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High prevalence of sexually transmitted infections, and high-risk sexual behaviors among indigenous adolescents of the Comarca Ngäbe-Buglé, Panama

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Short summary (WC=28 of 30):

The burden of STI in Comarca Ngäbe-Buglé high-school adolescents, is similar or higher than in urban Panama. There is urgent need to implement targeted screening and other interventions.

Abstract

Background: There is scant information on STI prevalence and risk factors among Latin American indigenous populations. We investigated STI prevalence and risk factors among adolescents of the Comarca Ngäbe-Buglé (CNB) indigenous region of Panama.

Methods: A population-based cross-sectional study was conducted among school-going adolescents aged 14-19-years. Eligible consenting participants self-completed a questionnaire and provided blood and urine samples. Females provided additional self-administered genital swabs. Seroprevalences of HIV, syphilis, hepatitis B (HBsAg, anti-HBc) and herpes simplex virus type-2 (HSV-2) were determined in all participants; genital *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) by PCR among participants who reported sexual experience or were seropositive for HIV/syphilis/HSV2/HBsAg; high-risk HPV by qualitative DNA assay and bacterial vaginosis (BV) by Gram-stain among females. Risk factors were identified by estimating adjusted odds-ratios (AOR) using random-effects logistic regression.

Results: We enrolled 700 participants (median age: 17 years [females], 18 years [males]) from 20 schools. Sexual experience was reported by 536 participants (76.6%). HIV/STI prevalences among females and males were: HIV 0.4% and 1.0%, high-titer active syphilis 1.3% and 6.6%, HSV-2 16.1% and 16.1%, HBsAg 1.3% and 1.4%, anti-HBc 3.2% and 1.4%, NG 1.8% and 1.7%, CT 17.5% and 10.7%; among females: BV 42.9% and HPV 33.2%. CT was independently associated with being female (AOR=2.02, 95%CI:1.20-3.41); high-titer active syphilis with being male (AOR=4.51, 95%CI:1.17-17.40). BV was associated with sexual behavior (≥3 lifetime sex partners, AOR=3.81, 95%CI:1.29-11.26), HPV with sexual experience (AOR=4.05, 95%CI:1.62-10.09).

Conclusions: School-going indigenous adolescents in rural Panama have substantial STI burden. Targeted STI screening is required.

Key words: STI, adolescents, indigenous populations, schools, Panama

Introduction

Sexually transmitted infections (STIs) are commonly acquired during adolescence and, if left untreated, can lead to poor sexual and reproductive outcomes, such as pelvic inflammatory disease, infertility and enhanced HIV vulnerability (1). Indigenous peoples, particularly those who live in rural areas, are especially vulnerable to STIs due to unequal access to healthcare, especially to STI treatment and care (2).

In Panama, indigenous peoples make up 12.2% of the total population. The Comarca Ngäbe-Bugle (CNB) is Panama's most populated indigenous region with over 200,000 individuals, with the country´s highest levels (93.4%) of multidimensional poverty (3). Prevalence of HIV among 15-24-year-old females and males in Panama is estimated at 0.3% and 0.5%, respectively (4). However, in CNB, Ministry of Health (MOH) data show that, between 2013-2017, 2.1% (868/41,982) of rapid HIV tests performed were positive, with 82.0% of HIV infections in males, and 16.7% in 14-19-year-old male and females (5). As in other low- and middle-income countries, most STIs are managed syndromically in Panama, with little STI screening or etiological surveillance, except for prenatal MOH data which estimated maternal syphilis as 1.94% in 2017 (6). Furthermore, CNB-MOH data indicate low prevalence of hepatitis B virus (HBV), whilst no data exists for *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG), or high-risk human papillomavirus (HR-HPV) (6). Vaccination against HPV genotypes 16 and 18 was rolled out in 2008 through a school-based program targeting 10-year-old females (7). In 2015, the tetravalent vaccine was substituted in the same age group; in 2016, 10-year-old males were included (8). Despite universal rollout of HPV vaccination, monitoring of uptake is not

available. While some national STI data are stratified by region, they are not by ethnicity. Specifically, there are no MOH data on STIs among indigenous youth of CNB.

The World Health Organization (WHO) Strategy on STIs 2016-21 defines the global strategy for the prevention and control of STIs (9). The first strategic direction is to collect laboratory diagnosed epidemiological data on STIs, to plan, fund, and undertake effective targeted interventions. To inform this strategic direction, we conducted the first community-based prevalence study of STIs focused on school-going indigenous adolescents in CNB.

Methods

Between July-November 2018, we conducted a cross-sectional study among male and female adolescent students aged 14-19 years, enrolled in high-schools (7^{th}-12^{th} grades), using two-stage cluster sample design with random sampling of clusters, and equal probability of selection (Figure 1).

Study procedures

The sampling frame was the 20 largest CNB high-schools, equating to 41.7% of all CNB high-school students. Schools were arranged in 5 groups of 4, in decreasing order by enrolment numbers. Two schools were randomly selected from each group. Then, all 7^{th}-12^{th} grade classrooms in selected schools were ordered by decreasing classroom size, arranged into groups of ten, from which two classrooms were selected until about 1100 14-19-year-old individuals were selected; we assumed two-thirds would agree to participate (10). The primary outcome of interest in the study was STI prevalence among adolescents 14-19y who had engaged in sexual

intercourse at least once. A final sample size of 700 14-19y students was estimated, based on an assumed design effect of 2, 5% precision for STI prevalence estimates, 20% prevalence of the most common STI (CT), assuming two-thirds of participants had engaged in sex, based on previous school-based sexual health studies in Panama (10).

Guardians of minor students (aged <18y) from selected classrooms were invited by letter to attend an informational meeting and were requested to bring their child's vaccine card. During the meeting, study objectives and procedures were explained. Guardians were then asked to provide signed informed consent. If available, details of HBV and HPV vaccinations were logged. After the meeting, eligible students were provided with information individually, asked to provide signed informed assent (if <18y) or consent (≥18y). Participants were assigned a unique identification code and given an appointment card with the date (within 3-4 weeks) to retrieve their laboratory results and treatment at a designated MOH clinic. At the schools, participants completed a self-administered questionnaire and provided blood and urine samples. All female participants went to the health center to provide additional self-collected genital swabs.

