Comparison of anal HPV natural history among men by country of residence: Brazil, Mexico, and the United States

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Abstract

OBJECTIVES.—Globally, anal cancer incidence is rare, but is increasing in some world regions. Our objective was to assess differences in anal HPV natural history in three countries.

METHODS.—Men aged 18–70 years were recruited from the US (n=634), Mexico (n=665), and Brazil (n=731). Anal specimens were collected every six-months. HPV genotyping was assessed by Linear Array. Anal HPV prevalence was compared using the Fisher's exact test. HPV infection incidence rates (IR) and 95% confidence intervals (CI) were calculated.

RESULTS.—Any anal HPV prevalence was highest among men from Brazil (24%) compared to Mexico (15%) and the US (15%). When stratified by sexual history, the prevalence of any HPV among MSM/MSMW was 43%, 37%, and 45% and 9%, 12%, and 10% for MSW from Brazil, Mexico, and US, respectively. Any HPV incidence was significantly higher among men from Brazil compared to US men (IRR= 2.4, 95% CI=1.7–3.4) and comparable between men from Mexico and the US (IRR=1.2, 95% CI=0.8–1.8).

CONCLUSION.—Men in Brazil and Mexico often have similar, if not higher incidence of anal HPV compared to men from the U.S., and may benefit from gender neutral HPV vaccine policies.

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Keywords

HIM Study; human papillomavirus (HPV); HIV-negative

Introduction

The incidence of anal cancer globally is rare with annual age-adjusted incidence rates of less than 2 per 100,000 in the general population.(1–3) Globally, age-adjusted anal cancer incidence ranged from less than 1 per 100,000 men per year in developed and developing countries to 3.6 per 100,000 men per year among the Indigenous Australians in the Northern Territory.(3, 4) While rare, anal cancer incidence has been shown to be increasing over time in both men and women in more developed world regions.(1, 5)

The increase in anal cancer incidence may be attributable to changing sexual practices that include earlier age of sexual intercourse and larger numbers of sexual partners.(1) Certain populations have been documented to have a higher incidence of anal cancer, specifically men who have sex with men (MSM), persons living with HIV/AIDS, transplant recipients, and women with prior HPV-associated cervical disease.(3) Anal cancer incidence among HIV-positive MSM in the US is comparable to cervical cancer incidence among women in sub-Saharan Africa.(6) There are currently no uniform screening guidelines for anal cancer, but there are screening tools that are used by some healthcare professionals among populations at highest risk for anal cancer, including digital ano-rectal exam, anal Pap cytology and high resolution anoscopy.

The majority of incident anal cancers can be attributed to HPV with 88% of tumors testing HPV positive.(7) In a meta-analysis, high-risk (HR-HPV) HPV anal prevalence among HIV-positive MSM was 74% and among HIV-negative MSM was 37%.(8) Anal HPV infection is not limited to those that engage in receptive anal sex. We previously reported 12% anal HPV prevalence among HIV-negative men who have sex exclusively with women (MSW).(9) The majority of reports focusing on anal HPV prevalence and incidence are among high-risk populations in developed countries. Our objective was to assess the natural history of anal HPV by country of residence among a general population of men residing in Tampa, Florida, US; Cuernavaca, Mexico; and Sao Paulo, Brazil. This information is needed to inform HPV vaccine policy discussion for men in each of the countries.

Methods

Study Population

The *HIM Study* enrolled 4123 men aged 18–70 years living in Tampa, Florida, US; Cuernavaca, Mexico; and Sao Paulo, Brazil between July 2005 and June 2009. A full description of the study procedures has been published.(10, 11) All men in the current analysis reported they were HIV-negative at baseline and all follow-up visits; we did not clinically assess HIV serostatus. Participants returned for study visits every six months and were given a physical exam where specimens for laboratory analyses were obtained. From the overall *HIM Study*, 14% of participants chose not to provide an anal specimen at

baseline and not all anal specimens provided have been HPV genotyped. A sub-cohort of men who had two or more study visits with anal swabs were selected to be HPV genotyped based on chronological enrollment in the *HIM study* were included in this analysis (n=2030). Among these 2030 men, 731 were from Brazil, 665 from Mexico, and 634 from US.

All participants provided written informed consent. Study protocols were approved by the Institutional Review Boards at the University of South Florida (Tampa, FL, US), the Ludwig Institute for Cancer Research, the Centro de Referencia e Treinamento em Doencas Sexualmente Transmissiveis e AIDS (Sao Paulo, Brazil), and the Instituto Nacional de Salud Publica (Cuernavaca, Mexico).

Anal specimen collection for HPV detection—Participants underwent a clinical examination at each visit. Using a pre-wetted Dacron swab, 360 degrees of the anal canal epithelium was swabbed between the anal os and the anal canal dentate line, after which the swab was placed into standard transport medium and stored at −80C.(12, 13) Specimens underwent DNA extraction (Qiagen Media Kit), PCR analysis, and HPV genotyping (Roche Linear Array) (14). If samples tested positive for β-globin or an HPV genotype, they were considered adequate and were included in the analysis. The Linear Array assay tests for 37 HPV types, classified as high-risk (HR-HPV; types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68) or low-risk (LR-HPV; types 6, 11, 26, 40, 42, 53, 54, 55, 61, 62, 64, 66, 67, 69, 70, 71, 72, 73, 81, 82, 82 subtype IS39, 83, 84, and 89).(15) The HPV genotypes were further classified as the HPV types in the 4vHPV vaccine (6/11/16/18) and the 9vHPV vaccine (6/11/16/18/31/3¾5/52/58) target.

Statistical Analysis

In the *HIM Study*, sexual orientation was purposefully not asked to decrease risk of reporting bias of sexual behavior. Instead detailed information regarding sexual behavior was assessed and sex was defined as oral, vaginal or anal sex. Using responses to these questions at baseline, we defined MSM as only having sex with a man during their lifetime, MSWM as having sex with both women and men, MSW as only having sex with women during their lifetime, and virgins as those that reported no sex with men or women. Both prevalence and incidence analyses were stratified by two sexual history groups: MSM/MSWM and MSW, virgin data was not included in the stratified analyses.

