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Risk Factors for Incidence of Sexually Transmitted Infections Among Women in a Human Immunodeficiency Virus Chemoprevention Trial: VOICE (MTN-003)

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Abstract

Background—In sub-Saharan Africa, there are limited data on the incidence of sexually transmitted infections (STIs) among women, largely because routine screening for asymptomatic infection is not performed. We conducted a secondary analysis to measure STI incidence rates and determine risk factors for new STI acquisition among women enrolled in the VOICE trial.

Methods—We analyzed data from 4843 women screened for chlamydia, gonorrhoea, syphilis, and trichomonas infection at baseline, annually, at interim visits when clinically indicated and at their study termination visit. Risk reduction counseling and condoms were provided throughout the trial.

Results—Twenty percent of evaluable participants had one or more curable STIs at baseline. Over 5660 person-years at risk (PYAR) of observation, incidence rates were 13.8% (95% confidence interval [CI], 12.7–14.8) PYAR for chlamydia, 3.5% (95% CI, 3.0–4.1) PYAR gonorrhea, 0.1% (95% CI, 0.6–1.1) PYAR syphilis, and 6.6% (95% CI, 5.8–7.2) PYAR trichomoniasis. South African sites had the highest incidence of chlamydia. The Uganda site had the highest incidence of gonorrhoea and syphilis, and Zimbabwe the lowest incidence overall. The majority of these cases were diagnosed at a routine scheduled testing visit. In multivariate analysis, positive baseline STI, younger than 25 years, being unmarried, and some alcohol consumption were associated with acquiring a new STI.

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Conclusions—We observed high rates of STIs during follow up among women in the VOICE study. Women living in human immunodeficiency virus endemic countries should be screened for common STIs.

The burden of sexually transmitted infections (STIs) remains high, affecting an estimated 340 million people globally each year.[1] The presence of curable STI (chlamydia, gonorrhoea, syphilis, trichomoniasis) and other reproductive tract infections is associated with multiple adverse reproductive health outcomes that include pelvic inflammatory disease (PID), infertility, chronic pelvic pain,[2] and a 2-fold to 3-fold increased risk of human immunodeficiency virus (HIV) acquisition.[3,4] The majority of incident STI infections occur in developing countries including those in the Sub-Saharan Africa region that is the epicenter of the HIV pandemic. The current HIV pandemic is fueled by uncontrolled rates of STIs and other reproductive tract infections in the same communities.

Evaluating the impact of global STI prevention and control programs requires quality surveillance data that remain largely inadequate in developing countries due to lack of capacity.[2] Current efforts to contain the spread of STIs including HIV rely on interventions that aim to reduce risky sexual behavior and provision of condoms, along with screening and treatment of STIs.[5] In low resource settings, women who present with symptomatic vaginal discharge are treated under the guidelines of “syndromic management” based on presenting symptoms and clinical judgment, in absence of identified etiological organism. These guidelines typically recommend empirical anti-microbial coverage for suspected pathogens using World Health Organization–recommended flowcharts.[6] However, syndromic management fails to detect the large majority of STIs which are asymptomatic. Among 242 HIV uninfected women enrolled in Durban, South Africa, and followed up for 2 years, only 12% of women having a laboratory-diagnosed STI (gonorrhoea, chlamydia, trichomoniasis) were symptomatic, suggesting that reliance on syndromic management misses more than 80% of STIs in women.[7]

The VOICE study provided an opportunity to measure prevalence of STIs at baseline and follow-up among women who were provided risk reduction counseling and condoms throughout the duration of the trial. This secondary analysis aimed to evaluate STI burden and determine common risk factors in the presence of risk reduction counseling and condom provision within the scope of a clinical trial.