Data were obtained for socio-demographics and sexual behavior including vaginal/anal/oral sex, forced sex, and same-sex sexual activity, (further defined in **Supplementary Table 1)** with a self-completed questionnaire using a tablet computer (Kobo Toolbox, Harvard Humanitarian Initiative, MA, USA). All participants, regardless of reported sexual behavior, were asked to give blood and urine samples, and self-collected swab samples (females only). Participants were

expected to complete the questionnaire and biological sampling on the same day as consent/assent; however, if necessary, some activities were completed the following day.

Blood samples (8ml) were tested with rapid HIV and syphilis tests in the field laboratory; confirmatory tests for these infections and HBV and HSV-2 serologies were performed at the Provincial MOH blood bank laboratory in nearby Santiago. Participants were asked to provide a 40ml first-void urine sample in a sterile cup for CT/NG testing. To limit costs, we only included CT/NG testing in participants who reported sexual experience, or tested positive for any HIV/STI serology (syphilis, HBV or HSV-2). All female participants were instructed to provide two self-collected vaginal swabs (11), a high-vaginal Dacron swab (5cm insertion) for HPV testing, and a dry-cotton lower-vaginal swab (3cm insertion) for BV testing. Dacron swabs were placed immediately in a CerviCollect transportation tube (Abbott Molecular, IL, USA), and transported to the Gorgas Memorial Laboratory in Panama City at weekly intervals. Lower-vaginal swabs (Copan Diagnostics Inc., CA, USA) were rolled onto a glass slide by a health technician, air-dried, fixed with methanol, transported weekly to the MOH Microbiology Laboratory in Santiago. Participants were offered a minimum 3-hour group education session, which included the topics: self-esteem, sexual decision making, dating violence, transmission and prevention of HIV/STIs.

Within one day of submitting their sample, participants testing HIV-positive by rapid test were counselled and referred to the closest HIV clinic for assessment and antiretroviral therapy (ART) initiation. All treponemal antibody-positive cases were offered treatment upon receiving confirmation within 5 days of submitting their sample. All participants were reminded by school

counselors to collect other test results during their scheduled appointment. All participants with a positive test for a curable STI were provided standardized STI treatment and patient-initiated notification, according to Panama guidelines (12). Participants with positive CT or NG who did not retrieve their results were traced and treated as per MOH guidelines (12).

Laboratory methods

Blood samples were collected at each school. A temporary study laboratory was housed within the closest MOH clinic for HIV and syphilis testing. HIV testing was undertaken according to national guidelines (13) using two rapid tests from different manufacturers: Alere Determine HIV-1/2 Ab (Inverness Medical Japan Co, Chiba, Japan), confirmatory testing using SD Bioline HIV-1/2 3.0 (Standard Diagnostics, Inc., Gyeonggi-do, South Korea). For syphilis testing, a point-of-care treponemal assay (Alere Determine^{TM} TP, Inverness Medical Japan Co, Chiba, Japan) was used, with confirmation using a non-treponemal assay (VDRL, Weiner Lab, Rosario, Argentina) with assay titration. Treponemal seroreactivity was defined as positivity to the treponemal assay, whilst active syphilis was defined as the dual positivity to treponemal and non-treponemal assays independent of titration, although titers were recorded with reactivity at ≥1:8 concentration considered 'high-titer'. Participants with positive treponemal and non-treponemal (any titer) assays were treated. External control for HIV was performed with the College of American Pathologists (CAP) schemes, where concordance with other CAP users was 98.8%. External control of syphilis testing was undertaken using 24 panels from the Curie Laboratory in Panama, with 100% concordance.

At the Santiago MOH Bloodbank Laboratory, serological samples were tested to detect HSV-2 antibodies (Focus Diagnostic, Cypress, CA), HBV surface antigen [HBsAg] and total HBV core antibodies [anti-HBc] (Bio-Rad Laboratories, Hercules, CA, USA). The laboratory participated in quarterly MOH Quality Assurance testing for bloodborne infections (HBsAg, anti-HBc), where performance has been certified as "Excellent" in 9 assessments prior to the study; HSV-2 testing concordance with other CAP laboratory users was 100%.

At the Santiago MOH Microbiology Laboratory, vaginal swabs were Gram-stained and analyzed using the Nugent's score: 0-3 was classified as healthy; 4-6 as intermediate microbiota; and 7-10 as BV (13). Study microbiologists (MH and GH) were trained at University of Alabama, USA, read the slides independently and undertook double reading in ~20% of slides.

At the Gorgas Genomics laboratory in Panama City, urine samples were tested for CT and NG using RealTi*me* CT/NG polymerase chain reaction (Abbott Molecular, IL, USA). High-vaginal swabs were tested with a qualitative high-risk HPV genotypes detection assay (Abbott RealTi*m*e High-Risk HPV, Abbott Molecular, IL, USA) that distinguishes HPV16 and/or HPV18 from 12 other high-risk/probable HR-types (31,33,35,39,45,51,52,56,58,59,66,68). The laboratory enrolled in the CAP CT/NG and HPV testing schemes; concordance with other CAP users was 98.2% for HPV, 100% for both CT and NG.

Statistical methods

Questionnaires were uploaded into the Kobo Toolbox cloud, imported and analyzed in STATA V15.0 (StataCorp, TX, USA). Participants who completed the questionnaire and gave at least

one biological sample were included in the analyses. We used the χ^2 test to evaluate the difference in STI prevalence between males and females, age, and key sexual behavior variables, and Fisher's Exact Test where appropriate. Kruskal-Wallis Test was used to evaluate associative trends in age, biological sex, and sexual behavior variables. Missing data were excluded.

Random-effects logistic regression was used to calculate odds-ratios (OR) and 95% confidence interval (CI) for each pathogen adjusting for school-level clustering (14). Variables associated with each pathogen at $p<0.2$ in univariable analyses were included in initial multivariable models adjusting for sex and age (*a-priori*). In the model, distal variables were included first, then proximal variables (15). The final model included variables independently associated with outcomes at $p<0.1$.

Ethics

The research was approved by the Comité Nacional de Bioética de la Investigación de Panamá (EC-CNBI-2016-05-25, November 2017), and the London School of Hygiene & Tropical Medicine, UK (Ref:14558; January 2018).

Results

Study population

Overall, 2006 students were assessed for eligibility, of whom 1101 (55%) were eligible (aged 14-19y). A total of 380/380 (100%) eligible minor participants had guardian consent, signed their assent, and were present during the week the study team visited the community; one minor subsequently withdrew assent. Separately, a total of 321/354 (90.7%) eligible 18-19y adolescents

consented to participate and were available during the visit week **(Figure 1)**. Overall, we included 316 (45.1%) female and 384 (54.9%) male participants (**Table 1)**, median age was 17y (interquartile range [IQR], 14-19) for females, 18y (IQR, 16-18) for males. The majority of participants (91.3%) were of Ngäbe ethnicity (**Table 1**).