Prevalence—Differences in demographic and sexual behavior characteristics between men who did or did not have a prevalent HPV infection (any HPV type) at baseline were calculated within each country using Monte Carlo estimation of the exact Pearson Chi-square test (Table 1). We also calculated differences in demographic and sexual behavior characteristics between men who did or did not have a prevalent HPV infection (any HPV type) at baseline between the three countries (global p-value) using the Wald Chi-square test. Prevalence of each HPV genotype was compared between the three countries using the Fisher's exact test.

Incidence—Differences in baseline demographic and sexual behavior characteristics between men with and without an incident HPV infection (any HPV type) were calculated within each country using Monte Carlo estimation of the exact Pearson Chi-square test. We also calculated differences in baseline characteristics between men with and without an incident HPV infection between the three countries (global p-value) using the Wald Chi-square test. Men with a prevalent HPV infection would be classified as having incident infections only for the HPV types not present at the baseline visit.

Person time for newly acquired HPV infection was estimated by use of the time from study entry to the date of the first detection of HPV DNA, assuming a new infection arose at the date of detection. For individual and grouped HPV incidence analyses, only the first acquired infection was considered for a given HPV type or group. Incidence analyses included only men who tested negative for a given individual HPV type or grouped HPV infection category at baseline. For example, only men who were anal HPV negative for any HPV type were included in the grouped "any HPV" anal HPV incidence analysis. The calculation of the exact 95% CIs for incidence estimates was based on the number of events modelled as a Poisson variable for the total person-months. Incidence rate ratios (IRR) and 95% CIs were also calculated based on Poisson assumptions comparing incidence rates between countries.

Results

Prevalence

Overall, anal HPV (any type) prevalence was 18.3% among the sub-cohort of 2030 men participating in the *HIM Study* (Table 1). The prevalence of any HPV type significantly differed (p<0.001) by country with Brazil (24.1%) having the highest prevalence compared to Mexico (15.0%) and the US (15.0%) (Table 2). Prevalence of any anal HPV was significantly associated with sexual history and lifetime number of male anal sexual partners in all three countries (Table 1). Age and marital status were significantly associated with prevalence of anal HPV in Brazil and Mexico, but not in the US. In Brazil, education (p=0.004) and number of lifetime female sexual partners (<0.0001) was associated with prevalence of anal HPV. Race (p=0.01) and smoking status (p=0.002) were associated with anal HPV prevalence in the US. When comparing demographic and sexual characteristics across the three countries, race (p=0.02), marital status (p=0.003), smoking status (p=0.003), monthly alcohol use (p=0.002), and total number of female sexual partners (p<0.0001) were differentially associated with anal HPV prevalence (Table 1, global p-value).

HPV genotype prevalence by country is described in Table 2. Prevalence of several HPV types significantly differed by country. Overall, HPV16 prevalence was highest among men from the US (4.3%) compared to men from Mexico (1.4%) and Brazil (3.7%). When stratified by sexual history, the prevalence of HPV16 was highest among MSM/MSWM (p=0.02) and MSW (p=0.0001) from the US (Table 2). Overall, anal HPV6 prevalence was comparable between the three countries (p=0.27); however when stratified by sexual history, prevalence was highest among MSM/MSWM from Mexico (p=0.03) and lowest among MSW from Brazil (p=0.01). Overall, the men from Brazil (8.2%) and the US (7.3%) had a higher proportion of having one or more of the 4vHPV types detected at the anal canal

compared to men from Mexico (4.4%). Prevalence of 4vHPV types among MSM/MSWM was highest among men from US (22.4%) compared to men from Brazil (16.5%) and Mexico (14.9%, p=0.006), and among MSW was highest among men from the US (5.2%) compared to men from Brazil (1.8%) and Mexico (2.8%, p=0.0005).

Incidence

The median follow-up time for all 2030 men was 7.1 months (interquartile range (IQR): 6.5–18.8). Median follow-up time for men from Brazil was 7.6 months (IQR: 6.4–24.4), 7.2 months (IQR: 6.7–14.4) for men from Mexico, and 6.8 months (IQR: 6.5–7.9) for men from the US. Among the 2030 men, 27% of men from Brazil, 13% of men from Mexico, and 9% of men from the US had an incident HPV (any type) infection during follow-up. Table 3 describes differences in demographic and sexual characteristics at baseline associated with any anal HPV incidence. In all three countries lifetime number of male sexual partners and sexual history were significantly associated with any anal HPV incidence (Table 3). Marital status was significantly associated with any anal HPV incidence in Brazil and Mexico but not in the US. In Brazil, anal HPV incidence was associated with age (p<0.0001), education (p=0.0002), smoking status (p=0.04), monthly alcohol consumption (p=0.007) and lifetime number of female sexual partners (p<0.0001). When comparing demographic and sexual characteristics across the three countries, age (p=0.0002), marital status (p<0.0001), smoking status (p=0.004), alcohol consumption (p=0.02), sexual history (p<0.0001), lifetime number of female sexual partners (p<0.0001), and lifetime number of male sexual partners (p<0.0001) were differentially associated with anal HPV incidence (Table 3, global p-value).

Table 4 presents overall anal HPV incidence rates (IR) per 1000 person-months (pm). Incidence rate ratios (IRR) were calculated to compare anal HPV IR across countries. Table 5 presents anal HPV IR stratified by sexual history and country. Any anal HPV incidence was significantly higher among men from Brazil compared to men from the US (IRR= 2.4, 95% CI 1.7–3.4) and comparable between men from Mexico and the US (IRR=1.2, 95% CI 0.8–1.8, Table 4). Stratified analyses by sexual history for any anal HPV incidence was marginally higher among MSM/MSWM from Brazil compared to men from the US (Table 5). No difference in HPV16 or HPV6 incidence was observed between the three countries; stratified analyses by sexual history were also similar. Overall, Brazil had a significantly higher incidence of the HPV types that the 4vHPV and 9vHPV vaccines are directed against compared to the US and Mexico. When stratified by sexual history, incidence rates were similar between the three countries. In general, Brazil had the highest incidence of non-vaccine HPV types compared to the US and Mexico. Men from the US and Mexico were comparable in the incidence of non-vaccine HPV types.

