton General Hospital Faculty of Medicine Ethics Committee, the Hlabisa District Hospital and the AHRI Somkhele Community Advisory Board approved the study protocol. The STI survey was called *Ukuvikela impilo yetho yokuzalana eyigugu*, isiZulu for "protecting our precious reproductive health." The AHRI Community Engagement Team disseminated information about the study in community dialogues and road shows. Potential

participants were contacted at home and invited to participate. Written parental consent was required for participants <18 years old with participant written assent. Participants aged 18 years or older proved written consent. Participants consented separately for each sample type (vaginal swab [women], urine [men] and blood); participants who did not consent for a sample could still enrol in the study. Participants were asked for permission to link their STI survey data with the data collected in the annual routine household and individual surveillance.

Study procedures

The study team consisted of 2 field workers (1 male and 1 female), 2 female licensed practical nurses, 1 male licensed practical nurse and 1 male registered nurse team leader with an intention to match same sex nurse to participants whenever possible. The field work was conducted Tuesday to Saturday from 11am to 7pm to maximise finding participants at home.

After informed consent/assent, the participant had a short computer-assisted personal interview by the study nurse [15]. The interview obtained data on demographics, substance use, sexual behaviour, violence, circumcision (young men only), family planning (young women only), genital hygiene, and genital symptoms. For questions about sexual behaviour and violence, the participant was asked to self-interview using a tablet device; however, the study nurse was available to support the participant if needed. If a participant reported genital complaints, they were referred to our study nurse in a local primary health clinic for syndromic management as per South African STI Management Guidelines (2015) [16].

All participants had 8.5 ml of blood drawn for syphilis and HSV-2. For young women, the research nurse explained the procedure to self-collect a total of 5 vaginal swabs for testing for chlamydia, gonorrhoea, trichomoniasis and BV. Swab collection took place in a private setting identified by the participant. Young men collected a urine sample for testing for chlamydia, gonorrhoea, and trichomoniasis.

After the sample collection, participants were asked to rate their agreement with 10 statements using visual analogue scales (VAS) ranging from 0 (easy/agree) to 100 (difficult/disagree) to assess the ease of understanding of consent for the study, the instructions for collecting the sample, and the participant's experience of participation.

All participants were asked to provide contact information for test results, including their preferred mode of contact for both positive and negative results (e.g. telephone call, text or WhatsApp Messenger), and ideal hours for contact. We attempted to contact all participants with the results of the laboratory-diagnosed curable STIs (chlamydia, gonorrhoea, trichomoniasis, syphilis). All participants with mobile phones were provided 5 South Africa Rand (0.37 US Dollar) of air time to contact the study nurses with questions if needed. Participants who had a positive test for a curable STI were referred for free treatment; reimbursement for travel was provided. We traced all cases who were not contactable or did not come to clinic for treatment. We used the British Association for Sexual Health and HIV (BASHH) guidelines for the treatment of laboratory diagnosed chlamydia, gonorrhoea, and trichomoniasis [17–19], and South African STI Management Guidelines for the treatment of syphilis [16].

Laboratory methods

Laboratory testing was performed according to manufacturer's instructions and standard operating procedures in the central AHRI laboratory and Global Clinical and Viral Laboratory in Durban. Serum samples were used to test for IgG antibodies for HSV-2 by a type specific ELISA (Kalon Biological Ltd., Guildford, UK). Syphilis was determined by the Determine™ Syphilis TP rapid test (Alere Inc, USA) in the central AHRI laboratory. All positives were confirmed at the Global Clinical and Viral Laboratory with *Treponema pallidum* haemagglutination (TPHA) (Randox Laboratories, UK) and tested with venereal disease research laboratory (VDRL) (Omega Diagnostics, UK) using a reverse algorithm as per South African STI Management Guidelines[16] due to the young age of participants (i.e. unlikely to have treated past infections). Syphilis was defined as follows: negative (TPHA-/VDRL-); early or

previously treated infection (TPHA +/VDRL-); active syphilis (TPHA +/VDRL+ low titre [<1:8]; TPHA +/VDRL+ high titre [≥1:8])

Vaginal swabs were used to prepare a slide at the home and air dried. Slides were transported to the central ARHI laboratory , methanol-affixed, Gram stained, and examined for BV using the Nugent score [20]. A Nugent score of 0-3 indicated normal microbiota, 4-6 indicated intermediate microbiota and 7-10 indicated BV. Vaginal swabs (women) and urine (men) were sent to Global Clinical and Viral Laboratory for testing by real-time PCR for *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Trichomonas vaginalis.* Detection was carried out using the Lightmix Kit *Neisseria gonorrhoeae,* the Lightmix Kit *Chlamydia trachomatis* and the Lightmix Kit *Trichomonas vaginalis* (TIB MOLBIOL, Germany) following manufacturer's instructions. All positive tests for *N. gonorrhoeae* were confirmed using GeneXpert (Cepheid Inc, USA). External quality controls are carried out quarterly for real-time PCR with the College of American Pathology.

Data management and statistical methods

Data were captured electronically using REDCap software [21]; range and consistency checks were done automatically during data capture; further data cleaning and analysis was done using Stata 14 (College Station, USA). All questions were required to minimise missing data, although participants could reply 'don't know' or 'prefer not to say'.

The statistical analysis plan was prepared prior to the statistical analysis (S1 Statistical Analysis Plan). Changes in response to peer review of this paper included the inclusion of other STIs to the BV risk factor analysis, and the inclusion of transactional sex in each risk factor analysis. Continuous variables were summarised using means, standard deviations, medians and inter-quartile ranges; categorical data were summarised using frequency counts and percentages. Missing data were not inputted.

Acceptability and feasibility of our survey were measured by the following outcomes: proportion of participants who were selected and contactable; the proportion of those contacted who agreed to

participate; the proportion who agreed to each sample collection (e.g. blood, vaginal swabs and urine); median and interquartile range of responses to a VAS measuring acceptability post-sampling; and proportion of cases who presented for treatment. We also estimated STI/BV prevalence and explored factors associated with any curable STI (chlamydia, gonorrhoea, syphilis, and trichomoniasis), HSV-2, and BV.

The number of individuals who were successfully contacted, and who consented to participate, were tabulated by sex, age group, residence location (urban/peri-urban/rural), household socioeconomic status, education level and HIV status using linked data from the HDSS. Characteristics of individuals who participated and the remainder in the eligibility list were compared using Chi-squared tests.

The prevalence estimate of each STI/BV, and its 95% confidence interval (CI), was calculated overall and by sex; prevalence estimates were weighted to account for the stratified sample design and non-response, calculated as the inverse probability of study participation in strata defined by age group, sex and residence location (urban/peri-urban/rural). We compared these results to unweighted prevalence and prevalence weighted for the stratified sample design only.

Logistic regression was used to estimate odds ratios and 95% CIs for factors associated with the presence of any curable STI (chlamydia, gonorrhoea, syphilis or trichomoniasis), of HSV-2 and of BV; separate models were developed for each outcome. Potential factors associated with curable STIs, HSV-2 and BV were examined using a conceptual framework with 3 levels: sociodemographic factors, modifiable behavioural factors (including genital hygiene), and sexual behaviour. For each outcome, age and sex (except for BV, which was in women only) were considered *a priori* confounders and were included in all models. First, sociodemographic factors whose age- and sex-adjusted associations with the outcome were significant at $p<0.10$ were included in a multivariable model; those remaining associated at $p<0.10$ were retained in a core model. Behavioural factors were then added to this core model one by one; those that were associated with the outcome at $p<0.10$, after adjusting for sociodemographic factors, were included in a multivariable model and retained if they remained

associated at p<0.10. Associations with sexual behavioural factors were subsequently determined in a similar way. Many of the questions about sexual relationships were only asked if participants reported having ever had sex; therefore, the analysis of these variables were restricted to that subgroup.