Few participants had vaccination records and brought them to the study (22.8%, [72/316] females, 19.0% [73/384] males). Of these, 61.1% (44/72) females and 69.9% (51/73) males had ≥1 HBV vaccine dose; and 33.3% and 32.9% had full 3-dose vaccination. For HPV vaccination, 38.9%, 15.3% and 11.1% of females had full (three), two, one dose, respectively. Male participants were too old to have been included in the country-wide HPV vaccination, therefore none had HPV vaccination records.

Sexual behavior

Most participants reported previous sexual experience: 74.1% [234/316] of females, 78.7% [302/384] of males. Those who reported sexual experience were older (92.4% of 19 year-olds versus 52.9% of 14 year-olds) and studying in the coastal region (Ño Kribo) compared to those from the mountainous southern regions (86.6% versus 63.2%, $p<0.01$) **(Table 1)**. The median age of sexual debut was 15y (IQR, 14-16) among females, and 16y (IQR, 14-17) among males (**Table 2**). A high proportion of both sexes reported forced sex, although females were more likely to report this than males (36.2% versus 18.2%, $p<0.01$) (**Table 2)**. History of pregnancy was reported by 11.3% of females, whilst 6.0% of males reported having impregnated a partner. Ten male participants reported no sexual experience, although they were HSV-2 seropositive, and thus assumed to be sexually-experienced in further analyses (**Table 3)**.

HIV and STI prevalence

All HIV cases (females 0.4%, males 1.0%) were new diagnoses. Among all participants, treponemal seroreactivity was more prevalent among males than females (7.7% versus 3.5%; p=0.05), as was high-titer (≥1:8) active syphilis (6.6% versus 1.3%; p=0.003), with the following titer distribution: 9.1% (2/22) had 1:2, 9.1% (2/22) had 1:8, 13.6% (3/22) had 1:16, 22.7% (5/22) each had 1:32, 1:64 and 1:128 titers. There were no differences in seroprevalence of HBV markers by sex (HBsAg females: 1.3%; males: 1.4%; p=0.93), anti-HBc females: 3.2%; males: 1.4%; p=0.18); and in HSV-2 seroprevalence (females: 16.1%; males 16.1%; p=0.99).

Among participants who were sexually-experienced, prevalence of CT was higher in females (17.4% versus 10.7%; p=0.03) (**Table 3**), whilst NG prevalence was similar in both sexes (females 1.8% versus males 1.7%; p=0.95).

Among females, no HPV genotypes 16 or 18 were detected, however 27.9% (95%CI:22.7-33.9) of all females, and 33.2% (95%CI:26.8-40.2) of those who reported sexual experience tested positive for other HR-HPV genotypes.

Overall, 100% of NG and 64% of CT-positive cases were treated within four weeks, and 93% CT-positive within 8 weeks. Within four weeks, 51% of HR-HPV returned for their results, 46% of BV-positive cases returned and were treated.

Factors associated with STIs

There were no statistical significant associations between participant´s age, age of sexual debut, partner´s age at sexual debut, or reported condom use at last coitus with any STI

(Supplementary Figure 1). After adjusting for age, CT was associated with female sex (adjusted odds-ratio [AOR]=2.02, 95%CI:1.20-3.41) (**Supplementary Table 1**). Active syphilis was strongly associated with being male (AOR=4.51, 95%CI:1.17-17.40), weakly associated with reported forced sex (AOR=2.43, 95%CI:0.89-6.62), and reported transactional sex (AOR=2.49, 95%CI:0.82-7.57, **Supplementary Table 2)**. Among male participants, active syphilis was independently associated with reported forced sex (7/52 [13.5%] versus no-forced sex 11/231 [4.8%], AOR=3.11, 95%CI:1.14-8.45) and weak evidence of association among those who reported transactional sex (5/40 [12.5%] versus no-transactional sex 13/247 [5.3%], AOR= 2.57, 95%CI:0.86-7.65), and those who reported same-sex sex (4/26 [15.4%] versus no report 11/204 [5.4%], AOR=1.52, 95%CI:0.84-2.75).

Region of CNB was strongly associated with HSV-2 seropositivity in both sexes, and BV prevalence among female participants, with highest prevalence of both infections among participants from the coastal region of Ño Kribo compared to the southern mountainous regions (**Supplementary Tables 3 and 4).**

Among females, there was a strong association between BV and reported sexual experience (AOR=2.86, 95%CI:1.39-5.91), number of lifetime sexual partners (≥3 compared to one, AOR=3.81, 95%CI:1.29-11.26), and same-sex sex (compared to non-report, AOR=4.68, 95%CI:0.87-25.11) (**Supplementary Table 5)**. HR-HPV infection was associated with reported sexual experience (AOR=4.05, 95%CI:1.62-10.09) (**Supplementary Table 6)**. In the adjusted analysis, participants who tested positive for HR-HPV had 1.81 times the odds of testing positive

for BV than those without HR-HPV (95%CI:1.02-3.22). Participants with NG had 14.73 times the odds of testing positive with CT (95%CI:3.47-62.4).

Discussion

We conducted the first study of HIV/STI prevalence and sexual behavior among indigenous adolescents living in a Comarcal area of Panama, and found a very high prevalence of chlamydia, syphilis, BV and HR-HPV in this population, indicating high vulnerability and great need for interventions. Understanding regional and national STI epidemics through the collection of STI prevalence data is essential to develop interventions targeted for high-risk groups to achieve STI control (9).

Syphilis prevalence was remarkably high (5.6% in both sexes combined) compared to that found in a similar study conducted in 2015 among sexually-experienced school-going adolescents (14-19y) living in urban areas of Panama (0.0% overall) (10). High-titer treponemal infection was particularly high among male adolescents. Results were comparable to, or higher than, adult indigenous peoples of Honduras and the Peruvian Amazon (16). In the absence of reported yaws cases in Panama since 1977 (17) and given the high proportion of high-titer active syphilis found exclusively among sexually-experienced adolescents, it can be inferred that this is recent exposure to sexually-transmitted treponemal infection. Among males, same-sex sex was weakly associated with active syphilis, which accords with the general epidemiology of syphilis among men who have sex with men (MSM) in Latin America (18). We found high prevalence of forced sex among both sexes, and among male participants this activity was strongly associated with active syphilis infection, similar to that found among young men in Ecuador (19). The 0.8% HIV

prevalence is a worrying finding in this young population and was higher than among most adult indigenous populations in Latin America (16).