MATERIALS AND METHODS

Study Design and Participants

We analyzed prospective data from the VOICE trial (MTN-003) a randomized, placebo-controlled trial that investigated the safety and effectiveness of oral and topical tenofovir based preexposure prophylaxis for prevention of sexually transmitted HIV in women. Women aged 18 to 40 years were enrolled by targeting areas associated with high-risk behaviors “hot spots” such as night clubs, beerhalls, overcrowded resettlement (high density) areas and locations with marginalized populations from Uganda, Zimbabwe and South Africa from 2009 to 2011 and followed up until 2012. Women were scheduled to be followed up for a minimum of 12 months and a maximum of 34 months. Eligibility criteria

required that participants be HIV-uninfected, sexually active, nonpregnant, free of curable genitourinary infection, and willing to use effective contraception (oral contraceptive pills, injectable progestins, implantable devices containing progestins, intrauterine devices, or sterilization).[8] Women were not eligible if they reported allergy to latex condoms, were within 6 weeks of delivery or planning to get pregnant during follow-up. As has previously been reported, adherence to the VOICE study drugs was low, and no regimen significantly reduced HIV acquisition compared to placebo.[8]

Procedures

Participants provided written consent. Research ethics committees and institutional review boards in Zimbabwe, Uganda, South Africa, and the United States approved the VOICE trial.

Behavioral assessment interviews using standardized questionnaires were administered monthly to document number of sexual partners, frequency of intercourse, condom use, intra-vaginal practices and contraceptive use. Sensitive questions, like those assessing report of anal intercourse and alcohol use, were asked via audio computer-assisted self-interview at quarterly visits. Human immunodeficiency virus testing, pregnancy testing, and study product management were performed at monthly visits. All participants received a comprehensive HIV prevention package that included ongoing risk reduction counseling and provision of male and/or female condoms at each monthly visit throughout the trial.

Participants were screened for chlamydia, gonorrhea, syphilis, and trichomoniasis at baseline, annually, when clinically indicated and at their study termination visit. STI treatment was provided on-site. During the pelvic examination, a speculum was inserted, naked eye inspection for cervical-vaginal discharge, superficial lacerations, ulcers, and collection of specimens for diagnosis of genital infections were performed. Urine samples were collected for pregnancy tests and for screening for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. Participant's partners were offered HIV testing, STI screening, and treatment. Potential participants with curable STI and other genitourinary infections (except for asymptomatic candidiasis) diagnosed at screening were eligible for enrollment after completing treatment per World Health Organization guidelines. Consistent with local standards, test of cure was not performed routinely.

Laboratory Testing

A vaginal swab was used to perform the OSOM® Rapid Trichomonas (Sekisui Diagnostics, San Diego, Calif) test for *Trichomonas vaginalis*. Saline wet mount of a vaginal smear was examined onsite among women reporting symptoms for candidiasis; if clue cells or motile *T. vaginalis* was noted in the vaginal fluid, these were reported. Syphilis serology was performed first by rapid plasma reagin (RPR) with positives being titered and confirmed by treponemal-specific assay (TPHA or TPPA). Testing for HIV followed a protocol-defined algorithm. The Determine HIV 1/2 (Alere Diagnostics, Orlando FL, USA) and either the Oraquick (Orasure Technologies, Bethlehem, Pa) or Uni-Gold Recombigen HIV (Trinity Biotech PLC, Wicklow, Ireland) were performed on whole blood or EDTA plasma samples for initial HIV testing. All HIV positive samples were confirmed by a Genetic Systems

Western Blot (Bio-Rad Laboratories, Redmond, Wash). Herpes simplex virus type 2 (HSV-2) status at baseline, and exit was determined by central testing using the FOCUS EIA (Focus Technologies, Cypress, Calif).

The Strand Displacement Amplification by BD Probe Tec ET (Becton Dickinson, Franklin Lakes, NJ) system was used to test for *C. trachomatis* and *N. gonorrhoeae* from urine samples. Pregnancy status was ascertained with monthly urine hCG testing using the QuickVue One-Step or Combo kit (Quidel, San Diego, Calif).

Because women in the study could be randomized to oral tablets or vaginal gel products, all STI test systems and pregnancy tests were evaluated to ensure that the vaginal gel products did not interfere with test performance prior to the initiation of the study.

Statistical Methods

Data forms from each site were faxed to the Statistical Center for HIV/ADIS Research and Prevention for processing. Incidence rates were calculated as the number of incident events (allowing for multiple events per participant) divided by the total person-years at risk (PYAR). Results are presented as number of events/100 PYAR. The variance of the confidence interval (CI) was calculated based on methods by Stukel et al.[9] Because women with STIs and other genital infections at all sites received effective treatment, chlamydia, gonorrhea, and trichomoniasis infections detected during the follow-up period were regarded as new infections unless a positive result was within 10 days of a previous positive result. For data analysis of syphilis, a positive RPR test with a titer greater than 0, and a positive confirmatory test was considered as positive. All positive RPR test results from baseline were included. During follow-up, new syphilis infections were determined if no previous infection was reported or if the participant had adequate treatment for a previous syphilis diagnosis and had a 4-fold increase in titer from the previous event, and the titer was at least 8.