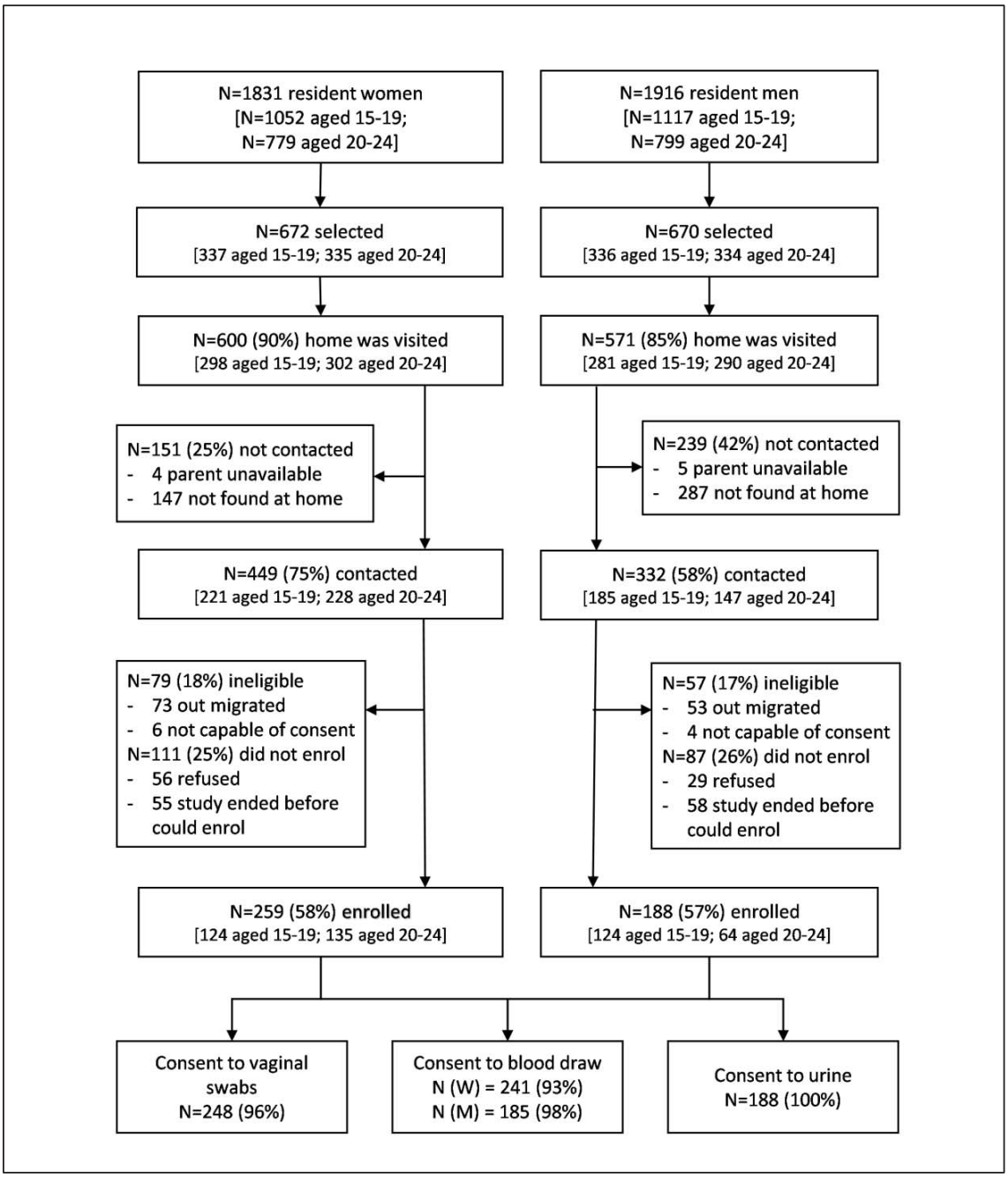
Results

Acceptability and feasibility

The field work took place from October 2016 to January 2017. Due to unexpected time limitations, only 1 visit attempt per selected individual was carried out from November to January to attempt coverage in subareas (a total of 14 subareas); however, not all selected young people were visited. 1171/1342 (87%) individuals had ≥1 attempted home visit, of whom 781(67%) were successfully contacted (Fig 1). Individuals aged 20–24 were less likely to be contacted than those aged 15–19 (63% vs 70% of those with an attempted visit, p=0.01), and less likely to be eligible after contact was made (mostly due to migration). Men were less likely to be contacted than women (58% vs 75%, p<0.001). Among those contacted, 447(57%, or 69% of those who were still eligible) enrolled. Overall, there was strong evidence that individuals who were sampled but did not enrol were more likely to be older, male, from rural or urban areas, and have completed secondary education or above, compared with those who enrolled (Supplementary Table S1).

285 Fig 1. Flow diagram for enrolment in a population-based STI survey among young people aged 15-24

286 years in rural Kwa-Zulu Natal



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288 Of those enrolled, 96% women provided all vaginal swabs and 93% provided blood samples; all men

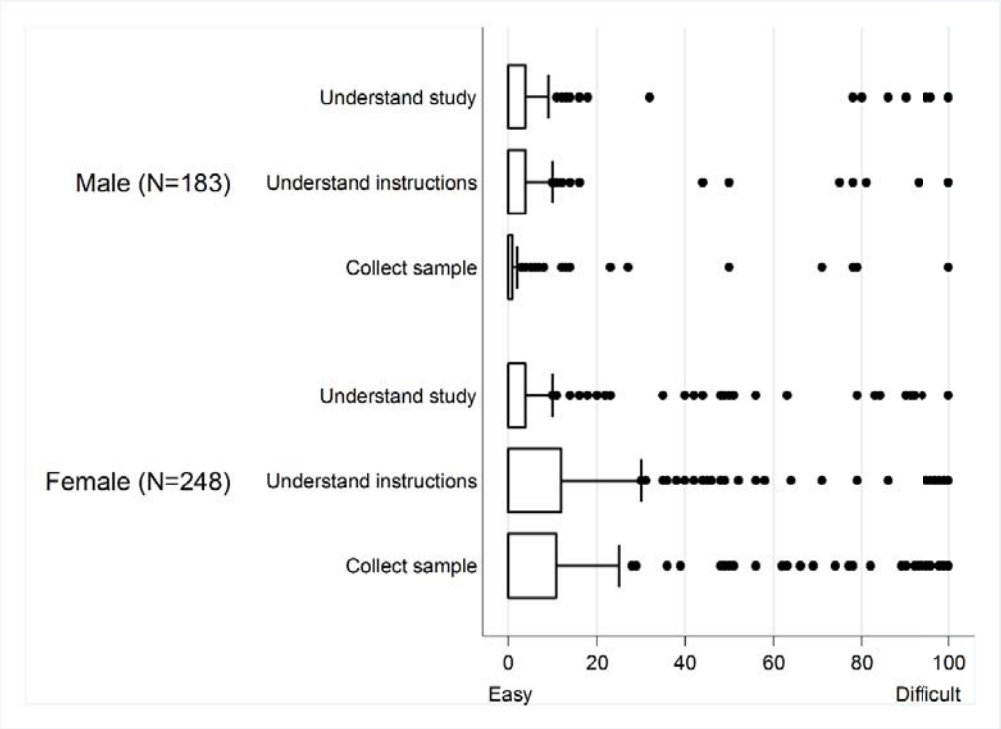
289 provided urines and 98% provided blood samples. Both men and women reported that it was easy to

290 understand how to collect urine / vaginal swabs, respectively (Fig 2a). Participants agreed they felt

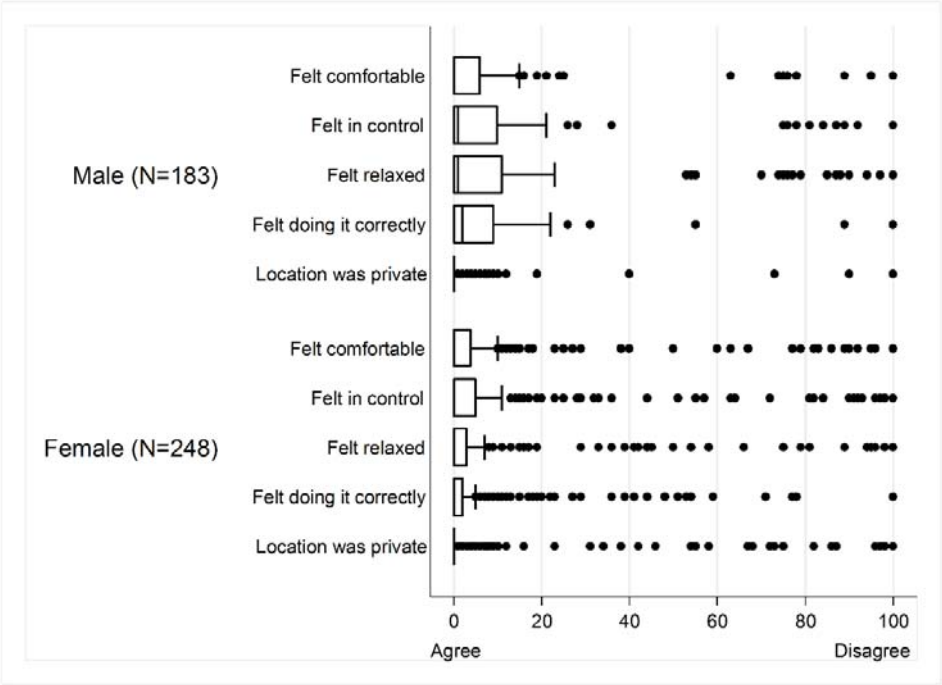
comfortable, in control, relaxed, and confident of their ability to collect the sample correctly (Fig 2b). Participants disagreed that that sampling was painful. Most men disagreed that they felt anxious or embarrassed or; and over half of women disagreed that they were anxious or embarrassed (Fig 2c).

Fig 2. Box and whisker plots of the acceptability of sampling in a population-based STI/BV survey among young people aged 15-24 years in rural KwaZulu-Natal. The vertical line within the box indicates the median, boundaries of the box indicate the interquartile range (25th and 75th percentiles), and the whiskers indicates values that are within 1.5 times the interquartile range above the 75th percentile, or 1.5 times the interquartile range below the 25th percentile. Values outside that range are plotted as individual points. E.g. the medians for Fig 2a equal 0.

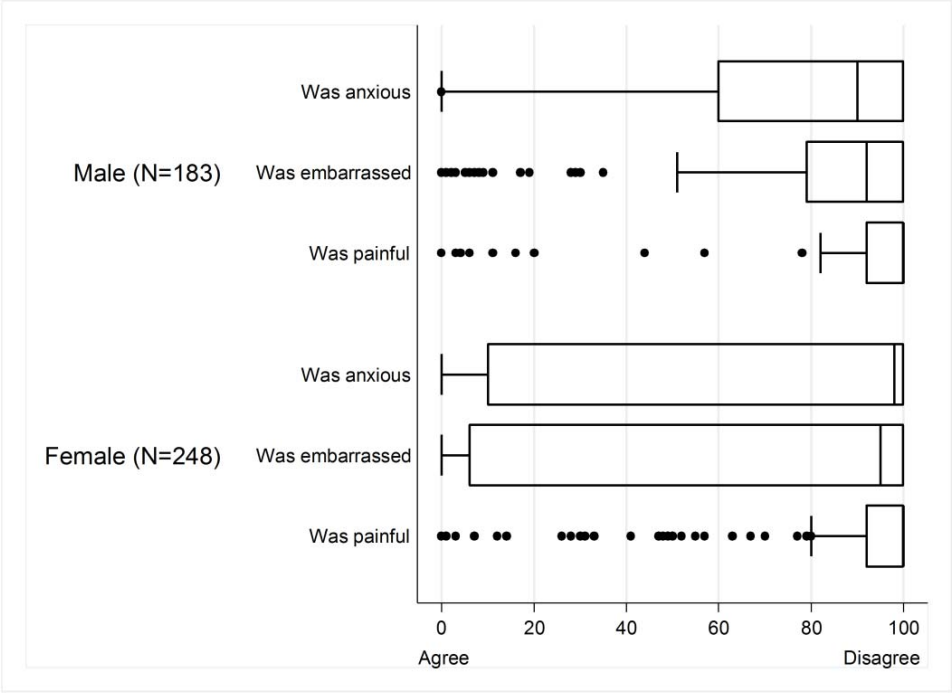
a. Ease of understanding the study and instructions, and the ease of sample collection



b. Experience of self-collecting urine (males) or vaginal swabs (women) - Positive Items



c. Experience of self-collecting urine (males) or vaginal swabs (women) - Negative items



Of those who provided samples, 206/245(84%) of 15–19 year olds and 184/192(96%) of 20–24 year olds enrolled had access to a telephone to receive results. Of those, the majority preferred a telephone

call for both positive and negative results (59% or 57%, respectively) followed by an SMS message (37% or 39%, respectively). Few choose to receive their results (positive or negative) by WhatsApp Messenger (4% or 4%, respectively). These were similar by sex and age, although a higher proportion of males than females preferred to receive their results by telephone (S2 Table).