Chlamydia prevalence was also high in both sexes, although lower for females than in the study of adolescents in Panama City (30.9% in females, 6.2% in males) (10). Sex differences are comparable to those observed worldwide (1). Despite the impact of CT on sexual and reproductive health, there are limited control options for chlamydia infection which impact sequelae (1, 20). Specifically, there are no CT screening programs in Panama, as CT/NG infections are managed syndromically (12).

The prevalence of BV was also high in our study population, greater than among adolescents in Ecuador (21), but comparable to BV prevalence among adolescent females in South Africa and Tanzania (22, 23). It is likely that some BV-associated bacteria are sexually-transmitted (24), yet school-based studies have reported prevalent BV among females who reported never having penile-vaginal sex (23). This may be due to under-reporting of sexual activity (25). In our study, BV was strongly associated with reported sexual activity, but was also found among those who did not report any type of sexual activity. Similarly, we found several cases of HSV-2 seropositivity among males who did not report sexual activity, although oral-genital transmission may explain some cases. Study staff emphasized confidentiality of results to both parents and participants, although students may still have feared disclosure. Interestingly, we found BV to be associated with HR-HPV infection. A causal link has been hypothesized in a recent meta-analysis, where BV has been found to be associated with HR-HPV persistence and the development of high-grade cervical neoplasia (26).

The absence of HPV16/18 genotypes among female adolescents is encouraging and had not been previously documented in Panama. It suggests possible success of the universal school-based HPV vaccination program that was rolled-out in 2008. However, it is difficult to ascribe a direct effect of the vaccination program, as too few participants produced vaccination records, and a large proportion of female participants had not received the recommended full-dose vaccination regimen, although it is plausible that a suboptimal number of doses may still provide sufficient protection (27). The high prevalence of other HR-HPV genotypes indicates this population is still highly vulnerable, as reported elsewhere (28). Additionally, if elimination of cervical and other HPV-related cancers were to be achieved, Panama will need to include a broader range of high-risk genotypes in the country-wide vaccination (29). Prevalence of HBV was low compared to other studies among adult indigenous populations in Latin America (16). Hepatitis B vaccination has been rolled out among infants in Panama since 2002, although in the few vaccination records produced, compliance with vaccination schedule appeared low. Catch-up vaccination for both HPV and HBV may be advantageous for those who have incomplete vaccination records.

Strengths of our study included testing a large panel of STIs among a highly vulnerable under-researched indigenous population, using population-based sampling and laboratories with excellent EQA results. We used electronic data-capture and self-completed questionnaires to mitigate reporting bias inherent in collecting sensitive behavior data. This study had some limitations. Firstly, we may have encountered selection bias due to the school-based sampling; only about half of guardians consented their minor child's enrolment. More at-risk adolescents may have thus been excluded, leading to an underestimated STI prevalence. Moreover, male participants were over-represented in our sample, as more males attend school. Finally, for

logistical reasons, only the 20 largest schools were included in the sampling, which would have excluded adolescents who do not attend school or attend smaller schools. Second, CT/NG testing was not extended to the entire population, but only to those reporting sexual debut or found to be seropositive for an STI. Among females, genital self-swabbing was optional and nearly a quarter (23.1%) declined. To overcome these possible reporting and selection biases, we tested samples of participants who were positive for any of the serological markers, regardless of reported sexual debut. Few participants with HPV (n=6) or BV (n=10) were additionally identified. HPV transmission may still be possible in sexually-inexperienced females through fomites and non-penile-vaginal sex (30). Third, reporting biases may have arisen from the self-reported nature of the questionnaire. We carefully piloted the use of the tablet-computers with consistent results, and other studies have demonstrated high rates of disclosure of sensitive behavior using such methods (31s).

In line with the first target of the worldwide WHO Strategy for STI Control, this study has collected data which estimate the epidemiological STI burden among a vulnerable indigenous population in rural Panama. Our results underscore the need for swift coordinated action, focusing on the development of control programs for the WHO-prioritized infections, ie HIV, syphilis, HBV and HPV. Specifically, programs should be developed for CT screening among at-risk youth. In developing these interventions, it will be imperative to take Ngäbe and Buglé culture into account, as culturally congruent messages are more effective in delivering sexuality education curricula (32s).

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Figure 1 Study flow chart, Comarca Ngäbe-Bugle, Panama, 2018