Discussion

In this multinational cohort of 2,030 HIV-negative men, we compared the natural history of HPV at the anal canal by country of residence. We and others have shown that MSW have anal HPV present at the anal canal; however the prevalence is dramatically lower compared to MSM/MSMW.(13, 16) Therefore, we stratified the analyses by sexual history at baseline.

In this cohort, Brazil had a larger sample size of MSM/MSWM. HPV16 is the most common HPV genotype detected within pre-malignant anal lesions (~67%) and anal cancer (~76%). (17, 18) We found that the US had the highest prevalence of HPV16 while HPV16 incidence was highest among men from Brazil and Mexico. Other HR-HPV genotypes and HPV6 and 11 are also detected within pre-malignant anal lesions that would have been prevented with the 9v-HPV vaccine.(17, 18) In this study population, 15.2%, 7.2%, and 5.4% of men from Brazil, Mexico and the US, respectively had an incident HPV infection covered by the 9vHPV vaccine. When we stratify by sexual history, 28.5%, 28.7%, 25.9% of MSM/MSWM and 4.2%, 4.1%, 2.3% MSW from Brazil, Mexico and the US, respectively had an incident HPV infection that the 9vHPV vaccine protects against; thus, after controlling for sexual behavior, incidence was comparable.

The majority of research focusing on anal HPV has been conducted among high-risk populations in developed countries. Few studies have assessed the natural history of anal HPV among MSW. While the prevalence and incidence of anal HPV was lower among MSW compared to MSM/MSWM, HPV genotypes that are known to cause anal disease were detected among MSW. Previously, we reported that the duration of those infections is significantly lower among MSW compared to MSM, which could explain the differences in disease risk for anal cancer among those groups.(13) Two other studies assessed anal HPV prevalence among MSW; a study of men from Amsterdam detected anal HPV in 1.2% of participants, (19) and study of men with HPV-positive female sexual partners from Sao Paulo, Brazil detected anal HPV in 8% of participants.(20) This was comparable to the anal HPV prevalence among the MSW study population from Sao Paulo (8.7%) in the current study. If MSW are not engaging in receptive anal intercourse, then how is HPV infecting that anatomic site? We recently assessed the role of autoinoculation as a potential mechanism for anal HPV infection among MSW.(21) MSW with a prior genital HPV infection were at a higher risk for a subsequent type-specific anal infection compared to men without a genital infection.(21) Similar results have been observed among women in that those with a cervical HPV infection were more likely to have a subsequent anal infection even after controlling for receptive anal sex.(22–24) Autoinoculation or partner-assisted inoculation may explain the presence of anal HPV among MSW.

Anal HPV prevalence and incidence among MSM/MSWM in our population is lower than what has been reported in other studies. Anal HPV16 prevalence reported in a recent meta-analysis was 12.5% (range 6.3–26.9%) among HIV-negative MSM with the majority of included studies having been conducted in United States (5 studies), China, the Netherlands, and Australia.(8) In contrast, in the *HIM Study* population HPV16 prevalence among MSM/MSWM was lower than those reported in the meta-analysis (8) with prevalence at 4.6%, 6.7%, and 8.2% among men from Mexico, Brazil and US, respectively. The lower HPV16 prevalence in our study is likely not due to combining MSM with MSWM as previously reported no significant differences in HPV16 prevalence or 12-month cumulative incidence rates between MSM and MSWM.(25) Two other studies have reported anal HPV incidence among HIV-negative MSM.(26, 27) In Seattle, Washington among 16–30 year olds (n=94), anal HPV16 incidence was 10.3 per 1000pm.(26) In Rome, Italy among 155 HIV-negative MSM, anal HPV16 incidence was 9.1 per 1000pm. HPV16 incidence among HIV-negative MSM/MSWM in our population was 3.8, 3.9, and 2.9 per 1000pm among men from Brazil,

Mexico, and US, respectively. The higher incidence among the young MSM from Seattle and Italy is likely due to the difference in age and lifetime number of sexual partners between the populations and methods of recruitment (HIM Study did not recruit MSM in gay bars, bathhouses, etc.).

While rare, anal cancer incidence is increasing worldwide, specifically in developed countries. The age standardized anal cancer incidence rate in Brazil was 1.0 per 100,000 men per year and among men from Florida, US was 1.1 per 100,000 men per year; no information was reported for Mexico.(4) In Latin America (Chile, Colombia, Ecuador, Guatemala, Honduras, Mexico, and Paraguay) 77.4% of invasive anal cancers were HPV16-positive and in North America (US) 84.7% was HPV16-positive.(18) Other HPV types found in anal cancer were 18, 31, 33, 45, 58 in the USA and 18, 31, 33, 35, 39, 45, 52, 58, 59 in Latin America with the majority of these HR-HPV types being targeted by the 9vHPV vaccine.(18) As we previously mentioned, in our population 28.5%, 28.7%, 25.9% of MSM/ MSWM and 4.2%, 4.1%, 2.3% MSW from Brazil, Mexico and the US, respectively had an incident HPV infection covered by the 9vHPV vaccine. We currently cannot predict whether these HPV infections will persist and progress to anal intraepithelial neoplasia (AIN) or cancer. There is no treatment for HPV infections, but we can treat cancer, if we can detect it. Anal HPV can be prevented by both the 4vHPV and 9vHPV vaccines, significantly reducing rates of AIN.(28, 29)

This study has several strengths including the large sample size, duration of follow-up, and data collection from three international clinical sites. Data collection and specimen processing was consistent across the three clinical sites. The *HIM Study* is not a population-based study, but the demographics such as age, ethnicity, and education of the men included at each clinical site are similar to the underlying population of men aged 18–70 years in their respective communities.(11) Brazil had a much large sample size of MSM/MSWM than what may exist in the general population in Sao Paulo. Therefore, a potential limitation of the cohort is that the findings may not be generalizable to all men in each country. HPV incidence was based on clinic visits that occurred every six-months and may not accurately reflect the exact timing of infection. We stratified analyses based on sexual history at baseline, which was defined as either MSM/MSWM or MSW. Potentially a subject in the MSW (n=1324) categorization may have moved into the MSWM category during follow-up depending on the timing of the anal HPV infection. Time-dependent analyses would be required to account for these time-varying covariates.