To assess associations between STI acquisition and study arm and between STI acquisition and baseline risk factors, a generalized estimating equation (GEE) method was employed. The baseline factors used in these analyses are summarized in Table 1. The GEE models use the Poisson distribution, a log link, an exchangeable correlation structure and follow-up time as the offset. All models, except for those assessing the risk by country, were adjusted by site. In the multivariable GEE models, backward selection was used to retain only the factors significant at the 0.05 level in the final adjusted model. All statistical analyses were performed using SAS 9.4 (SAS Institute, Inc., NC).

RESULTS

Among 5029 participants enrolled in the VOICE study, 164 (3%) participants had no testing for any of the curable STIs after enrollment, and another 22 (<1%) were found to be HIV positive at baseline and excluded from this analysis, leaving 4843 (96%) evaluable participants who contributed 5660.6 PYAR of follow-up for this analysis. Of the 164 participants excluded from the analysis, 63 (38%) withdrew from study, 58 (35%) were lost to follow-up, 30 (18%) relocated, 9 (5%) terminated at the scheduled exit visit before and/or

with a missed annual testing visit, and 4 (2%) terminated for other causes including death and investigator decision.

Selected baseline and demographic risk factors by country are summarized in Table 1. The average age was 25.4 years. The majority of participants 3824 (79%) were unmarried with 1078 (22%) reporting 1 or more partners in addition to their primary sex partner. At least some alcohol consumption was reported by 1266 (26%) of women and 1046 (24%) reported sex without condoms in the last 7 days before that visit. Ugandan women reported the highest rates of some consumption of alcohol 188 (61%) of 310. Across all sites, participants reported a mean of 2.5 episodes of vaginal intercourse during the 7 days before enrollment,[7] whereas 837 (18%) reported any anal sex in past 3 months. Ugandan and Zimbabwean women reported the highest rates of condomless sex, 133 (48%) of 277 and 289 (48%) of 600, respectively.

Of the 4843 evaluable participants, 956 (20%) participants had one or more STIs at baseline, 114 (12%) participants had 2 STIs and 14 (2%) had 3 STIs at baseline.

The baseline prevalence of STIs by country is displayed in Table 1.

A total of 1352 cases of STIs (763 chlamydia, 196 gonorrhea, 48 syphilis, 345 trichomoniasis) were diagnosed during follow-up visits. The majority of these cases were diagnosed at a scheduled visit which included routine STI testing (91% of chlamydia, 88% gonorrhea, 96% syphilis, 69% trichomoniasis) rather than a visit at which new problems or symptoms were addressed. The number of STI and HIV events and the HIV incidence is displayed in Table 2. The incidence of STIs by all of the baseline factors is displayed in Table 3. During follow-up visits, 763 cases of *C. trachomatis* were reported, resulting in an incidence of 13.8 events/100 PYAR across all 3 countries, with South African sites reporting the highest incidence at 15.9 events/100 PYAR (Table 3). The highest HIV incidence (6.9 events/100 PYAR) was also observed in the South African sites. Zimbabwean women had the lowest incidence rates of STIs and HIV (0.8/100 PYAR). Ugandan women had the highest incident rates of gonorrhea (5.9 events/100 PYAR) and syphilis (4.0 events/100 PYAR), trichomoniasis (7.4/100 PAYR) and low HIV incidence (2.1/100 PYAR).

Among the participants who tested positive for each of the STIs during follow-up, a significant percentage had tested positive for the same STI at screening (baseline) before study enrollment. Because these participants were treated for the infection before enrolling in the study, these infections during follow-up most likely represented new infections. Chlamydia and gonorrhea test results were available at baseline and follow-up for 4789 participants. Of those participants, 577 (12%) had chlamydia at baseline and 174 (30%) of 577 had a repeat chlamydia infection during follow-up. For gonorrhea, 154 (3%) tested positive at baseline and 15 (10%) of 154 had a repeat gonorrhea infection during follow-up. Of the 4781 participants with baseline and follow-up syphilis test results available, 67 (1%) had syphilis at baseline and 8 (12%) of 67 had a repeat syphilis infection during follow-up. Of the 4572 participants with baseline and follow-up trichomoniasis test results available, 277 (6%) had trichomoniasis at baseline, and 71 (26%) of 277 had a repeat trichomonas infection during follow-up.