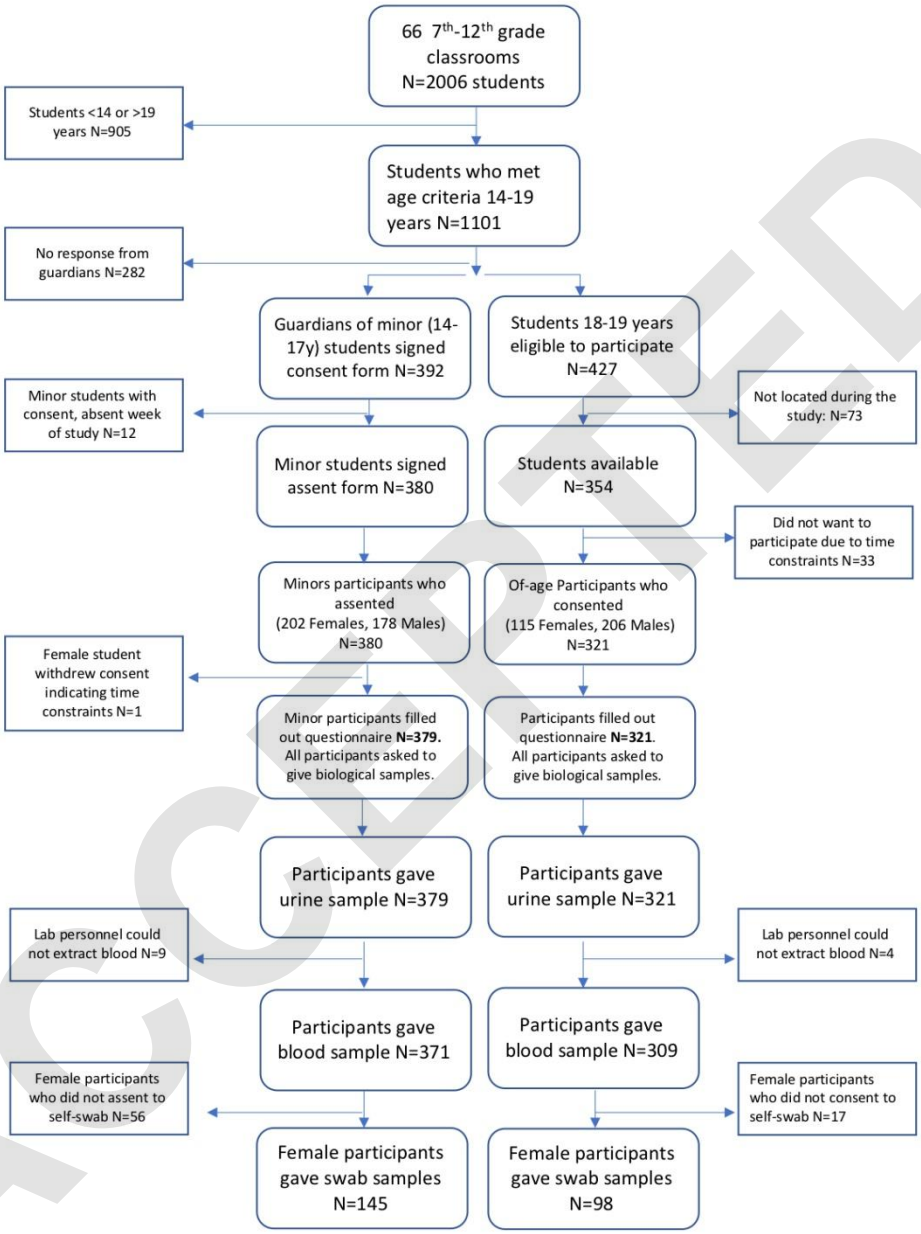


Table 1: Characteristics of participants, by reported history of sexual activity, Comarca Ngäbe-Bugle, Panama, 2018

	All Participants[1]		Reported sexual activity				p-value[2]
			No		Yes		
	n/N	%	n/N	%	n/N	%	
Participant sex							0.15
Female	316/700	45.1	82/316	27.9	234/316	74.1	
Male	384/700	54.9	82/384	21.4	302/384	78.7	
Age							**<0.01**
14-15 years	157/700	22.4	74/157	47.1	83/157	52.9	
16 years	100/700	14.3	31/100	31.0	69/100	69.0	
17 years	122/700	17.4	24/122	19.7	98/122	80.3	
18 years	203/700	29.0	27/202	13.4	175/202	86.6	
19 years	118/700	16.9	9/118	7.6	109/118	92.4	
Ethnicity							0.42
Ngäbe	607/665	91.3	133/606	21.9	473/606	78.1	
Bugle	23/665	3.5	5/23	21.7	18/23	78.3	
Mixed Latino/Ngäbe/Bugle	35/665	5.3	11/35	31.4	24/35	68.6	
School grade							**<0.01**
7-9th	168/698	24.1	70/167	41.9	97/167	58.1	
10	119/698	17.0	34/119	28.6	85/119	71.4	
11	162/698	23.2	26/162	16.0	136/162	84.0	
12	249/698	35.7	35/249	14.1	214/249	85.9	
Comarcal Region							**<0.01**
Nidrini (previously Chiriquí)	335/700	47.9	80/335	23.9	255/335	76.1	
Kädridri (previously Veraguas)	155/700	22.1	57/155	36.8	98/155	63.2	
Ño Kribo (previously Bocas del Toro)	210/700	30.0	28/209	13.4	181/209	86.6	
Access to cellular phone							0.70
Personal cell phone	295/675	43.7	67/295	22.7	228/295	77.3	
Shared cell phone	149/675	22.1	34/149	22.8	115/149	77.2	
No access	231/675	34.2	59/230	25.7	171/230	74.4	

[1] Denominators differ for each variable due to missing data
[2] Difference between those who reported sexual activity and those who did not

Table 2: Reported sexual behaviors among those who report history of sexual activity, by participant sex, Comarca Ngäbe-Bugle, Panama, 2018

	All participants[3]		Sex				
			Female		Male		p-value[4]
	n/N	%	n/N	%	n/N	%	
Reported age of sexual debut							0.58
≤12 years	31/372	8.3	11/149	7.4	20/223	9.0	
13-16 years	248/372	66.7	104/149	69.8	144/223	64.6	
17-19 years	93/372	25.0	34/149	22.8	59/223	26.5	
Reported age of partner at sexual debut							**<0.01**
8-13 years	34/356	9.6	4/143	2.8	30/213	14.1	
14-19 years	283/356	79.5	109/143	76.2	174/213	81.7	
≥20 years	39/356	11.0	30/143	21.0	9/213	4.2	
Reported total number of sex partners in lifetime							**<0.01**
1	153/333	46.0	77/138	55.8	76/195	39.0	
2	67/333	20.1	28/138	20.3	39/195	20.0	
≥3	113/333	33.9	33/138	23.9	80/195	41.0	
Reported number of partners in past month							0.06
0	218/488	44.7	90/211	42.7	128/277	46.2	
1	191/488	39.1	95/211	45.0	96/277	34.7	
2	52/488	10.7	16/211	7.6	36/277	13.0	
≥3	27/488	5.5	10/211	4.7	17/277	6.1	

[3] Denominators differ for each variable due to missing data
[4] Difference between male and female participants

Reported same-sex sex partner							**0.09**
No	359/395	90.9	152/162	93.8	207/233	88.8	
Yes	36/395	9.1	10/162	6.2	26/233	11.2	
Reported condom use at last sexual intercourse							**<0.01**
No	247/312	79.2	101/133	75.9	146/179	81.6	
During part of the time	48/312	15.4	18/133	13.5	30/179	16.8	
During the whole act	17/312	5.4	14/133	10.5	3/179	1.7	
Has experienced forced sex[5]							**<0.01**
Never	371/503	73.8	139/218	63.8	232/285	81.4	
Yes, at least once	132/503	26.2	79/218	36.2	53/285	18.6	
Has been offered something in exchange for sex[6]							0.26
No	429/509	84.3	180/219	82.2	249/290	85.9	
Yes	80/509	15.7	39/219	17.8	41/290	14.1	

[5] Has been physically forced to engage in sex

[6] Has been offered something (money, food, housing, a better grade) in exchange for sex.