In summary, men from Brazil and Mexico often have similar, if not higher incidence of anal HPV compared to men from the U.S. Among MSM/MSWM, the prevalence of HR-HPV types was highest among men from the US while the incidence of HR-HPV types was highest among men from Brazil and Mexico. Among the MSW, the prevalence of HR-HPV types was highest among men from Mexico and incidence of HR-HPV was comparable between the three countries. Although MSM/MSWM had a higher prevalence and incidence of anal HPV, we still detected anal HPV among 10% of MSW. Globally, only six countries have national gender-neutral vaccine policies: the U.S., Austria, Australia, Israel, Panama, and some provinces in Canada. Results presented here indicate that men from Brazil,

Mexico and the U.S. are infected with anal HPV and men from Brazil and Mexico may benefit from gender neutral HPV vaccine policies similar to the U.S.

Acknowledgements

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Table 1.

Demographic characteristics at HIM Study baseline comparing men with and without any prevalent HPV infection at the anal canal by country

	Brazil (n=731)			Mexico (n=665)			US (n=634)			
	No infection N=555	Infection N=176	P Value [a]	No infection N=565	Infection N=100	P Value [a]	No infection N=539	Infection N=95	P Value [a]	Global Pvalue [b]
Age			0.0002			0.03			0.12	0.55
18–30	198(68.3)	92(31.7)		219(80.8)	52(19.2)		312(87.4)	45(12.6)		
31–44	272(79.8)	69(20.2)		262(86.8)	40(13.2)		129(80.6)	31(19.4)		
45–70	85(85.0)	15(15.0)		84(91.3)	8(8.7)		98(83.8)	19(16.2)		
Race			0.09			0.48			0.01	0.02
White	332(73.1)	122(26.9)		13(76.5)	4(23.5)		400(87.1)	59(12.9)		
Black	173(81.2)	40(18.8)		1(100.0)	0(0.0)		74(76.3)	23(23.7)		
Asian/PI	6(66.7)	3(33.3)		0(0.0)	0(0.0)		30(93.8)	2(6.3)		
Other	33(84.6)	6(15.4)		538(85.4)	92(14.6)		20(74.1)	7(25.9)		
Refused	11(68.8)	5(31.3)		13(76.5)	4(23.5)		15(78.9)	4(21.1)		
Ethnicity			0.04			1.00			0.14	0.39
Hispanic	132(70.6)	55(29.4)		563(84.9)	100(15.1)		70(79.5)	18(20.5)		
Non-Hispanic	410(78.2)	114(21.8)		1(100.0)	0(0.0)		468(86)	76(14)		
Missing	13(65.0)	7(35.0)		1(100.0)	0(0.0)		1(50.0)	1(50.0)		
Years of Education			0.004			0.24			0.4	0.29
12 Years	344(80.4)	84(19.6)		328(83.5)	65(16.5)		91(85.0)	16(15.0)		
13–15 Years	72(67.9)	34(32.1)		59(89.4)	7(10.6)		284(86.6)	44(13.4)		
16 Years	138(70.8)	57(29.2)		177(87.6)	25(12.4)		162(82.2)	35(17.8)		
Missing	1(50.0)	1(50.0)		1(25.0)	3(75.0)		2(100.0)	0(0.0)		
Marital Status			<.0001			0.01			0.11	0.003
Single	214(64.1)	120(35.9)		130(79.3)	34(20.7)		337(87.1)	50(12.9)		
Married/Cohabiting	283(87.6)	40(12.4)		410(87.6)	58(12.4)		131(82.9)	27(17.1)		
Divorced/Separated/Widowed	55(77.5)	16(22.5)		23(74.2)	8(25.8)		67(78.8)	18(21.2)		
Missing	3(100.0)	0(0.0)		2(100.0)	0(0.0)		4(100.0)	0(0.0)		
Current Smoker			0.22			0.12			0.002	0.003