After adjusting for site, we identified a number of independent risk factors for acquisition of STIs during follow-up (Table 4). Having an STI at baseline was the strongest predictive risk factor for incident infection with any of the 4 STIs during follow-up. Trichomoniasis was 5.6 times more likely to be diagnosed during study follow-up when it was present at baseline. Syphilis was 6.8 times more likely to be diagnosed during follow-up when present at baseline, whereas chlamydia and gonorrhea were twice as likely to be diagnosed during follow-up when present at baseline. Younger age and marital status were also important risk factors for incident STIs, with participants younger than 25 years being twice as likely and unmarried participants being 1.5 times more likely to acquire chlamydia. Diagnosis of gonorrhea was also twice as common in women younger than 25 years, but was also 70% more likely in women who consumed some alcohol. Trichomoniasis was more likely to occur in participants who were positive for HSV-2 at baseline. There were no significant differences in STI incidence rates in the active product arms compared with placebo arms.

DISCUSSION

In this subanalysis of women who participated in the VOICE study, we observed a high rate of curable STIs during follow-up among women who were provided ongoing risk reduction counseling and free condoms throughout the trial. Critically, and of importance for consideration of implementation of routine STI screening in such women, the vast majority of these infections were detected at routinely scheduled visits not visits prompted by symptoms. A significant number of these cases were diagnosed among women who received treatment after testing positive at screening, thus implying that most of these cases represented repeat infections rather than treatment failure. However, although routine partner treatment was offered in this study, no data were collected to capture the number of partners who were not successfully treated, nor was a test of cure performed after treatment to ensure that there was high adherence to STI treatment medications.

The STI incidence rates were highest at South African sites that also recorded the highest HIV incidence rates. Women younger than 25 years had the highest incidence rates for both curable STIs and HIV. Study retention in the VOICE was high at 91%,[8] thus most participants would have received ongoing risk reduction counseling and also collected their condom supply during scheduled visits. Despite this provision, high-risk sexual behaviors were common as evidenced by high rates of curable STIs. Negotiating condom use among women in these male-dominated communities remains a challenge as reported in several studies.[10] The provision of testing for STIs at baseline, annually, and when clinically indicated provided us opportunity to accurately determine the frequency of STIs among high-risk women in low resource settings where syndromic management of STIs is the standard of care.

Our study supports the observation that a significant number of women with laboratory confirmed STIs are likely asymptomatic and therefore will miss the opportunity to be offered treatment using current syndromic management recommendations in low resource settings.[7,11] In this population with a high number of repeat infections during follow-up, untreated cases may progress and cause a significant future burden in reproductive morbidity that includes chronic pelvic pain, infertility and ectopic pregnancy. Chlamydia is associated

with 16% progression to PID in untreated women followed up prospectively.[12] In HIV-negative women, presence of STIs increases susceptibility of HIV by recruiting HIV pro-inflammatory cells to genital epithelium and disrupting mucosal barriers,[3,4,13] a major concern that impedes current progress for HIV control in sub-Saharan Africa. Gonorrhea and chlamydia both facilitate HIV transmission; therefore, control of these treatable STIs as part of a HIV combination prevention strategy is essential. In this subanalysis of data from the VOICE study, we estimate that only a small proportion of women who tested positive for chlamydia, gonorrhoea, syphilis, or trichomoniasis were symptomatic at time of diagnosis, because the majority tested positive at routine scheduled testing visits.

We identified several independent risk factors associated with recurrent curable STIs among women enrolled in the VOICE study. Even though participants with baseline STIs comprised a small percentage of participants with the same STI during follow-up, having a curable STI at baseline remained the strongest predictive risk factor for being diagnosed with the same STI type (not necessarily the same organism) during follow-up (Table 4). The high baseline STI prevalence presumably reflects underlying community burden of preventable infections. We were however unsuccessful in reducing high-risk behaviors in this population as evidenced by the high incidence of the four types of STIs during follow-up. A limitation of our study analysis is the long duration between study visits resulting in potential likely underestimates of STI incidence. However, the associations we observed should remain valid as diagnostic testing was done consistently throughout the study. In the absence of a test of cure for diagnosed STIs, we are not able to determine if some of the incident cases were from treatment failure or reinfections from untreated partners.