55 had ≥1 curable STI and were invited to the clinic for management: 52 (95%) came on their own, and 3 had to be traced.

Results of behavioural questionnaire

Most participants were currently enrolled in school (Table 1). Few participants were working (9% of men and 5% of women). Proportionally, more men aged 20-24 years reported having ever smoked a cigarette compared to women of the same age (17% vs 8%, respectively). Conversely, proportionally fewer men compared to women reported having ever had at least 1drink of alcohol (23% vs 51%, respectively). A small proportion of participants reported cannabis use 8% among men aged 20-24 years, and less than 2% of participants reported using other drugs.

321 Table 1. Baseline characteristics of participants in a population-based STI survey among young people aged 15-24 years in rural KwaZulu-Natal (N=447)

	Male			Female			Overall		
	15-19	**20-24**	**Total**	**15-19**	**20-24**	**Total**	**15-19**	**20-24**	**Total**
Total	124	64	188	124	135	259	248	199	447
Characteristics[1]									
Highest level of education									
Primary	16 (12.9%)	3 (4.7 %)	19 (10.1%)	5 (4.0 %)	9 (6.7 %)	14 (5.4 %)	21(8.5 %)	12 (6.0 %)	33(7.4 %)
Secondary	90 (72.6%)	21 (32.8%)	111 (59.0%)	106 (85.5%)	52 (38.5%)	158 (61.0%)	196(79.0%)	73 (36.7%)	269(60.2%)
Matric or above	18 (14.5%)	40 (62.5%)	58 (30.9%)	13 (10.5%)	74 (54.8%)	87 (33.6%)	31(12.5%)	114 (57.3%)	145(32.4%)
Socio-economic status									
Low	53 (42.7%)	27 (42.2%)	80 (42.6%)	57 (46.3%)	60 (44.8%)	117 (45.5%)	110(44.5%)	87 (43.9%)	197 (44.3%)
Middle	30 (24.2%)	18 (28.1%)	48 (25.5%)	24 (19.5%)	38 (28.4%)	62 (24.1%)	54 (21.9%)	56 (28.3%)	110 (24.7%)
High	41 (33.1%)	19 (29.7%)	60 (31.9%)	42 (34.2%)	36 (26.9%)	78 (30.4%)	83 (33.6%0	55 (27.8%)	138 (31.0%)
Currently in school									
Yes	114 (91.9%)	30 (46.9%)	144 (76.6%)	112 (90.3%)	47 (35.1%)	159 (61.6%)	226(91.1%)	77 (38.9%)	303(67.9%)
Working									
Yes	12 (9.8 %)	8 (12.5 %)	20 (8.6 %)	7 (5.7 %)	7 (5.2 %)	14 (5.4 %)	19(7.7 %)	15 (7.5 %)	34(7.6%)
Ever smoked cigarette									
Yes	3 (2.5 %)	11 (17.2%)	14 (7.5 %)	13 (10.6%)	11 (8.1 %)	24 (9.3 %)	16(6.5 %)	22 (11.1%)	38(8.6 %)
Ever used cannabis									
Yes	1 (0.8%)	5 (7.8%)	6 (3.2%)	8 (6.5%)	5 (3.7%)	13 (5.0%)	9 (3.6%)	10 (5.0%)	19 (4.3%)
Use other drugs									
Yes	2 (1.6 %)	--	2 (1.1 %)	1 (0.8 %)	2 (1.5 %)	3 (1.2 %)	3(1.2 %)	2 (1.0 %)	5(1.1 %)
Ever drunk 1 drink of alcohol									
Yes	26 (21.7%)	17 (26.6%)	43 (23.4%)	57 (47.1%)	73 (54.5%)	130 (51.0%)	83(34.4%)	90 (45.5%)	173(39.4%)
Ever been circumcised									
Yes	71 (57.3%)	25 (39.1%)	96 (51.1%)	--	--	--	--	--	--
Cleanse inside vagina									
Yes	--	--	--	13 (10.7%)	28 (20.9%)	41 (16.1%)	--	--	--

Use contraception									
Yes	--	--	--	27 (22.5%)	67 (50.4%)	94 (37.2%)	--	--	--
Ever had sex									
Yes	29 (23.6%)	32 (52.5%)	61 (33.2%)	54 (46.2%)	101 (77.7%)	155 (62.8%)	83(34.6%)	133 (69.6%)	216(50.1%)
Condom at last sex									
Yes	16 (55.2%)	20 (60.6%)	36 (58.1%)	26 (49.1%)	36 (36.4%)	62 (40.8%)	42(51.2%)	56 (42.4%)	98(45.8%)
Partner discuss their HIV status									
Yes	8 (27.6%)	13 (44.8%)	21 (36.2%)	25 (46.3%)	60 (61.2%)	85 (55.9%)	33(39.8%)	73 (57.5%)	106(50.5%)
Know partner's HIV status									
Yes	9 (31.0%)	13 (43.3%)	22 (37.3%)	28 (49.1%)	59 (59.0%)	87 (55.4%)	37(43.0%)	72 (55.4%)	109(50.5%)
Discuss your HIV status with partner									
Yes	12 (50.0%)	14 (46.7%)	26 (48.1%)	28 (53.8%)	62 (68.9%)	90 (63.4%)	40(52.6%)	76 (63.3%)	116(59.2%)
Number of current sexual partners									
None	94 (78.3%)	29 (49.2%)	123 (68.7%)	63 (57.3%)	29 (23.2%)	92 (39.1%)	157(68.3%)	58 (31.5%)	215(51.9%)
1	21 (17.5%)	21 (35.6%)	42 (23.5%)	44 (40.0%)	91 (72.8%)	135 (57.4%)	65(28.3%)	112 (60.9%)	177(42.8%)
2 or more	5 (4.2 %)	9 (15.3%)	14 (7.8 %)	3 (2.7 %)	5 (4.0 %)	8 (3.4 %)	8(3.5 %)	14 (7.6 %)	22(5.3 %)
Oral sex, receive									
Yes	9 (7.3 %)	7 (11.5%)	16 (8.7 %)	11 (9.2 %)	38 (30.2%)	49 (19.9%)	20(8.2 %)	45 (24.1%)	65(15.1%)
Oral sex, provide									
Yes	12 (9.7 %)	8 (12.9%)	20 (10.8%)	21 (17.5%)	59 (46.1%)	80 (32.3%)	33(13.5%)	67 (35.3%)	100(23.0%)
Ever had anal sex									
Yes	2 (1.6 %)	--	2 (1.1 %)	6 (5.0 %)	6 (4.7 %)	12 (4.8 %)	8(3.3 %)	6 (3.2 %)	14(3.2 %)
Violence (perpetrator)									
Yes	5 (4.1%)	3 (4.9%)	8 (4.4%)	3 (2.6%)	8 (6.2%)	11 (4.3%)	8 (3.4%)	11 (5.8%)	19 (4.4%)
Violence (victim)									
Yes	6 (6.4%)	3 (4.8%)	11 (5.9%)	7 (5.8%)	19 (15.1%)	26 (10.5%)	15 (6.1%)	22 (11.7%)	37 98.7%)
HIV status[2]									
Positive	2 (3.6%)	5 (19.2%)	7 (8.5%)	6 (8.6%)	23 (29.5%)	29 (19.6%)	8 (6.4%)	28 (26.9%)	36 (15.7%)
Negative	54 (96.4%)	21 (80.8%)	75 (91.5%)	64 (91.4%)	55 (70.5%)	119 (80.4%)	118(93.6%)	76 (73.1%)	194 (84.3%)

[1]Proportions of individuals who responded to study questions (excluding those who preferred not to answer). [2] Among individuals who participated in the 2016 serosurvey

51% men reported circumcision: younger men were more likely to be circumcised (Table 1). 16% women reported using intravaginal cleansing, older women were more likely to report intravaginal cleansing. 23% of women aged 15-19 and 50% of women aged 20-24 reported contraceptive use.

61 (33%) men and 155 (63%) women reported having had sexual intercourse; of these, the median(IQR) of lifetime partners was 4(2-6) for men and 3(2-3) for women. A larger proportion of men than women reported having used a condom at last intercourse 58% vs 41%, respectively). A smaller proportion of men than women reported knowing their last partner's HIV status (37% vs 55%, respectively), and a smaller proportion of men than women reported discussing their own HIV status with their last partner (48% of men vs 63% of women).

More women aged 20-24 years reported providing (32%) or receiving oral sex (20%) than men of the same age group (11% and 9%, respectively). Few participants reported ever having anal sex, fewer men than women (1% vs 5%). Among men who participated in the 2016 HIV serosurvey, the prevalence of HIV among those aged 15-19 years was 4%, aged 20-24 years was 19%. Among women the prevalence of HIV among those aged 15-19 years was 9%, and aged 20-24 years was 30%.