		Brazil (n=731)			Mexico (n=665)			US (n=634)			Global Pvalue[b]
		No infection N=555	Infection N=176	P Value[a]	No infection N=565	Infection N=100	P Value[a]	No infection N=539	Infection N=95	P Value[a]	
	Current	104(70.7)	43(29.3)		174(82.5)	37(17.5)		83(74.8)	28(25.2)		
	Former	96(79.3)	25(20.7)		135(90.0)	15(10.0)		105(83.3)	21(16.7)		
	Never	353(76.6)	108(23.4)		256(84.2)	48(15.8)		350(88.4)	46(11.6)		
	Missing	2(100.0)	0(0.0)					1(100.0)	0(0.0)		
Monthly Alcohol				0.51			0.7			0.66	0.002
	0 drinks	154(76.2)	48(23.8)		117(86.7)	18(13.3)		96(85.7)	16(14.3)		
	1 – 30 drinks	246(77.4)	72(22.6)		312(85.0)	55(15.0)		242(83.7)	47(16.3)		
	31+ drinks	128(72.7)	48(27.3)		112(83.0)	23(17.0)		194(86.6)	30(13.4)		
	Missing	27(77.1)	8(22.9)		24(85.7)	4(14.3)		7(77.8)	2(22.2)		
Sexual History				<.0001			<.0001			<.0001	0.39
	MSW	305(91.3)	29(8.7)		447(88.0)	61(12.0)		433(89.8)	49(10.2)		
	MSM	45(48.4)	48(51.6)		9(56.3)	7(43.8)		10(47.6)	11(52.4)		
	MSMW	134(60.1)	89(39.9)		46(64.8)	25(35.2)		37(57.8)	27(42.2)		
	Virgins	30(85.7)	5(14.3)		34(89.5)	4(10.5)		35(92.1)	3(7.9)		
	Missing	41(89.1)	5(10.9)		29(90.6)	3(9.4)		24(82.8)	5(17.2)		
Circumcised				0.82			0.47			0.16	0.62
	No	464(75.7)	149(24.3)		467(84.4)	86(15.6)		95(80.5)	23(19.5)		
	Yes	91(77.1)	27(22.9)		98(87.5)	14(12.5)		444(86.0)	72(14.0)		
Lifetime # of Female Partners				<.0001			0.21			0.12	<.0001
	0–1	98(62)	60(38)		88(84.6)	16(15.4)		103(83.7)	20(16.3)		
	2–9	139(70.6)	58(29.4)		311(86.1)	50(13.9)		209(88.9)	26(11.1)		
	10–49	222(85.7)	37(14.3)		130(82.8)	27(17.2)		174(84.1)	33(15.9)		
	50+	43(81.1)	10(18.9)		7(63.6)	4(36.4)		40(78.4)	11(21.6)		
	Refused	53(82.8)	11(17.2)		29(90.6)	3(9.4)		13(72.2)	5(27.8)		
Lifetime # of Male Anal Sex Partners				<.0001			<.0001			<.0001	0.77
	0	390(90.3)	42(9.7)		513(87.7)	72(12.3)		495(88.6)	64(11.4)		
	1–9	109(70.8)	45(29.2)		43(69.4)	19(30.6)		31(62.0)	19(38.0)		

	Brazil (n=731)			Mexico (n=665)			US (n=634)			
	No infection N=555	Infection N=176	P Value[a]	No infection N=565	Infection N=100	P Value[a]	No infection N=539	Infection N=95	P Value[a]	Global Pvalue[b]
10+	40(35.4)	73(64.6)		4(33.3)	8(66.7)		5(33.3)	10(66.7)		
Missing	16(50.0)	16(50.0)		5(83.3)	1(16.7)		8(80.0)	2(20.0)		

Abbreviations: MSW: Men who have sex with only women; MSM: Men who have sex with only men; MSMW: men who have sex with men and women; Virgins: reported no sexual contact with male or female

[a]P values were calculated using Monte Carlo estimation of exact Pearson chi-square tests comparing characteristics of men with and without HPV within each country. Missing values were not included in p value calculations.

[b]Global p values were calculated using the Wald chi-square tests comparing the characteristics of men with and without HPV across the three countries. Missing values were not included in p value calculations.

Table 2.

Type distribution of prevalent HPV infections overall and by country among 2030 HIM Study participants by sexual history