To have an impact on STIs and HIV in young women, there is an urgent need to develop innovative interventions which incorporate sexual and reproductive health promotion and evaluation of new vaccines.[14] In many high-income countries, there is evidence of a decline in pelvic inflammatory disease observed after implementing annual programs to screen and treat chlamydia and gonorrhea among women younger than 25 years.[15,16] Randomized controlled trials have confirmed that screening and treatment for *C. trachomatis* can prevent pelvic inflammatory disease.[16–18] Nucleic acid amplification tests with high sensitivity (>90%) and high specificity (>90%)[16] are now available as rapid tests that can be implemented in programs suitable for point of care testing for chlamydia, gonorrhea and trichomoniasis.[19,20] There is an urgent need for validation of accurate easy to use point of care tests in low resource settings that will result in more timely targeted treatment and earlier partner management.[21] Our data strongly support a recommendation to transition from syndromic management to targeted annual and repeat testing for STIs among high-risk young women living in HIV endemic communities. Moreover, the high rate of repeat infection speaks to the lack of partner management services available in these settings. Implementing feasible and affordable tests in screening programs for chlamydia and gonorrhea, along with partner management, should accelerate control of STI in these women at high risk for HIV acquisition. Evidence of improved uptake of STI screening through integrated services for STI/HIV in health care facilities like family planning, postnatal and STI clinics speaks to the potential of this approach in targeting women in the years of reproductive health.[22]

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TABLE 1

Baseline Demographics and Baseline Curable STIs Among Evaluable Participants

	All Countries	South Africa	Uganda	Zimbabwe
Evaluable participants	4843	3918	310	615
Age				
Mean (SD)	25.4 (5.2)	24.7 (5.1)	28.2 (4.8)	28.1 (4.7)
Min, max	18.0, 40.0	18.0, 40.0	19.0, 40.0	18.0, 39.0
< 21 y	918 (19%)	872 (22%)	17 (5%)	29 (5%)
21–24 y	1536 (32%)	1357 (35%)	60 (19%)	119 (19%)
25–30 y	1514 (31%)	1118 (29%)	127 (41%)	269 (44%)
> 30 y	875 (18%)	571 (15%)	106 (34%)	198 (32%)
Currently married	1019/4843 (21%)	271/3918 (7%)	169/310 (55%)	579/615 (94%)
No. partners in addition to primary sex partner				
0	3731/4809 (78%)	3033/3884 (78%)	121/310 (39%)	577/615 (94%)
1	792 (16%)	691 (18%)	71 (23%)	30 (5%)
2	157 (3%)	108 (3%)	43 (14%)	6 (1%)
3 or more	129 (3%)	52 (1%)	75 (24%)	2 (<1%)
Education: primary school or less	387/4839 (8%)	147/3914 (4%)	187/310 (60%)	53/615 (9%)
Children: 1 or more	4114/4842 (85%)	3198/3917 (82%)	303/310 (98%)	613/615 (>99%)
Earns own income	2792/4843 (58%)	2281/3918 (58%)	230/310 (74%)	281/615 (46%)
Alcohol consumption*: At least some	1266/4808 (26%)	1039/3883 (27%)	188/310 (61%)	39/615 (6%)
Any anal sex (in the past 3 mo)	837/4773 (18%)	767/3854 (20%)	23/306 (8%)	47/613 (8%)
Any vaginal sex without condoms in past 7 d†	1046/4403 (24%)	624/3526 (18%)	133/277 (48%)	289/600 (48%)
HSV-2–positive	2210/4834 (46%)	1817/3909 (46%)	196/310 (63%)	197/615 (32%)
Baseline curable STIs				
Chlamydia	584 (12%)	550 (14%)	18 (6%)	16 (3%)
Gonorrhoea	155 (3%)	131 (3%)	17 (5%)	7 (1%)
Syphilis	67 (1%)	42 (1%)	20 (6%)	5 (1%)
Trichomoniasis	292 (6%)	230 (6%)	22 (7%)	40 (7%)
Any of these STIs	956 (20%)	827 (21%)	67 (22%)	62 (10%)

*Participants indicated any amount of alcohol consumption in contrast to never drinking alcohol.