Prevalence of STI/BVs

Weighted prevalence from Table 2 shows a high prevalence of chlamydia in men aged 20-24 (12.6%; 95% CI 6.5%-23.3%), and women in both age groups (15-19 years: 11.7%; 95%CI 6.8%-19.3%; 20-24 years: 10.2%; 95%CI 6.0%-176.9%). The prevalence of gonorrhoea was relatively low from 0% (no cases) among men aged 20-24 to 3.2% (95% CI 1.2%-8.2%) in women of the same age group. There was 1 case of active syphilis - the overall prevalence of active syphilis was 0.2%. There were 5 treponemal - / VDRL + samples. The prevalence of trichomoniasis was lower in men compared to women (0.6% [95%CI 0.1%-4%] vs 5% [95%CI 3%-8%]); the highest prevalence among women aged 20-24 years. 14% had a curable STI (chlamydia, gonorrhoea, syphilis and trichomoniasis). Of these, 75% reported no symptoms. The prevalence of HSV-2 was lower in men compared to women (17% [95%CI 11%-24%] vs 29% [95%CI 23%-25%]) with the highest prevalence among women aged 20-24

348 years. The prevalence of BV was 41% (95%CI 32%-50%) among women aged 15 to 19 years and 44%
349 (95%CI 35%-53% among women 20-24 years. Prevalence weighted for sampling and non-response
350 (Table 2) were similar to unweighted prevalence and prevalence using sampling weights only (S3
351 Table).

352 Table 2. Prevalence of STIs weighted for sampling and non-response in a population-based STI survey among young people aged 15-24 years in rural
353 KwaZulu-Natal (N=447)

	Male			Female			All participants		
	15–19 years (N=124)	**20–24 years (N=64)**	**All males (N=188)**	**15–19 years (N=124)**	**20–24 years (N=135)**	**All females (N=259)**	**15–19 years (N=248)**	**20–24 years (N=199)**	**All participants (N=477)**
Chlamydia									
Positive	1.6% (0.4-6.1)	12.6% (6.5-23.3)	5.3% (3.0-9.4)	11.7% (6.8-19.3)	10.2% (6.0-16.9)	11.2% (7.5-16.4)	6.2% (3.8-10.1)	11.5% (7.4-17.5)	8.1% (5.8-11.1)
Gonorrhoea									
Positive	2.3% (0.7-7.0)	0	1.5% (0.5-4.7)	1.1% (0.3-4.5)	3.2% (1.2-8.2)	1.8% (0.8-4.1)	1.8% (0.7-4.3)	1.5% (0.6-3.9)	1.7% (0.8-3.3)
Syphilis									
Active	0	0	0	0	0.8% (0.1-5.7)	0.4% (0.0-2.5)	0	0.5% (0.1-3.4)	0.2% (0.0-1.2)
Early/previously treated	0	1.4% (0.2-9.5)	0.4% (0.0-2.5)	0	3.2% (1.2-8.2)	1.4% (0.5-3.6)	0	2.4% (1.0-5.8)	0.8% (0.3-1.9)
Trichomoniasis									
Positive	0	1.7% (0.2-11.1)	0.6% (0.1-4.0)	2.0% (0.5-7.7)	9.4% (5.4-16.0)	4.6% (2.6-7.9)	0.9% (0.2-3.6)	5.3% (3.0-9.2)	2.4% (1.4-4.2)
HSV-2									
Positive	12.1% (7.3-19.2)	25.8% (14.3-41.9)	16.8% (11.3-24.1)	18.1% (11.8-26.7)	48.0% (39.2-56.9)	28.7% (23.3-34.8)	14.8% (10.7-20.1)	36.1% (28.4-44.6)	22.2% (18.2-26.8)
Bacterial vaginosis									
Intermediate	-	-	-	9.9% (5.5-17.2)	11.3% (6.8-18.3)	10.4% (6.8-15.4)	-	-	-
Positive	-	-	-	41.1% (32.3-50.4)	44.2% (35.5-53.2)	42.1% (35.5-49.0)	-	-	-

354

Factors associated with STI/BV

In the adjusted analysis of factors associated with curable STIs (chlamydia, gonorrhoea, syphilis and trichomoniasis), participants aged 20-24 years and women had more than twice the odds of having a curable STI compared to participants aged 15-19 years or men (Table 3). Increasing number of lifetime sexual partners was associated with a curable STI (p=0.034). Reporting having had sexual intercourse was strongly associated with a curable STI.

Table 3. Factors associated with chlamydia, gonorrhoea, syphilis and trichomoniasis in a population-based STI survey among young people aged 15-24 years in rural KwaZulu-Natal (N=447)

	No. with any curable STI/N(%)	Crude OR (95% CI)	Age-sex adj OR (95%CI)	Adjusted OR[1] (95% CI)
Socio-demographic				
Age group		P<0.0001	P=0.001	**P=0.001**
15-19	20 / 245 (8.2 %)	1	1.00 (1.00 -1.00)	**1**
20-24	40 / 191 (20.9%)	2.98 (1.68 -5.30)	2.64 (1.47 -4.73)	**2.64 (1.47 -4.73)**
Sex		P=0.001	P=0.006	**P=0.006**
Male	14 / 188 (7.4 %)	1	1	**1**
Female	46 / 248 (18.5%)	2.83 (1.50 -5.32)	2.45 (1.29 -4.65)	**2.45 (1.29 -4.65)**
In school or working		P=0.001	P=0.268	P=0.268
No	29 / 128 (22.7%)	1	1	1
Yes	31 / 308 (10.1%)	0.38 (0.22 -0.67)	0.69 (0.35 -1.33)	0.69 (0.35 -1.33)
Socio-economic status		P=0.276	P=0.287	P=0.287
Low	32 / 192 (16.7%)	1	1	1
Middle	14 / 109 (12.8%)	0.74 (0.37 -1.45)	0.68 (0.34 -1.36)	0.68 (0.34 -1.36)
High	14 / 133 (10.5%)	0.59 (0.30 -1.15)	0.61 (0.30 -1.21)	0.61 (0.30 -1.21)
Highest level of education completed		P=0.485	P=0.774	P=0.774
Primary	5 / 33 (15.2%)	1	1	1
Secondary	32 / 263 (12.2%)	0.78 (0.28 -2.15)	0.79 (0.27 -2.31)	0.79 (0.27 -2.31)
Matric or above	23 / 140 (16.4%)	1.10 (0.38 -3.15)	0.68 (0.22 -2.07)	0.68 (0.22 -2.07)
Behaviour				
Ever smoked cigarette		P=0.718	P=0.915	P=0.827
No	54 / 395 (13.7%)	1	1	1
Yes	6 / 38 (15.8%)	1.18 (0.47 -2.97)	1.05 (0.41 -2.68)	0.90 (0.34 -2.35)
Ever drank alcohol		P=0.014	P=0.150	P=0.150
No	27 / 259 (10.4%)	1	1	1
Yes	32 / 169 (18.9%)	2.01 (1.15 -3.49)	1.54 (0.86 -2.75)	1.54 (0.86 -2.75)
Sexual behaviour and violence				
Genital touching		P=0.001	P=0.044	P=0.296
No	24 / 258 (9.3 %)	1	1	1

Yes	36 / 178 (20.2%)	2.47 (1.42 -4.31)	1.82 (1.02 -3.26)	1.48 (0.71 -3.09)
Oral sex (receive)		P=0.106	P=0.963	P=0.201
No	39 / 326 (12.0%)	1	1	1
Yes	18 / 98 (18.4%)	1.66 (0.90 -3.05)	0.98 (0.51 -1.91)	0.62 (0.30 -1.29)
Oral sex (provide)		P=0.156	P=0.850	P=0.626
No	45 / 357 (12.6%)	1	1	1
Yes	12 / 62 (19.4%)	1.66 (0.82 -3.36)	1.07 (0.51 -2.26)	0.83 (0.38 -1.79)
Ever had sex		P<0.0001	P=0.004	**P=0.009**
No	13 / 210 (6.2 %)	1	1	**1**
Yes	45 / 210 (21.4%)	4.13 (2.16 -7.92)	2.77 (1.38 -5.55)	**2.67 (1.28 -5.55)**
Number of lifetime sexual partners		P<0.0001	P=0.014	**P=0.038**
None	13 / 210 (6.2 %)	1	1	**1**
1	17 / 82 (20.7%)	3.96 (1.83 -8.60)	2.81 (1.25 -6.33)	**2.78 (1.19 -6.50)**
2 or more	23 / 104 (22.1%)	4.30 (2.08 -8.91)	2.88 (1.32 -6.28)	**2.47 (1.07 -5.70)**
Violence-perpetrator		P=0.681	P=0.891	P=0.395
No	53 / 399 (13.3%)	1	1	1
Yes	3 / 18 (16.7%)	1.31 (0.37 -4.66)	1.10 (0.29 -4.09)	0.49 (0.09 -2.55)
Violence-victim		P=0.006	P=0.040	P=0.126
No	45 / 387 (11.6%)	1	1	1
Yes	10 / 35 (28.6%)	3.04 (1.37 -6.74)	2.39 (1.04 -5.49)	1.96 (0.83 -4.65)

[1] Sociodemographic variables adjusted for age and gender. Behavioural variables adjusted for age, gender and ever drunk alcohol. Sexual behaviour and violence variables adjusted for age, gender, ever drank alcohol, ever had sex and violence (victim). Number of lifetime sexual partners was not included for the adjustment with sexual behaviour due to collinearity with ever had sex.

In the adjusted analysis of factors associated with HSV-2, participants aged 20-24 years and women had twice the odds of HSV-2 infection compared to participants aged 15-19 years or men (Table 4). Participants currently enrolled in school or working had less than half the odds of HSV-2 infection compared to those who were neither in school nor working.