Table 3: Prevalence of sexually transmitted infections by sex, among sexually experienced 14-19-year-old school-going participants from the Comarca Ngäbe-Buglé, Panama, 2018

	No reported sexual experience				Reported sexual experience				
	Females		Males		Females		Males		p-Value[7]
	n/N[8]	% (95%CI)	n/N	% (95%CI)	n/N[9]	% (95%CI)	n/N	% (95%CI)	
Chlamydia trachomatis	-	-	-	-	39/224	**17.4 (13.0-23.0)**	31/291	10.7 (7.6-14.8)	**0.03**
Neisseria gonorrhoeae	-	-	-	-	4/224	1.8 (0.7-4.7)	5/291	1.7 (0.7-4.1)	0.95
Syphilis									
Treponemal seroreactivity[10]	0/83	0.0	0/89	0.0	8/228	3.5 (1.8-6.9)	22/287	**7.7 (5.1-11.4)**	**0.05**
Active syphilis[11]	0/83	0.0	0/89	0.0	3/228	1.3 (0.4-4.0)	19/287	**6.6 (4.3-10.2)**	**<0.01[12]**
Hepatitis B virus (HBV)									
HBsAg	0/82	0.0	0/90	0.0	3/233	1.3 (0.4-3.9)	4/293	1.4 (0.5-3.6)	0.93
anti-HBc Ab	0/76	0.0	2/89	2.3 (0.6-8.7)	7/218	3.2 (1.5-6.6)	4/278	1.4 (0.5-3.8)	0.18
HIV	0/83	0.0	0/90	0.0	1/228	0.4 (0.0-3.1)	3/287	1.0 (0.3-3.2)	0.44
Herpes simplex virus type 2 (HSV-2)	0/63	0.0	10/69	**14.5 (7.9-25.1)**	28/174	16.1 (11.3-22.4)	35/217	16.1 (11.8-21.7)	0.99
Vaginal flora in all girls – Nugent's score									
Normal (Score 0-3)	40/61	65.6 (52.6-76.6)	-	-	84/182	46.2 (39.0-53.5)	-	-	-
Intermediate (Score 4-6)	9/61	14.8 (7.8-26.3)	-	-	20/182	11.0 (7.2-16.5)	-	-	-
BV (Score 7-10)	12/61	19.7 (11.4-31.8)	-	-	78/182	42.9 (35.8-50.2)	-	-	-

[7] $\chi 2$ was used to evaluate differences between in prevalence between male and female participants
[8] Differences in the total number of tests taken due to lack of quality sample in some instances
[9] Differences in the total number of tests taken due to lack of quality sample in some instances
[10] Positive syphilis rapid test
[11] Treponemal antibody confirmed active syphilis cases with VDRL
[12] Kruskal-Wallis Test for trend statistically significant at $p<0.05$ are presented in bold

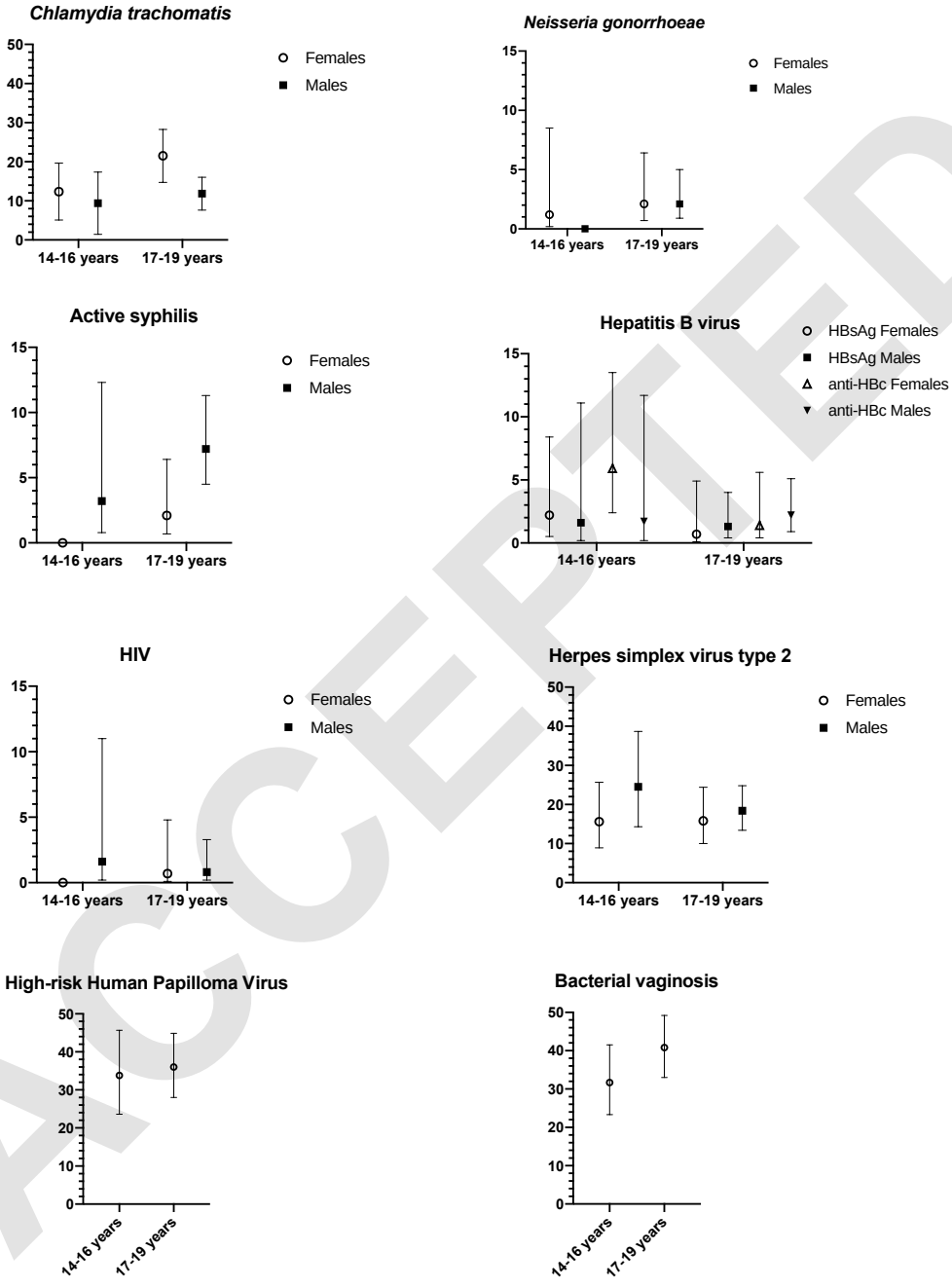
High-risk HPV in all girls									
Genotype 16	0/0	0.0	-	-	0/0	0.0	-	-	-
Genotype 18	0/0	0.0	-	-	0/0	0.0			-
Other HR genotypes[13]	6/57	10.5 (4.7-21.8)	-	-	63/190	33.2 (26.8-40.2)	-	-	-