HPV Type	Overall (n=2030)				MSM/MSWM (n=488)				MSW (n=1324)			
	Brazil (n=731)	Mexico (n=665)	US (n=634)	Pvalue[a]	Brazil (n=316)	Mexico (n=87)	US (n=85)	Pvalue[a]	Brazil (n=334)	Mexico (n=508)	US (n=482)	Pvalue[a]
Any	176 (24.1)	100 (15.0)	95 (15.0)	**<.0001**	137 (43.35)	32 (36.8)	38 (44.7)	**0.005**	29 (8.7)	61 (12.0)	49 (10.2)	**0.002**
HR	105 (14.4)	56 (8.4)	59 (9.3)	**0.0004**	85 (26.9)	19 (21.8)	29 (34.1)	**0.002**	16 (4.8)	31 (6.1)	26 (5.4)	**0.009**
16	27 (3.7)	9 (1.4)	27 (4.3)	**0.004**	21 (6.7)	4 (4.6)	7 (8.2)	**0.02**	4 (1.2)	4 (0.8)	18 (3.7)	**0.0001**
18	14 (1.9)	3 (0.5)	5 (0.8)	**0.02**	14 (4.4)	1 (1.2)	5 (5.9)	**0.01**	0 (0.0)	1 (0.2)	0 (0.0)	0.38
31	6 (0.8)	1 (0.2)	2 (0.3)	0.16	4 (1.3)	0 (0.0)	1 (1.2)	0.15	2 (0.6)	1 (0.2)	1 (0.2)	0.11
33	4 (0.5)	4 (0.6)	1 (0.2)	0.49	3 (1.0)	1 (1.2)	1 (1.2)	0.17	0 (0.0)	2 (0.4)	0 (0.0)	0.15
35	8 (1.1)	2 (0.3)	3 (0.5)	0.14	8 (2.5)	1 (1.2)	2 (2.4)	0.08	0 (0.0)	1 (0.2)	0 (0.0)	0.38
39	6 (0.8)	8 (1.2)	4 (0.6)	0.56	6 (1.9)	4 (4.6)	4 (4.7)	**0.01**	0 (0.0)	3 (0.6)	0 (0.0)	0.06
45	10 (1.4)	4 (0.6)	9 (1.4)	0.28	10 (3.2)	2 (2.3)	7 (8.2)	**0.006**	0 (0.0)	2 (0.4)	2 (0.4)	0.12
51	22 (3.0)	12 (1.8)	8 (1.3)	0.06	14 (4.4)	5 (5.8)	6 (7.1)	**0.02**	7 (2.1)	7 (1.4)	2 (0.4)	**0.004**
52	7 (1.0)	5 (0.8)	3 (0.5)	0.62	7 (2.2)	4 (4.6)	2 (2.4)	**0.04**	0 (0.0)	1 (0.2)	1 (0.2)	0.28
56	9 (1.2)	7 (1.1)	3 (0.5)	0.36	8 (2.5)	3 (3.5)	1 (1.2)	0.06	1 (0.3)	4 (0.8)	2 (0.4)	0.08
58	8 (1.1)	5 (0.8)	3 (0.5)	0.45	6 (1.9)	1 (1.2)	1 (1.2)	0.13	2 (0.6)	0 (0.0)	1 (0.2)	0.07
59	16 (2.2)	10 (1.5)	4 (0.6)	0.06	14 (4.4)	2 (2.3)	3 (3.5)	0.05	2 (0.6)	8 (1.6)	1 (0.2)	**0.005**
68	7 (1.0)	6 (0.9)	5 (0.8)	0.96	7 (2.2)	3 (3.5)	3 (3.5)	0.05	0 (0.0)	2 (0.4)	1 (0.2)	0.16
LR	139 (19)	71 (10.7)	55 (8.7)	**<.0001**	113 (35.8)	22 (25.3)	23 (27.1)	**0.001**	18 (5.4)	44 (8.7)	28 (5.8)	**0.001**
6	25 (3.4)	15 (2.3)	14 (2.2)	0.27	23 (7.3)	7 (8.1)	5 (5.9)	**0.03**	2 (0.6)	8 (1.6)	9 (1.9)	**0.01**
11	3 (0.4)	4 (0.6)	3 (0.5)	0.92	3 (1.0)	2 (2.3)	3 (3.5)	**0.03**	0 (0.0)	1 (0.2)	0 (0.0)	0.38
26	1 (0.1)	0 (0.0)	0 (0.0)	1.00	1 (0.3)	0 (0.0)	0 (0.0)	0.65	0 (0.0)	0 (0.0)	0 (0.0)	N.E.
40	2 (0.3)	1 (0.2)	5 (0.8)	0.18	2 (0.6)	1 (1.2)	1 (1.2)	0.16	0 (0.0)	0 (0.0)	3 (0.6)	0.05
42	4 (0.5)	2 (0.3)	0 (0.0)	0.22	2 (0.6)	1 (1.2)	0 (0.0)	0.22	2 (0.6)	0 (0.0)	0 (0.0)	0.06
53	29 (4.0)	6 (0.9)	5 (0.8)	**<.0001**	26 (8.2)	4 (4.6)	2 (2.4)	**0.005**	3 (0.9)	1 (0.2)	2 (0.4)	0.05
54	8 (1.1)	7 (1.1)	2 (0.3)	0.23	8 (2.5)	3 (3.5)	0 (0.0)	**0.03**	0 (0.0)	3 (0.6)	2 (0.4)	0.07
55	7 (1.0)	3 (0.5)	1 (0.2)	0.13	7 (2.2)	1 (1.2)	0 (0.0)	0.07	0 (0.0)	1 (0.2)	1 (0.2)	0.28
61	17 (2.3)	10 (1.5)	4 (0.6)	**0.04**	13 (4.1)	3 (3.5)	2 (2.4)	0.05	2 (0.6)	6 (1.2)	2 (0.4)	**0.03**

HPV Type	Overall (n=2030)				MSM/MSWM (n=488)				MSW (n=1324)			
	Brazil (n=731)	Mexico (n=665)	US (n=634)	Pvalue[a]	Brazil (n=316)	Mexico (n=87)	US (n=85)	Pvalue[a]	Brazil (n=334)	Mexico (n=508)	US (n=482)	Pvalue[a]
62	20 (2.7)	5 (0.8)	9 (1.4)	**0.01**	14(4.4)	2(2.3)	2(2.4)	**0.04**	5(1.5)	3(0.6)	7(1.5)	**0.02**
64	20 (2.7)	5 (0.8)	9 (1.4)	**0.01**	0(0.0)	0(0.0)	0(0.0)	N.E.	0(0.0)	0(0.0)	0(0.0)	N.E.
66	7 (1.0)	7 (1.1)	5 (0.8)	0.92	6(1.9)	2(2.3)	3(3.5)	0.06	0(0.0)	5(1.0)	2(0.4)	**0.02**
67	0 (0.0)	0 (0.0)	3 (0.5)	**0.03**	0(0.0)	0(0.0)	2(2.4)	**0.03**	0(0.0)	0(0.0)	1(0.2)	0.36
69	2 (0.3)	0 (0.0)	0 (0.0)	0.34	2(0.6)	0(0.0)	0(0.0)	0.42	0(0.0)	0(0.0)	0(0.0)	N.E.
70	12 (1.6)	3 (0.5)	1 (0.2)	**0.003**	11(3.5)	2(2.3)	1(1.2)	0.05	0(0.0)	1(0.2)	0(0.0)	0.38
71	8 (1.1)	6 (0.9)	0 (0.0)	**0.03**	7(2.2)	2(2.3)	0(0.0)	0.05	1(0.3)	4(0.8)	0(0.0)	**0.03**
72	8 (1.1)	2 (0.3)	1 (0.2)	**0.03**	6(1.9)	1(1.2)	1(1.2)	0.13	1(0.3)	1(0.2)	0(0.0)	0.19
73	14 (1.9)	3 (0.5)	1 (0.2)	**0.0007**	12(3.8)	1(1.2)	1(1.2)	**0.03**	1(0.3)	2(0.4)	0(0.0)	0.11
81	14 (1.9)	9 (1.4)	2 (0.3)	**0.02**	13(4.1)	4(4.6)	1(1.2)	**0.03**	1(0.3)	3(0.6)	1(0.2)	0.10
82	1 (0.1)	1 (0.2)	4 (0.6)	0.19	1(0.3)	1(1.2)	3(3.5)	**0.01**	0(0.0)	0(0.0)	1(0.2)	0.36
82s[b]	1 (0.1)	1 (0.2)	2 (0.3)	0.69	1(0.3)	1(1.2)	1(1.2)	0.12	0(0.0)	0(0.0)	1(0.2)	0.36
83	9 (1.2)	3 (0.5)	5 (0.8)	0.27	8(2.5)	1(1.2)	3(3.5)	0.06	0(0.0)	2(0.4)	2(0.4)	0.12
84	25 (3.4)	14 (2.1)	7 (1.1)	**0.01**	23(7.3)	6(6.9)	5(5.9)	**0.03**	1(0.3)	7(1.4)	1(0.2)	**0.008**
89	25 (3.4)	12 (1.8)	2 (0.3)	**0.0001**	17(5.4)	2(2.3)	1(1.2)	**0.01**	6(1.8)	8(1.6)	0(0.0)	**0.02**
4vHPV[c]	60 (8.2)	29 (4.4)	46 (7.3)	**0.01**	52(16.5)	13(14.9)	19(22.4)	**0.006**	6(1.8)	14(2.8)	25(5.2)	**0.0005**
9vHPV[d]	81 (11.1)	42 (6.3)	56 (8.8)	**0.006**	68(21.5)	17(19.5)	24(28.2)	**0.004**	10(3.0)	20(3.9)	29(6.0)	**0.002**