Table 4. Factors associated with herpes simplex virus-2 in a population-based STI survey among young people aged 15-24 years in rural Kwa-Zulu Natal (N=419[1])

	No. with HSV-2/N(%)	Crude OR (95% CI)	Age-sex adj OR (95%CI)	Adjusted OR[2] (95% CI)
Socio-demographic				
Age group		P<0.0001	P<0.0001	**P=0.004**
15-19	35 / 233 (15.0%)	1	1	**1**
20-24	73 / 186 (39.2%)	3.65 (2.30 -5.82)	3.29 (2.05 -5.28)	**2.23 (1.29 -3.83)**
Sex		P<0.0001	P=0.001	**P=0.006**
Male	29 / 183 (15.8%)	1	1	**1**
Female	79 / 236 (33.5%)	2.67 (1.65 -4.32)	2.28 (1.39 -3.74)	**2.03 (1.22 -3.37)**
In school or working		P<0.0001	P=0.003	**P=0.003**
No	57 / 125 (45.6%)	1	1	**1**
Yes	51 / 294 (17.3%)	0.25 (0.16 -0.40)	0.44 (0.25 -0.75)	**0.44 (0.25 -0.75)**

Socio-economic status		P=0.437	P=0.550	P=0.691
Low	51 / 184 (27.7%)	1	1	1
Middle	29 / 105 (27.6%)	1.00 (0.58 -1.70)	0.92 (0.52 -1.62)	0.85 (0.47 -1.52)
High	28 / 129 (21.7%)	0.72 (0.43 -1.23)	0.73 (0.42 -1.28)	0.79 (0.45 -1.39)
Highest level of education completed		P=0.007	P=0.413	P=0.743
Primary	9 / 31 (29.0%)	1	1	1
Secondary	51 / 251 (20.3%)	0.62 (0.27 -1.44)	0.59 (0.24 -1.45)	0.72 (0.28 -1.80)
Matric or above	48 / 137 (35.0%)	1.32 (0.56 -3.09)	0.76 (0.30 -1.93)	0.70 (0.27 -1.80)
Behaviour				
Ever smoked cigarette		P=0.289	P=0.488	P=0.400
No	96 / 381 (25.2%)	1	1	1
Yes	12 / 36 (33.3%)	1.48 (0.71 -3.08)	1.31 (0.61 -2.80)	1.40 (0.64 -3.04)
Ever drank alcohol		P=0.009	P=0.244	P=0.204
No	52 / 250 (20.8%)	1	1	1
Yes	52 / 161 (32.3%)	1.82 (1.16 -2.85)	1.34 (0.82 -2.18)	1.38 (0.84 -2.27)
Sexual behaviour and violence				
Genital touching		P<0.0001	P=0.001	P=0.255
No	42 / 247 (17.0%)	1	1	1
Yes	66 / 172 (38.4%)	3.04 (1.93 -4.78)	2.24 (1.39 -3.61)	1.40 (0.78 -2.52)
Oral sex (receive)		P=0.008	P=0.741	P=0.503
No	73 / 314 (23.2%)	1	1	1
Yes	35 / 94 (37.2%)	1.96 (1.20 -3.21)	1.10 (0.63 -1.90)	0.82 (0.46 -1.47)
Oral sex (provide)		P=0.022	P=0.577	P=0.859
No	81 / 343 (23.6%)	1	1	1
Yes	23 / 61 (37.7%)	1.96 (1.10 -3.48)	1.19 (0.64 -2.22)	0.94 (0.49 -1.81)
Ever had sex		P<0.0001	P=0.004	**P=0.012**
No	31 / 204 (15.2%)	1	1	**1**
Yes	76 / 201 (37.8%)	3.39 (2.11 -5.47)	2.14 (1.27 -3.58)	**1.96 (1.16 -3.32)**
Number of lifetime sexual partners		P<0.0001	P=0.035	P=0.085
None	31 / 204 (15.2%)	1	1	1
1	21 / 78 (26.9%)	2.06 (1.10 -3.86)	1.40 (0.72 -2.73)	1.29 (0.65 -2.56)
2 or more	39 / 100 (39.0%)	3.57 (2.05 -6.21)	2.22 (1.21 -4.06)	2.01 (1.08 -3.73)
Violence-perpetrator		P=0.791	P=0.558	P=0.394
No	102 / 386 (26.4%)	1	1	1
Yes	4 / 17 (23.5%)	0.86 (0.27 -2.69)	0.70 (0.21 -2.33)	0.59 (0.18 -1.98)
Violence-victim		P=0.102	P=0.400	P=0.532
No	94 / 373 (25.2%)	1	1	1
Yes	13 / 34 (38.2%)	1.84 (0.89 -3.81)	1.40 (0.64 -3.08)	1.29 (0.58 -2.83)

[1] Number less than 447 due to the number of samples collected for testing for HSV-2. [2] Socio-demographic variables adjusted for age, gender and in school/working. Behaviour variable adjusted for age, gender and in school/working. Sexual behaviour and violence variables adjusted for age, gender, in school/working and ever had sex. Number of lifetime sexual partners was not included for the adjustment with sexual behaviour due to collinearity with ever had sex.

In the adjusted analysis of factors associated with BV, there was weak evidence that being currently enrolled in school or working was associated with a diagnosis BV. Those having ever drunk alcohol had twice the odds of a diagnosis of BV, and there was weak evidence that having ever smoked a cigarette was associated with a diagnosis of BV. Independently, those reporting genital touching and having

382 ever had sex had twice the odds of a diagnosis of BV. Participants who were HSV-2 seropositive had

383 four times the odds of a diagnosis with BV.

384 Table 5. Factors associated with bacterial vaginosis in young women in a population-based STI survey
385 among young people aged 15-24 years in rural Kwa-Zulu Natal (N=239[1])

	No. with BV/N(%)	crude OR (95% CI)	Age adj OR (95%CI)	Adjusted OR[2] (95% CI)
Socio-demographic				
Age group		P=0.640	P=0.640	P=0.469
15-19	49 / 119 (41.2%)	1	1	1
20-24	53 / 120 (44.2%)	1.13 (0.68 -1.89)	1.13 (0.68 -1.89)	0.79 (0.42 -1.49)
In school or working		P=0.059	P=0.050	**P=0.050**
No	45 / 89 (50.6%)	1	1	**1**
Yes	57 / 150 (38.0%)	0.60 (0.35 -1.02)	0.52 (0.27 -1.00)	**0.52 (0.27 -1.00)**
Socio-economic status		P=0.092	P=0.090	P=0.128
Low	54 / 107 (50.5%)	1	1	1
Middle	24 / 60 (40.0%)	0.65 (0.34 -1.24)	0.64 (0.34 -1.23)	0.61 (0.31 -1.16)
High	24 / 70 (34.3%)	0.51 (0.27 -0.95)	0.51 (0.28 -0.96)	0.56 (0.30 -1.06)
Highest level of education completed		P=0.582	P=0.643	P=0.816
Primary	7 / 13 (53.8%)	1	1	1
Secondary	60 / 148 (40.5%)	0.58 (0.19 -1.83)	0.59 (0.19 -1.87)	0.73 (0.22 -2.39)
Matric or above	35 / 78 (44.9%)	0.70 (0.21 -2.27)	0.69 (0.21 -2.26)	0.68 (0.20 -2.24)
Behaviour				
Ever smoked cigarette		P=0.027	P=0.027	P=0.104
No	87 / 215 (40.5%)	1	1	1
Yes	15 / 23 (65.2%)	2.76 (1.12 -6.79)	2.77 (1.13 -6.82)	2.19 (0.85 -5.61)
Ever drunk alcohol		P=0.012	P=0.014	**P=0.009**
No	39 / 114 (34.2%)	1	1	**1**
Yes	61 / 121 (50.4%)	1.96 (1.16 -3.31)	1.94 (1.15 -3.29)	**2.04 (1.19 -3.48)**
Ever cleanse inside vagina		P=0.569	P=0.545	P=0.861
No	88 / 200 (44.0%)	1	1	1
Yes	14 / 36 (38.9%)	0.81 (0.39 -1.67)	0.80 (0.38 -1.66)	0.93 (0.44 -1.99)
Use hormonal contraception		P=0.425	P=0.467	P=0.876
No	84 / 202 (41.6%)	1	1	1
Yes	18 / 37 (48.6%)	1.33 (0.66 -2.69)	1.30 (0.64 -2.66)	1.06 (0.49 -2.29)
Sexual behaviour and violence				
Genital touching		P<0.0001	P<0.0001	**P=0.021**
No	36 / 122 (29.5%)	1	1	**1**
Yes	66 / 117 (56.4%)	3.09 (1.81 -5.27)	3.12 (1.82 -5.35)	**2.12 (1.12 -4.02)**
Oral sex (receive)		P=0.014	P=0.013	P=0.682
No	57 / 158 (36.1%)	1	1	1
Yes	39 / 73 (53.4%)	2.03 (1.16 -3.57)	2.11 (1.17 -3.82)	1.16 (0.58 -2.31)
Oral sex (provide)		P=0.068	P=0.077	P=0.936
No	71 / 186 (38.2%)	1	1	1
Yes	23 / 43 (53.5%)	1.86 (0.95 -3.63)	1.86 (0.94 -3.71)	0.97 (0.45 -2.11)
Ever had sex		P<0.0001	P<0.0001	**P=0.031**
No	22 / 85 (25.9%)	1	1	**1**
Yes	74 / 143 (51.7%)	3.07 (1.71 -5.52)	3.43 (1.85 -6.38)	**2.14 (1.07 -4.27)**

Number of lifetime sexual partners		P=0.003	P=0.001	P=0.261
None	22 / 85 (25.9%)	1	1	1
One	31 / 64 (48.4%)	2.69 (1.35 -5.36)	2.93 (1.45 -5.93)	1.79 (0.82 -3.90)
Two or more	31 / 60 (51.7%)	3.06 (1.52 -6.17)	4.02 (1.85 -8.73)	1.91 (0.78 -4.69)
Violence-perpetrator		P=0.636	P=0.654	P=0.555
No	92 / 217 (42.4%)	1	1	1
Yes	5 / 10 (50.0%)	1.36 (0.38 -4.83)	1.34 (0.37 -4.81)	1.52 (0.38 -6.14)
Violence-victim		P=0.960	P=0.990	P=0.585
No	88 / 205 (42.9%)		1	1
Yes	10 / 23 (43.5%)	1.02 (0.43 -2.44)	1.01 (0.42 -2.43)	1.30 (0.51 -3.30)
STI				
HSV-2		P<0.0001	P<0.0001	**P<0.0001**
Negative	50 / 152 (32.9%)	1	1	**1**
Positive	49 / 74 (66.2%)	4.00 (2.22 -7.20)	4.52 (2.40 -8.50)	**4.08 (2.03 -8.19)**
N Gonorrheae/C trachomatis		P=0.044	P=0.044	P=0.768
Negative	84 / 209 (40.2%)	1	1	1
Positive	18 / 30 (60.0%)	2.23 (1.02 -4.87)	2.23 (1.02 -4.88)	1.15 (0.46 -2.89)
T vaginalis		P=0.989	P=0.944	P=0.287
Negative	96 / 225 (42.7%)	1	1	1
Positive	6 / 14 (42.9%)	1.01 (0.34 -3.00)	0.96 (0.32 -2.91)	0.51 (0.15 -1.77)

[1] Number less than 447 due to the number of samples collected for testing for BV. [2]Sociodemographic variables adjusted for age and in school/working. Behaviour variables adjusted for age, in school/working and ever drank alcohol. Sexual behaviour adjusted for age, in school/working, ever drank alcohol, genital touching ever had sex, and HSV-2. Number of lifetime sexual partners was not included for the adjustment with sexual behaviour due to collinearity with ever had sex.