[13] Other high-risk types include: 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68

Supplementary Table 1: Questions on sexual activity to indicate ´reported sexual activity´

	Question	Possible answers, reported sex activity in bold
Reported sexual activity	Have you ever engaged in sex?	No, never/**Yes**
	Have you ever had vaginal sex?	No, never/**Yes**
	Have you ever had oral sex?	No, never/**Yes**
	Have you ever had anal sex?	No, never/**Yes**
	Who have you had sex with?	I've never had sex, **boy/boys/man/men, a girl/girls/woman/women, an animal,** I don't want to answer
	Sexual network questions (in the last three romantic relationships, did you have sex with this person?)	No and it will never happen, No but in the future we will, **yes once, yes more than once,** I don't want to answer
	How many sex partners have you had ever?	0, **1, 2, 3, 4 or more**
	Sometime, when you didn't want to, did someone force you to have sex with them?	No, never, **yes once, yes more than once**
	Do you use a condom when you have sex?	I've never had sex, **No but I've only had sex once, yes but I've only had sex once, during part of the act, I always use a condom, I never use a condom**
Reported STI symptoms	Have you ever had any of the following symptoms in your intimate parts:	None of the below, discharge from vagina, **discharge from penis, an ulcer on genitals or anus, swollen groin lymph nodes**
Reported STI diagnosis	Has a doctor at a health center ever told you have any of the following problems:	None of the below, discharge from vagina, **discharge from penis, gonorrhea or chlamydia, syphilis, hepatitis B, genital herpes, HIV, I don't remember what they told me but they said I had an infection from having sex**

Supplementary Figure 1: Prevalence of infections, among adolescents who have engaged in sex, by age, Comarca Ngäbe-Buglé, Panamá, 2018



Supplementary Table 2: Risk factors of genital *Chlamydia trachomatis* (CT) infection among male and female sexually-experienced participants Comarca Ngäbe-Bugle, Panama, 2018

	Yes n/N (%)	p-value	OR (95%CI)	p-value	AOR (95%CI)	p-value
Participant sex		**0.03**	1.77 (1.06-2.94)	**0.03**	**2.02 (1.20-3.41)**	**<0.01**
Female	39/224 (17.4)					
Male	31/291 (10.7)					
Age		0.37	1.23 (1.00-1.51)	**0.05**	**1.30 (1.05-1.60)**	**0.02**
14-15 years	6/71 (8.5)					
16 years	7/65 (10.8)					
17 years	13/98 (13.3)					
18 years	24/173 (13.9)					
19 years	20/108 (18.5)				3.0 (1.12-8.07)	
Comarcal Region		0.43	1.20 (0.91-1.59)	**0.19**	1.21 (0.91-1.60)	0.2
Nidrini (Chiriquí)	29/248 (11.7)					
Kädridri (Veraguas)	13/93 (14.0)					
Ño Kribo (Bocas del Toro)	28/174 (16.1)					
Forced sex[14]		0.47				
No	46/355 (13.0)					
Yes	20/129 (15.5)		0.72 (0.24-2.11)	0.55		
Transactional sex[15]		0.86				
No	55/410 (13.4)					
Yes	10/79 (12.7)					
Number of partners in lifetime		0.24	1.20 (0.85-1.69)	0.31		
1	17/152 (11.2)					
2	13/66 (19.7)					
3 or more	17/112 (15.2)					
Same-sex sex partner		0.54	1.06 (0.78-1.44)	0.71		
No	52/350 (14.9)					
Yes	4/36 (11.1)					

AOR= adjusted odds ratio; CI = confidence interval; OR = odds ratio

[1]Has been physically forced to engage in sex

[2]Has been offered something (money, food, housing, a better grade) in exchange for sex.

Supplementary Table 3: Risk factors of active syphilis among male and female sexually-experienced participants Comarca Ngäbe-Bugle, Panama, 2018

	Yes n/N (%)	p-value	OR (95%CI)	p-value	AOR (95%CI)	p-value
Sex of participant		**<0.01**	5.16 (1.50-17.76)	**0.01**	**4.51 (1.17-17.40)**	**0.02**
Female	3/235 (1.3)					
Male	19/299 (6.4)					
Age		0.18	1.49 (102-2.21)	**0.040**	1.08 (0.74-1.58)	0.14
14-15 years	1/85 (1.2)		1.00			
16 years	1/69 (1.5)		1.22 (0.07-20.14)			
17 years	5/97 (5.2)		4.62 (0.52-40.86)			
18 years	7/175 (4.0)		3.20 (0.38-27.23)			
19 years	8/108 (7.4)		6.35 (0.77-52.60)			
Comarcal Region			1.13 (0.60-2.13)	0.7		
Nidrini (Chiriquí)	9/255 (3.5)	0.54	1.00			
Kädridri (Veraguas)	6/98 (6.1)		1.71 (0.47-6.21)			
Ño Kribo (Bocas del Toro)	7/181 (3.9)		1.20 (0.36-4.08)			
Forced sex[16]		**0.08**	2.14 (0.88-5.24)	**0.09**	2.43 (0.89-6.62)	0.08
No	12/365 (3.3)					
Yes	9/131 (6.9)					
Transactional sex[17]		**0.02**	2.83 (1.09-7.29)	**0.03**	2.49 (0.82-7.57)	0.11
No	14/427 (3.3)					
Yes	7/79 (8.9)					
Number of partners in lifetime		0.84	1.03 (0.56-1.95)	0.89		
1	5/149 (3.4)		1.00			
2	4/66 (6.1)		1.86 (0.48-7.16)			
3 or more	4/113 (3.5)		1.06 (0.28-4.03)			
Same-sex sex partner		0.05	3.68 (1.06-12.81)	**0.04**	1.97 (0.53-7.32)	0.32
No	14/349 (4.0)					
Yes	4/36 (11.1)					

AOR= adjusted odds ratio; CI = confidence interval; OR = odds ratio

[16] Has been physically forced to engage in sex

[17] Has been offered something (money, food, housing, a better grade) in exchange for sex.