Abbreviations: MSW: Men who have sex with only women; MSM: Men who have sex with only men; MSMW: men who have sex with men and women; HR: High Risk HPV types; LR: Low Risk HPV types

[a]Pvalue calculated using the Fisher's exact test comparing HPV prevalence in all three countries. Values in bold denote statistical significance at p<0.05.

[b]HPV 82 subtype IS39

[c]4vHPV: one or more of the 4-valent HPV vaccine types (6, 11, 16, 18)

[d]9vHPV: one or more of the 4-valent HPV vaccine types (6, 11, 16, 18, 31, 33, 45, 52, 58)

Table 3.

Demographic characteristics of HIM study participants at baseline comparing men with and without an incident anal HPV infection during follow-up by country

	Brazil (n=731)			Mexico (n=665)			US (n=634)			Global P value [b]
	No infection	Infection	P Value [a]	No infection	Infection	P Value [a]	No infection	Infection	P Value [a]	
Age			<.0001			0.21			0.55	0.0002
18–30	183(63.1)	107(36.9)		230(84.9)	41(15.1)		326(91.3)	31(8.7)		
31–44	266(78.0)	75(22.0)		267(88.4)	35(11.6)		142(88.8)	18(11.3)		
45–70	82(82.0)	18(18.0)		84(91.3)	8(8.7)		108(92.3)	9(7.7)		
Race			0.08			0.69			0.12	0.12
White	317(69.8)	137(30.2)		14(82.4)	3(17.6)		421(91.7)	38(8.3)		
Black	165(77.5)	48(22.5)		1(100.0)	0(0.0)		84(86.6)	13(13.4)		
Asian/PI	6(66.7)	3(33.3)		0(0.0)	0(0.0)		31(96.9)	1(3.1)		
Other	33(84.6)	6(15.4)		552(87.6)	78(12.4)		25(92.6)	2(7.4)		
Refused	10(62.5)	6(37.5)		14(82.4)	3(17.6)		15(78.9)	4(21.1)		
Ethnicity			0.15			0.12			0.84	0.19
Hispanic	129(69.0)	58(31.0)		580(87.5)	83(12.5)		79(89.8)	9(10.2)		
Non-Hispanic	390(74.4)	134(25.6)		0(0.0)	1(100.0)		495(91)	49(9)		
Missing	12(60.0)	8(40.0)		1(100.0)	0(0.0)		2(100.0)	0(0.0)		
Years of Education			0.0002			0.94			0.05	0.09
12 Years	332(77.6)	96(22.4)		344(87.5)	49(12.5)		92(86)	15(14)		
13–15 Years	60(56.6)	46(43.4)		58(87.9)	8(12.1)		306(93.3)	22(6.7)		
16 Years	138(70.8)	57(29.2)		175(86.6)	27(13.4)		176(89.3)	21(10.7)		
Missing	1(50.0)	1(50.0)		4(100.0)	0(0.0)		2(100.0)	0(0.0)		
Marital Status			<.0001			<.0001			0.92	<.0001
Single	201(60.2)	133(39.8)		125(76.2)	39(23.8)		352(91)	35(9)		
Married/Cohabiting	269(83.3)	54(16.7)		426(91.0)	42(9.0)		144(91.1)	14(8.9)		
Divorced/Separated/Widowed	58(81.7)	13(18.3)		28(90.3)	3(9.7)		76(89.4)	9(10.6)		
Missing	3(100.0)	0(0.0)		2(100.0)	0(0.0)		4(100.0)	0(0.0)		