In the subgroup analysis among participants who reported having sex, there was weak evidence that discussing the last partner's HIV status was associated with not having a curable STI (aOR 0.48; 95%CI 0.23-1.00 [S4 Table]). There was no evidence that factors included in this subgroup analysis were associated with either HSV-2 infection or diagnosis of BV (S5-6 tables).

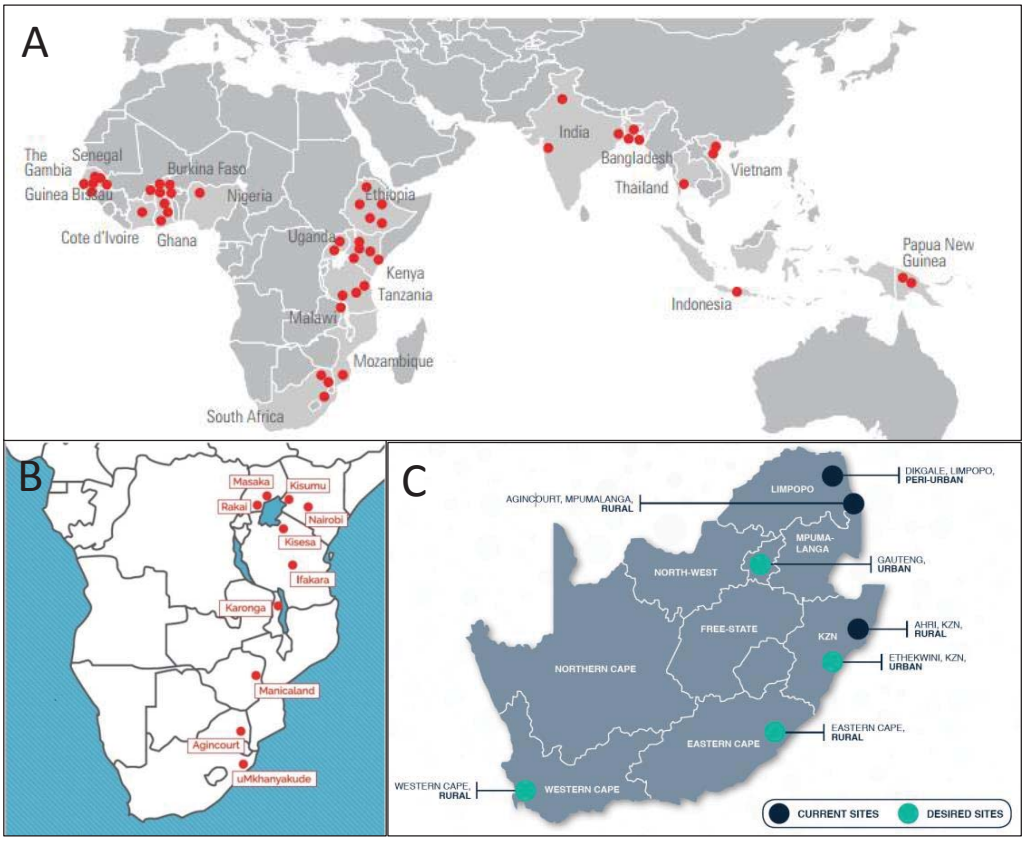
Discussion

We conducted a nested STI survey among young people aged 15 to 24 years in a rural HDSS in KwaZulu-Natal, and found it to be feasible and acceptable. The HDSS provided infrastructure and a sampling frame to carry out a population-based cross-sectional study of STI/BV prevalence. There was a high burden of STI/BV in this high HIV prevalence setting. Most of these were asymptomatic and would not have been identified or treated using national syndromic management guidelines.

This study is a proof-of-concept that STI surveys can be successfully conducted within HDSS networks such as the IN-DEPTH Network [11], the ALPHA Network [22], and the SAPRIN Network [23] (Fig 3).

403 The implementation of STI surveys within HDSS is an efficient use of resources and has two important
404 utilities. Firstly, STI surveys can be carried out in LMICs intermittently to contribute to the estimate of
405 the global burden of STIs and to evaluate local implementation of global STI control programmes at a
406 population level. Secondly, STI surveys can be carried out more frequently in settings with high HIV/STI
407 prevalence to monitor and evaluate enhanced STI/HIV control programmes. HDSS networks could
408 provide a strategic platform to strengthen STI surveillance and control in LMIC, especially in sub-
409 Saharan Africa where HIV and STI/BV prevalence are high. Importantly, while population-based data
410 are crucial for an effective STI prevention and control programme, these data must be complemented
411 by robust data from high-risk groups (e.g. female sex workers) to account for STI transmission
412 dynamics which depend on high rates of partner change [24].

413 Figure 3. Maps illustrating networks of health and demographic surveillance sites (HDSS) at the global,
414 regional and national level. A: IN-DEPTH Network, a network of 42 centres in 18 LMICs in Africa, Asia
415 and Oceania conducting population-based surveillance of the health status of communities
416 (www.indepth-network.org/member-centres). B: ALPHA Network, a network of 10 centres in sub-
417 Saharan Africa conducting population-based HIV surveillance (www.alpha.lshtm.ac.uk/partner-study-
418 institutions/). C: SAPRIN Network, an expanding network of HDSS in South Africa
419 (http://saprin.mrc.ac.za/SAPRINfactSHEET.pdf).



420

421 The burden of chlamydia was high in this STI survey among women of both age groups and among
422 men aged 20-24 years, ranging from 10-12%. Several studies report high prevalence of chlamydia in
423 South Africa [25–28]; both MTN-003 (VOICE) and HPTN 055 showed higher baseline chlamydia
424 prevalence and incidence among women in South Africa compared to other sites in the multi-site
425 studies, and both reported higher prevalence and incidence among women under 24 years old [26,27].
426 These studies uncover sub-regional or national differences in STI epidemics among young people that
427 could be further elucidated with the implementation of STI surveys in a network of HDSS. Importantly,
428 syndromic management is notably weak for identifying cases for chlamydia because most cases are
429 asymptomatic. Yet, asymptomatic chlamydia causes serious morbidity including pelvic inflammatory
430 disease in women contributing to chronic pelvic pain, ectopic pregnancy and tubal factor infertility
431 [29]. Etiological surveillance is, therefore, critical to understand the global burden of chlamydia.
432 However, etiological diagnosis outside of surveillance is unaffordable and inaccessible for most LMICs.

Rapid, accurate and affordable point of care tests may bridge this gap, but current point of care tests for chlamydia and gonorrhoea are either inaccurate (antigen detection in lateral flow format) or expensive (e.g. GeneXpert)[29]. Targeting high risk populations, including adolescents and young people, for chlamydia is important; the South African National Strategic Plan for HIV, TB and STIs 2017-2022 calls for the development, testing and validation of sexual history taking for different populations and different ages as the basis for screening tests and/or presumptive treatment to increase detection and treatment of asymptomatic STIs by 50% [30]. The development of tools such as these must be carried out in parallel with population-based STI surveys and analyses of risk factors.

The burden of HSV-2 was also high – almost twice as high for young women than for young men, and almost 50% in women aged 20-24 years. Rapid acquisition of HSV-2 after sexual debut has been shown in several studies [7,9], and can be a biological proxy for sexual activity. Another compelling case for surveillance of HSV-2 is the strong evidence that HSV-2 infection increases risk of HIV acquisition. There was also high prevalence of BV among young women in this study – over 40% of women had a diagnosis of BV. Factors associated with BV in our study (sexual debut, currently having more than one sex partner, and HSV-2 infection) are consistent with the literature [29]. Despite BV not being considered a traditional STI, there is an accumulating body of epidemiological and microbiological evidence suggesting that sexual transmission is an integral part to its pathogenesis [29]. In addition, BV has been shown to be highly prevalent in sub-Saharan Africa [31], and is associated with serious reproductive and obstetric sequelae, including preterm delivery and increased risk of STI and HIV acquisition and transmission of HIV [3,32–36]. Although not curable STIs, better control tools are needed for HSV-2 and BV, and we recommend continued integration of HSV-2 and BV in STI prevalence surveys.

Population-based demographic and behavioural data are also important for planning and evaluating STI prevention and control programmes [37]. In this HIV hyper-endemic setting it is reassuring that there was a higher prevalence of self-reported circumcision among younger aged men – suggesting

458 population impact of male medical circumcision programmes. However, the extremely low self-report
459 of condom use at last sex is a tremendous concern. In addition, few participants knew their last
460 partner's HIV status. In this STI survey, enrolment in school was protective for HSV-2 and trended
461 towards a protective effect for curable STIs and BV. These data mirror findings from the AHRI HDSS
462 which shows that out of school youth report earlier sexual debut and high-risk sex [38], suggesting
463 that interventions to keep adolescents in school are just as relevant for STIs as they are for HIV [39,40].

464 Strengths of this study include a high rate of acceptability for participation and sample collection, the
465 success in treating those with a curable STI, and the use of a population-based platform as a sampling
466 frame. There are several challenges for carrying out home-based studies, including contacting young
467 people during school hours and the provision of confidential results to participants; however, we
468 maximised contact by modifying the field work hours from 11:00 to 19:00 from Tuesday to Saturday,
469 and provide participants with a choice of mode for receiving results. Once contacted, enrolment into
470 a population-based study of STI/BV testing was acceptable among young people, as was home-based
471 testing and self-sampling. An additional strength of this study is that it was conducted in an area with
472 persistently high HIV incidence and prevalence. Results of this study could help to inform co-strategies
473 to address both HIV and STIs that synergize the transmission of HIV.