Supplementary Table 4: Risk factors of herpes simplex virus type-2 (HSV-2) infection among male and female sexually-experienced participants Comarca Ngäbe-Bugle, Panama, 2018

	Yes n/N (%)	p-value	OR (95%CI)	p-value	AOR (95%CI)	p-value
Participant sex		0.99	1.43 (0.81-2.50)	0.22	1.32 (0.75-2.33)	0.34
Female	28/174 (16.1)					
Male	35/217 (16.1)					
Age		0.97	1.05 (0.86-1.23)	0.62	0.97 (0.78-1.21)	0.82
14-15 years	13/70 (18.6)					
16 years	11/56 (19.6)					
17 years	13/81 (16.1)					
18 years	22/123 (17.9)					
19 years	14/76 (18.4)					
Comarcal Region		**<0.01**	2.12 (1.53-2.95)	**<0.01**	**2.10 (1.50-2.96)**	**<0.01**
Nidrini (Chiriquí)	27/247 (10.9)				1.0	
Kädridri (Veraguas)	10/59 (17.0)				1.71 (0.73-3.98)	
Ño Kribo (Bocas del Toro)	36/100 (36.0)				4.50 (2.38-8.52)	
Forced sex[18]		**0.19**	0.56 (0.27-1.14)	**0.11**	0.84 (0.39-1.80)	0.65
No	52/281 (18.5)					
Yes	12/95 (12.6)					
Transactional sex[19]		0.81	1.07 (0.50-2.27)	0.87		
No	57/328 (17.4)					
Yes	11/59 (18.6)					
Number of partners in lifetime		**0.61**	1.17 (0.78-1.76)	0.44		
1	15/113 (13.3)					
2	7/47 (15.9)					
3 or more	16/87 (18.4)					
Same-sex sex partner		0.39	2.14 (0.75-6.13)	**0.16**	2.41 (0.80-7.23)	0.12
No	41/259 (15.8)					
Yes	6/27 (22.2)					

AOR= adjusted odds ratio; CI = confidence interval; OR = odds ratio

[18] Has been physically forced to engage in sex

[19] Has been offered something (money, food, housing, a better grade) in exchange for sex.

Supplementary Table 5: Risk factors of bacterial vaginosis (BV) among all female participants Comarca Ngäbe-Bugle, Panama, 2018

	Yes n/N (%)	p-value	OR (95%CI)	p-value	AOR (95%CI)	p-value
Age		**0.15**	**1.15 (0.94-1.40)**	0.16	1.07 (0.87-1.31)	0.52
14-15 years	20/59 (33.9)		1.00			
16 years	12/42 (28.6)		0.68 (0.27-1.69)			
17 years	14/44 (31.8)		0.81 (0.34-1.93)			
18 years	32/64 (50.0)		1.93 (0.90-4.13)			
19 years	12/34 (35.3)		1.11 (0.45-2.77)			
Ever had sex		**<0.01**	**3.01 (1.48-6.11)**	**0.002**	2.86 (1.39-5.91)	<0.01
No	12/61 (19.7)					
Yes	78/182 (42.9)					
Comarcal Region		**0.06**	**1.39 (0.97-1.99)**	**0.07**	**1.36 (0.99-1.90)**	**0.02**
Nidrini (Chiriquí)	30/95 (31.6)		1.00		1.00	
Kädridri (Veraguas)	22/68 (32.4)		1.02 (0.49-2.14)		1.06 (0.52-2.17)	
Ño Kribo (Bocas del Toro)	38/80 (47.5)		**1.94 (0.99-3.81)**		**2.01 (1.06-3.86)**	
Forced sex[20]		0.47	0.90 (0.47-1.70)	0.74		
No	46/355 (13.0)					
Yes	20/129 (15.5)					
Transactional sex[21]		0.96	1.06 (0.49-2.29)	0.88		
No	73/193 (37.8)					
Yes	13/34 (38.2)					
Number of partners in lifetime		**0.03**	1.81 (1.14-2.89)	**0.01**	**1.86 (1.10-3.14)**	**0.02**
1	23/64 (35.9)		1.00		**1.00**	
2	11/26 (42.3)		1.31 (0.51-3.34)		1.13 (0.40-3.18)	
3 or more	18/27 (67.7)		**3.58 (1.38-9.30)**		**3.81 (1.29-11.26)**	
Same-sex sex partner		**0.05**	5.89 (1.04-33.39)	**0.07**	**4.68 (0.87-25.11)**	**0.07**
No	53/121 (43.8)					
Yes	7/9 (77.8)					

AOR= adjusted odds ratio; CI = confidence interval; OR = odds ratio

[20]Has been physically forced to engage in sex

[21]Has been offered something (money, food, housing, a better grade) in exchange for sex.

Supplementary Table 6: Risk factors of high-risk human papilloma virus (HPV) infection among all female participants of the Comarca Ngäbe-Bugle, Panama, 2018

	Yes n/N (%)	p-value	OR (95%CI)	p-value	AOR (95%CI)	p-value
Age		0.59				
14-15 years			1.14 (0.93-1.39)	0.20	1.05 (0.86-1.29)	0.63
16 years	13/60 (21.7)					
17 years	11/42 (26.2)					
18 years	12/43 (27.9)					
19 years	23/66 (34.9)					
Ever had sex	10/36 (27.8)	**<0.01**	4.22 (1.71-10.35)	**<0.01**	**4.05 (1.62-10.09)**	**<0.01**
No						
Yes	6/57 (10.5)					
Comarcal Region	63/190 (33.2)	0.55				
Nidrini (Chiriquí)			1.20 (0.86-1.66)	0.28		
Kädridri (Veraguas)	24/97 (24.7)					
Ño Kribo (Bocas del Toro)	19/69 (27.5)					
Forced sex[22]	4/9 (44.4)	0.35	0.64 (0.34-1.18)	0.42		
No						
Yes	41/92 (44.6)					
Transactional sex[23]	5/15 (33.3)	0.42				
No	3/12 (25.0)		1.30 (0.69-2.46)	0.42		
Yes						
Number of partners in lifetime	8/24 (33.3)	0.96	1.01 (0.64-1.58)	0.97		
1						
2	28/68 (41.2)					
3 or more	10/26 (38.5)					
Same-sex sex partner		0.74	1.26 (0.32-4.91)	0.74		
No	2/9 (22.2)					
Yes	49/126 (38.9)					

AOR= adjusted odds ratio; CI = confidence interval; OR = odds ratio

[22]Has been physically forced to engage in sex

[23]Has been offered something (money, food, housing, a better grade) in exchange for sex.