†Includes the participants who completed the questions on the Baseline Behavioral Assessment form regarding any vaginal sex in the past 7 days and the number of times a condom was used. If participants had vaginal sex in the last 7 days and used a condomless than 100% of the time they are included in this category as having unprotected sex (without condoms) in the 7 days.

TABLE 2

Curable STIs and HIV Events During Follow-Up

	All Countries	South Africa	Uganda	Zimbabwe
Evaluable ppts	4843	3918	310	615
Chlamydia				
ppts with chlamydia test follow-up after enrollment	4790	3871	310	609
Total follow-up time: PYAR	5543.7	4299.8	424.1	819.8
Total no. chlamydia events during follow-up (ppts)	763 (659)	685 (590)	41 (38)	37 (31)
Gonorrhoea				
ppts with gonorrhoea test follow-up after enrollment	4790	3871	310	609
Total follow-up time: PYAR	5543.7	4299.8	424.1	819.8
Total no. gonorrhoea events during follow-up (ppts)	196 (179)	162 (149)	25 (21)	9 (9)
Syphilis				
ppts with syphilis test follow-up after enrollment	4781	3862	310	609
Total follow-up time: PYAR	5533.0	4289.7	423.8	819.6
Total no. syphilis events during follow-up (ppts)	48 (47)	29 (28)	17 (17)	2 (2)
Trichomoniasis				
ppts with trichomoniasis test follow-up after enrollment	4577	3667	299	611
Total follow-up time: PYAR	5230.5	4001.7	406.9	822.0
Total no. trichomoniasis events during follow-up (ppts)	345 (300)	266 (232)	30 (27)	49 (41)
HIV *				
ppts with HIV test follow-up after enrollment	4842	3917	310	615
Total follow-up time: PYAR	5453.7	4205.7	422.0	826.0
No. ppts with HIV seroconversion	307	291	9	7
Incidence rate (per 100 person-years)	5.6	6.9	2.1	0.8
95% CI for incidence	(5.0–6.3)	(6.1–7.8)	(1.0–4.0)	(0.3–1.7)

* HIV results include follow-up time up to seroconversion since there are not multiple events per participant. In addition, HIV events are included only for the participants with STI test follow-up. Therefore, these results may be slightly different than the results given in the VOICE primary article.[8]

ppts, participants.