474 This study was not without limitations. The sample collection period was limited to 3.5 months by the
475 start of the next HDSS surveillance round and we did not reach our target of 800 young people. The
476 smaller sample size of 447 provided less precision for prevalence estimates and less power to
477 investigate factors associated with STI/BV. In addition, the overall coverage in the survey was low
478 increasing the potential for selection bias. It was challenging to find young men aged 20-24 years at
479 home. HPTN 017 (PopART), a cluster-randomized controlled trial offering home-based HIV counselling
480 and testing in South Africa and Zambia also reported that young men (32.7%) more than young women
481 (20.2%) were not at home at the time of visits [41]. Furthermore, many young people were not at
482 home due to migration. The AHRI individual survey of residents aged 17-49 approximately 1/5th of

men and women in any survey round have migrated at least once in the last 2 years, and persons with a recent migration history have a higher risk of HIV infection [42]; thus those with a recent migration history are likely to have a different risk profile. The AHRI HDSS was established in a highly mobile population with a severe HIV epidemic, in which characterisation of migration and mobility was central to its conceptual and data model [43]. Indeed, nesting STI surveys in HDSS may offer another advantage over one-off *de novo* STI prevalence surveys: the HDSS sampling frame has information about those who are not enrolled into the study. Additionally, while a one-time survey will miss some of those who have migrated; annual repeat cross-sectional surveys will ensure that most people will contribute data over time. Reassuringly, the STI/BV prevalence weighted for both sampling and non-response data was very similar to the unweighted data or data weighted for sampling only.

Another limitation was that there was evidence of underreporting sexual behaviours: 6% of participants with a curable STI and 15% of participants with HSV-2 reported never having had sex. Sexual behavioural questions were self-collected using a computer-assisted survey instrument, and study nurses were gender-matched and ensured that interviews were conducted in a private location. Yet underreporting of sexual behaviour is common, especially among adolescents.[44] While questionnaire delivery modes do affect self-reported sexual behaviour [15,45], underreporting was still a challenge. Further research is needed to assess factors affecting validity of self-reported behaviours among adolescents[46,47]. Importantly, underreporting of sexual behaviour highlights the need to have more robust biological measures of sexual risk, such as STI prevalence.

Finally, this survey is limited to the STI we tested for – future surveys should consider surveillance of *Mycoplasma genitalium* infection and *Neisseria gonorrhoeae* resistance in this population. In addition, surveillance of HPV infection and receipt of vaccination may be important to evaluate implementation of HPV vaccination programmes.

In conclusion, the global population of adolescents and young people is increasing, particularly in sub-Saharan Africa. STIs, including incident HIV, cluster in this population, especially among women. The

508 principles of 'epidemiology synergy' between STI and HIV strongly suggest that STI control must be
509 addressed if HIV is to be brought under effective control [48]. Yet, STI prevalence data are scarce, and
510 there is an urgent need for population-based, representative prevalence estimates of STIs, especially
511 in HIV endemic settings. These data should be complemented by robust prevalence estimates in key-
512 populations, often underrepresented in population-based surveys, to gain a full understanding of
513 burden of STIs and impact of interventions. Without robust prevalence estimates, moving an
514 international STI agenda forward will continue to be a challenge. Nesting STI prevalence surveys in the
515 HDSS could provide an efficient strategy for obtaining these data.

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Supporting Information

S1 Checklist	STROBE Statement—Checklist of items that should be included in reports of cross-sectional studies
S1 Statistical Analysis Plan	Statistical Analysis Plan for Protocol Title: A study to pilot the surveillance of reproductive tract infections among young people aged 15 to 24 years in the Africa Centre Demographic Surveillance Area
S1 Table	Comparison of selected characteristics of those who enrolled vs those who did not enrol in a population-based STI survey among young people aged 15-24 years in rural KwaZulu-Natal

S2 Table	Contact preferences for results by age and sex in population-based STI survey among young people aged 15-24 years in rural KwaZulu-Natal among participants who had access to a telephone
S3 Table	Prevalence of STIs in population-based STI survey among young people aged 15-24 years in rural KwaZulu-Natal: unweighted prevalence and with sampling weights only
S4 Table	Factors associated with gonorrhoea, chlamydia and trichomoniasis in a subgroup analysis among individuals who reported having had sex in a population-based STI survey among young people aged 15-24 years in rural KwaZulu-Natal
S5 Table	Factors associated with herpes simplex virus-2 in a subgroup analysis among individuals who reported having had sex in a population-based STI survey among young people aged 15-24 years in rural KwaZulu-Natal
S6 Table	Factors associated with bacterial vaginosis in a subgroup analysis among women who reported having had sex in a population-based STI survey among young people aged 15-24 years in rural KwaZulu-Natal

Figure 1

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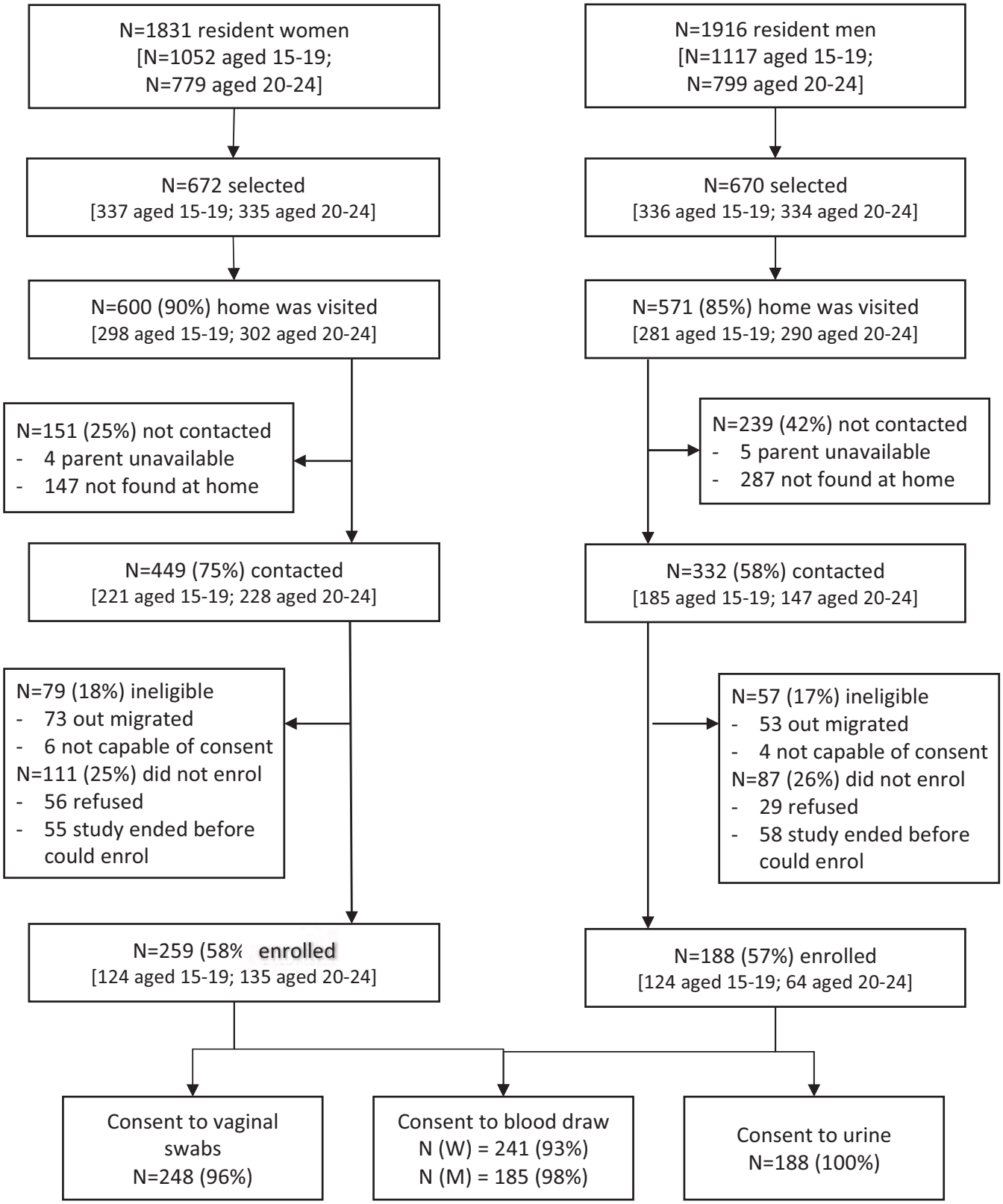