TABLE 3

Incidence Rates * for Curable STIs by Baseline Risk Factors

Baseline Risk Factor		Chlamydia Incidence (95% CI)	Gonorrhoea Incidence (95% CI)	Syphilis Incidence (95% CI)	Trichomoniasis Incidence (95% CI)
Participants with follow-up	STI results	4790	4790	4781	4577
PYAR		5543.7	5543.7	5533.0	5230.5
Country	South Africa	15.9 (14.7–17.2)	3.8 (3.1–4.4)	0.7 (0.4–0.9)	6.6 (5.7–7.5)
	Uganda	9.7 (6.7–12.7)	5.9 (3.2–8.6)	4.0 (2.2–5.8)	7.4 (4.4–10.3)
	Zimbabwe	4.5 (2.9–6.2)	1.1 (0.4–1.8)	0.2 (0–0.5)	6.0 (4.1–7.8)
Age	<21 y	26.8 (23.5–30.1)	6.8 (5.0–8.7)	1.0 (0.3–1.8)	7.9 (5.8–9.9)
	21–24 y	17.1 (15.0–19.1)	4.1 (3.1–5.1)	0.7 (0.4–1.1)	5.7 (4.5–6.9)
	25–30 y	9.2 (7.7–10.8)	2.3 (1.5–3.0)	0.7 (0.4–1.1)	6.4 (5.0–7.8)
	>30 years	3.7 (2.4–4.9)	1.5 (0.7–2.4)	1.2 (0.6–1.8)	7.2 (5.2–9.1)
Marital status	Unmarried	16.4 (15.1–17.7)	4.1 (3.5–4.8)	0.9 (0.6–1.2)	6.8 (5.9–7.8)
	Married	5.4 (4.0–6.8)	1.6 (0.8–2.4)	0.8 (0.4–1.3)	5.9 (4.4–7.3)
No. partners (in addition to primary sex partner)	0	13.7 (12.6–14.8)	3.4 (2.9–4.0)	0.7 (0.5–1.0)	6.6 (5.8–7.4)
	1 or more	14.8 (10.6–19.1)	5.3 (2.7–8.0)	3.0 (1.1–4.8)	6.4 (3.3–9.6)
Education	Primary school or less	9.5 (6.6–12.3)	4.3 (2.1–6.6)	2.6 (1.3–3.9)	7.7 (5.1–10.3)
	Secondary or more	14.2 (13.1–15.3)	3.5 (2.9–4.0)	0.7 (0.5–0.9)	6.5 (5.7–7.3)
Children	0	17.9 (14.8–21.0)	4.0 (2.5–5.6)	0.5 (0–1.1)	5.8 (4.0–7.6)
	1 or more	13.1 (12.0–14.2)	3.5 (2.9–4.0)	0.9 (0.7–1.2)	6.7 (5.9–7.6)
Earns own income	no	15.3 (13.6–17.0)	3.4 (2.6–4.3)	0.8 (0.4–1.2)	5.9 (4.8–7.1)
	yes	12.7 (11.4–14.0)	3.6 (2.9–4.3)	0.9 (0.6–1.2)	7.1 (6.0–8.1)
Alcohol consumption	None	12.7 (11.5–13.9)	2.9 (2.3–3.4)	0.7 (0.4–0.9)	6.5 (5.6–7.4)
	At least some	17.0 (14.8–19.2)	5.6 (4.2–6.9)	1.5 (0.9–2.1)	6.6 (5.1–8.2)
Any anal sex (past 3 mo)	No	13.2 (12.0–14.3)	3.5 (2.9–4.1)	0.8 (0.6–1.1)	6.5 (5.7–7.4)
	Yes	16.3 (13.6–19.0)	3.9 (2.5–5.2)	1.1 (0.4–1.7)	6.6 (4.7–8.5)
Any unprotected vaginal sex (past 7 d)	No	14.7 (13.4–16.0)	3.6 (2.9–4.2)	0.7 (0.5–1.0)	6.9 (6.0–7.9)
	Yes	10.0 (8.0–11.9)	3.4 (2.2–4.6)	1.3 (0.6–2.0)	5.4 (3.9–6.8)
Baseline HSV-2:	Negative	15.0 (13.5–16.5)	3.3 (2.6–4.0)	0.6 (0.3–0.9)	5.0 (4.1–5.8)
	Positive	12.3 (10.8–13.8)	3.9 (3.0–4.7)	1.2 (0.8–1.6)	8.5 (7.1–9.9)

* Not adjusted for any other baseline factors.

TABLE 4

Multivariable Models* With Baseline Risk Factors for Curable STIs

	Chlamydia	Gonorrhoea	Syphilis	Trichomoniasis
Participants included in the model	4789	4754	4781	4563
Baseline STI status†: positive versus negative				
IRR (95% CI)	2.1 (1.8–2.5)	2.1 (1.3–3.5)	6.8 (2.8–16.7)	5.6 (4.3–7.3)
P	<0.001	0.005	<0.001	<0.001
Age: < 25 y vs ≥ 25 y				
IRR (95% CI)	2.2 (1.9–2.6)	2.3 (1.6–3.2)	—	—
P	<0.001	<0.001	—	—
Marital status: unmarried versus married				
IRR (95% CI)	1.5 (1.1–2.1)	—	—	—
P	0.024	—	—	—
Alcohol consumption: some versus none				
IRR (95% CI)	—	1.7 (1.2–2.3)	—	—
P	—	0.003	—	—
Baseline HSV-2: positive vs negative				
IRR (95% CI)	—	—	—	1.6 (1.2–2.0)
P	—	—	—	<0.001

*Complete list of variables available in Table 3.

†The baseline STI status is from the same STI that is being modeled. (e.g. in the Chlamydia column, baseline STI status refers only to Chlamydia test results).

—, not retained in the final multivariable model since the factor is not significant at the 0.05 level; IRR, incident rate ratio.