Figure 2a

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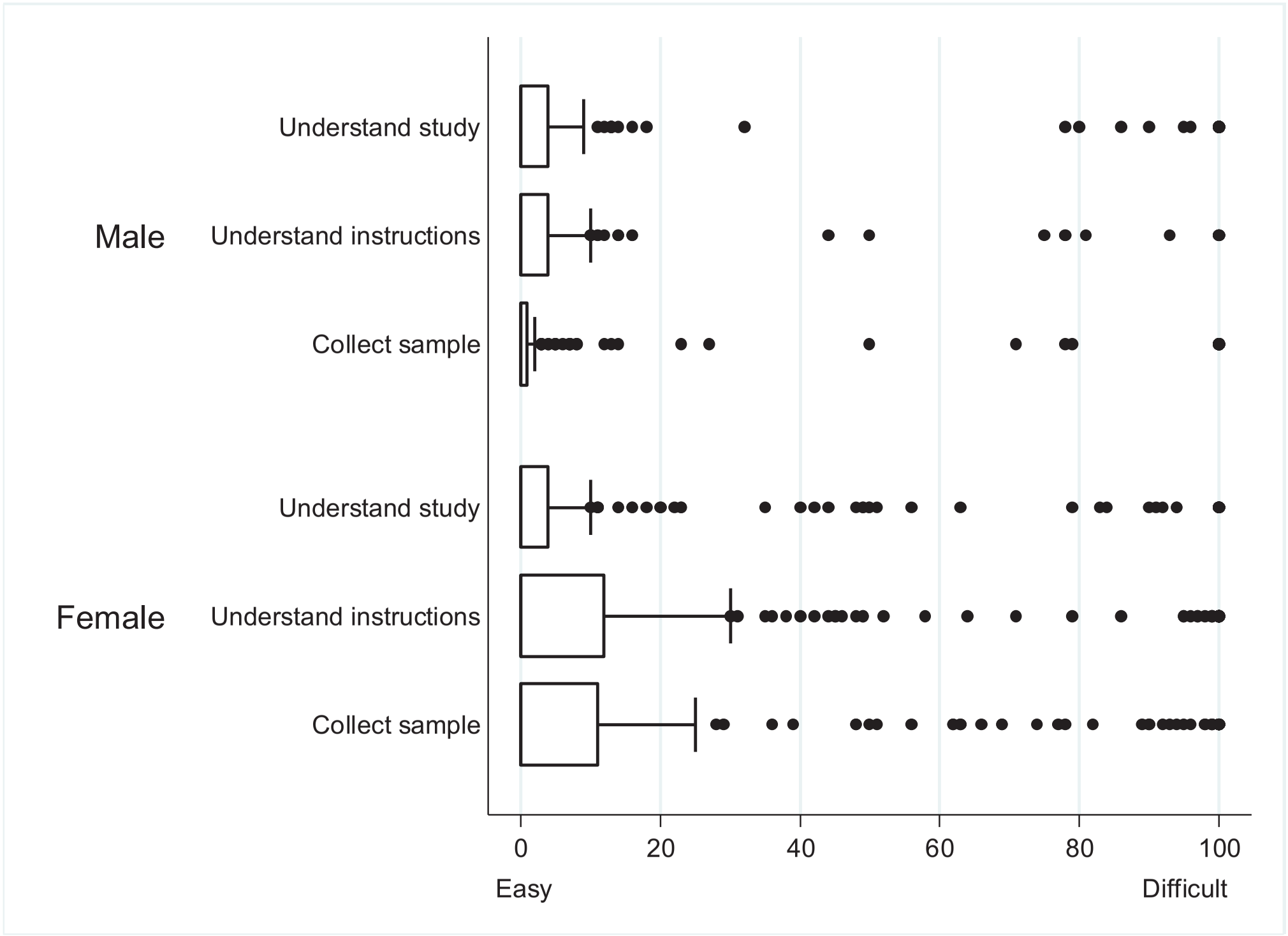

Figure 2b

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B. Positive Items

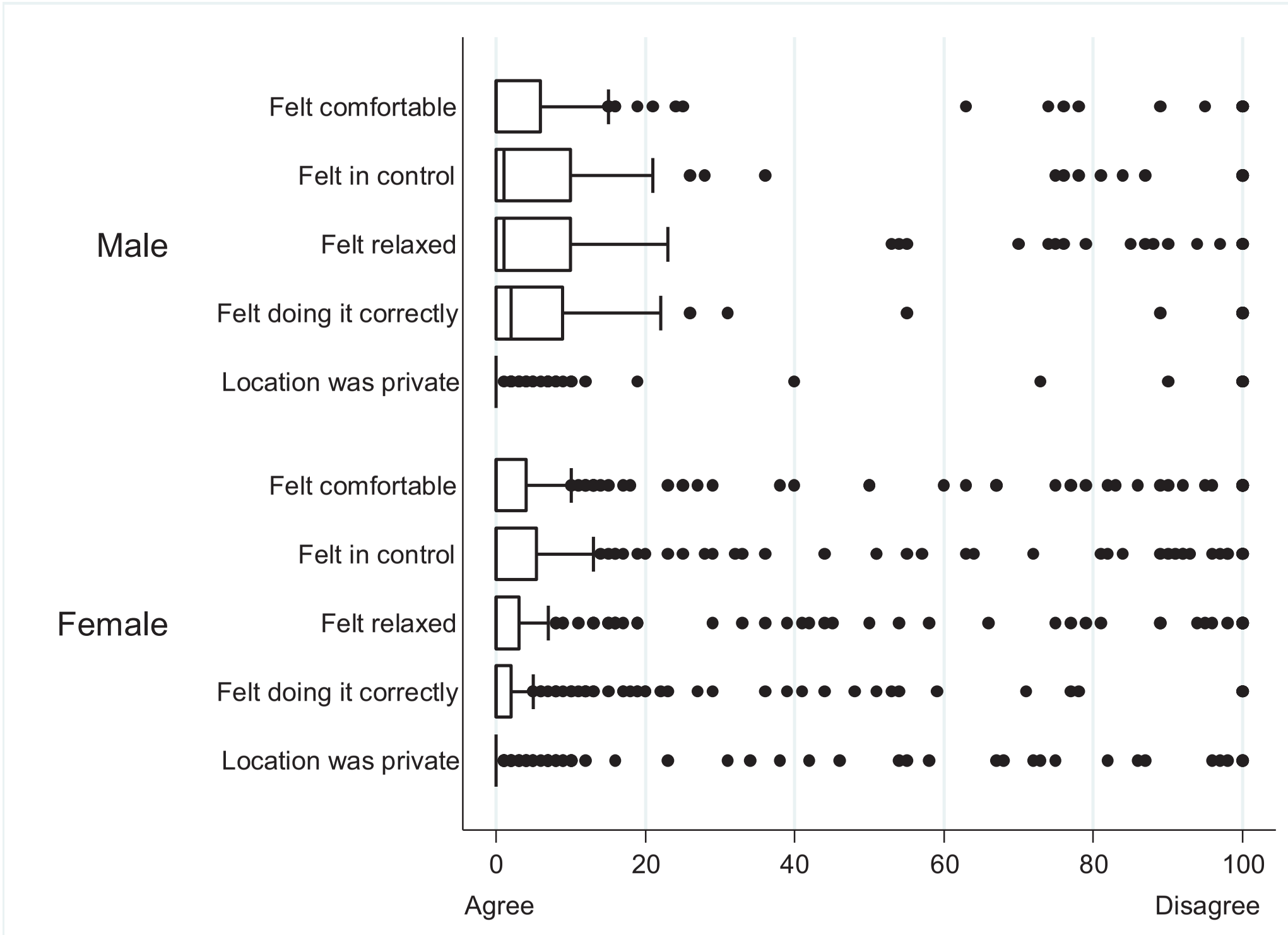

Figure 2c

C. Negative items

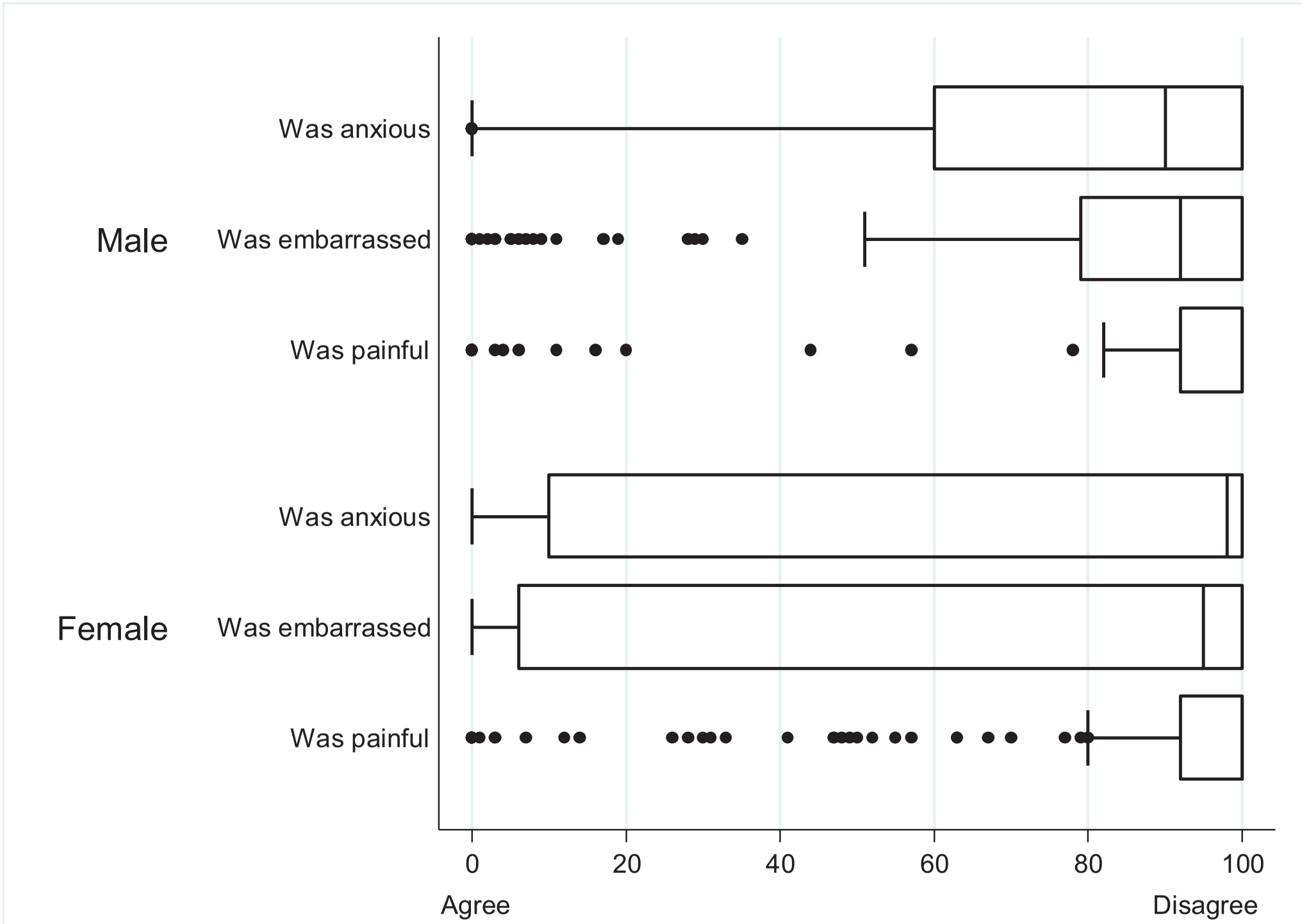

Figure 3

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