		Brazil (n=731)			Mexico (n=665)			US (n=634)			Global P value[b]
		No infection	Infection	P Value[a]	No infection	Infection	P Value[a]	No infection	Infection	P Value[a]	
Current Smoker				0.04			0.18			0.27	0.004
	Current	95(64.6)	52(35.4)		177(83.9)	34(16.1)		97(87.4)	14(12.6)		
	Former	94(77.7)	27(22.3)		134(89.3)	16(10.7)		113(89.7)	13(10.3)		
	Never	340(73.8)	121(26.2)		270(88.8)	34(11.2)		365(92.2)	31(7.8)		
	Missing	2(100.0)	0(0.0)					1(100.0)	0(0.0)		
Monthly Alcohol				0.007			0.17			0.44	0.02
	0 drinks	160(79.2)	42(20.8)		122(90.4)	13(9.6)		98(87.5)	14(12.5)		
	1 – 30 drinks	234(73.6)	84(26.4)		322(87.7)	45(12.3)		264(91.3)	25(8.7)		
	31+ drinks	114(64.8)	62(35.2)		112(83.0)	23(17.0)		205(91.5)	19(8.5)		
	Missing	23(65.7)	12(34.3)		25(89.3)	3(10.7)		9(100.0)	0(0.0)		
Sexual History				<.0001			<.0001			<.0001	
	MSW	306(91.6)	28(8.4)		465(91.5)	43(8.5)		460(95.4)	22(4.6)		
	MSM	32(34.4)	61(65.6)		4(25.0)	12(75.0)		12(57.1)	9(42.9)		
	MSMW	123(55.2)	100(44.8)		51(71.8)	20(28.2)		43(67.2)	21(32.8)		
	Virgins	30(85.7)	5(14.3)		34(89.5)	4(10.5)		36(94.7)	2(5.3)		
	Missing	40(87.0)	6(13.0)		27(84.4)	5(15.6)		25(86.2)	4(13.8)		
Circumcised				0.14			0.76			0.48	0.59
	No	452(73.7)	161(26.3)		482(87.2)	71(12.8)		105(89.0)	13(11.0)		
	Yes	79(66.9)	39(33.1)		99(88.4)	13(11.6)		471(91.3)	45(8.7)		
Lifetime # of Female Partners				<.0001			0.18			0.34	<.0001
	0–1	85(53.8)	73(46.2)		85(81.7)	19(18.3)		106(86.2)	17(13.8)		
	2–9	142(72.1)	55(27.9)		324(89.8)	37(10.2)		216(91.9)	19(8.1)		
	10–49	212(81.9)	47(18.1)		137(87.3)	20(12.7)		192(92.8)	15(7.2)		
	50+	43(81.1)	10(18.9)		9(81.8)	2(18.2)		46(90.2)	5(9.8)		
	Refused	49(76.6)	15(23.4)		26(81.3)	6(18.8)		16(88.9)	2(11.1)		
Lifetime # of Male Anal Sex Partners				<.0001			<.0001			<.0001	<.0001
	0	387(89.6)	45(10.4)		533(91.1)	52(8.9)		528(94.5)	31(5.5)		

	Brazil (n=731)			Mexico (n=665)			US (n=634)			Global P value [b]
	No infection	Infection	P Value [a]	No infection	Infection	P Value [a]	No infection	Infection	P Value [a]	
1–9	91(59.1)	63(40.9)		42(67.7)	20(32.3)		36(72.0)	14(28.0)		
10+	38(33.6)	75(66.4)		2(16.7)	10(83.3)		4(26.7)	11(73.3)		
Missing	15(46.9)	17(53.1)		4(66.7)	2(33.3)		8(80.0)	2(20.0)		

Abbreviations: MSW: Men who have sex with only women; MSM: Men who have sex with only men; MSMW: men who have sex with men and women; Virgins: reported no sexual contact with male or female

[a] P values were calculated using Monte Carlo estimation of exact Pearson chi-square tests comparing characteristics of men with and without HPV within each country. Missing values were not included in p value calculations.

[b] Global p values were calculated using the Wald chi-square tests comparing the characteristics of men with and without HPV across the three countries. Missing values were not included in p value calculations.

Table 4.

Incidence rates of anal HPV by country

HPV	Brazil		Mexico		United States		Brazil vs US	Mexico vs US
	no/pmonths[a]	IR (95%CI)	no/pmonths[a]	IR (95%CI)	no/pmonths[a]	IR (95%CI)	IRR (95%CI)	IRR (95%CI)
Any	143/6708	21.3(18.1–25.1)	67/6076	11.0(8.7–14.0)	40/4504	8.9(6.5–12.1)	**2.4(1.7–3.4)**	1.2(0.8–1.8)
HR	123/8944	13.8(11.5–16.4)	58/7461	7.8(6.0–10.1)	26/5258	4.9(3.4–7.3)	**2.8(1.8–4.2)**	1.6(0.9–2.5)
16	27/10186	2.7(1.8–3.9)	15/8447	1.8(1.1–2.9)	8/5742	1.4(0.7–2.8)	1.9(0.9–4.2)	1.3(0.5–3.0)
18	25/10698	2.3(1.6–3.5)	7/8675	0.8(0.4–1.7)	6/6022	1.0(0.4–2.2)	2.3(0.9–5.7)	0.8(0.3–2.4)
31	9/11050	0.8(0.4–1.6)	3/8793	0.3(0.1–1.1)	4/6138	0.7(0.2–1.7)	1.2(0.4–4.1)	0.5(0.1–2.3)
33	7/11075	0.6(0.3–1.3)	4/8611	0.5(0.2–1.2)	2/6142	0.3(0.1–1.3)	1.9(0.4–9.3)	1.4(0.3–7.8)
35	10/10853	0.9(0.5–1.7)	2/8761	0.2(0.1–0.9)	2/6162	0.3(0.1–1.3)	2.8(0.6–13.0)	0.7(0.1–5.0)
39	13/10976	1.2(0.7–2.0)	4/8532	0.5(0.2–1.2)	5/6066	0.8(0.3–2.0)	1.4(0.5–4.0)	0.6(0.2–2.1)
45	20/10770	1.9(1.2–2.9)	10/8639	1.2(0.6–2.2)	5/6001	0.8(0.3–2.0)	2.2(0.8–5.9)	1.4(0.5–4.1)
51	27/10405	2.6(1.8–3.8)	12/8362	1.4(0.8–2.5)	10/5953	1.7(0.9–3.1)	1.5(0.7–3.2)	0.9(0.4–2.0)
52	13/10966	1.2(0.7–2.0)	11/8528	1.3(0.7–2.3)	4/6114	0.7(0.2–1.7)	1.8(0.6–5.6)	2.0(0.6–6.2)
56	14/10923	1.3(0.8–2.2)	3/8605	0.4(0.1–1.1)	2/6147	0.3(0.1–1.3)	3.9(0.9–17.3)	1.1(0.2–6.4)
58	17/10957	1.6(1.0–2.5)	4/8628	0.5(0.2–1.2)	3/6110	0.5(0.2–1.5)	3.2(0.9–10.8)	0.9(0.2–4.2)
59	26/10562	2.5(1.7–3.6)	15/8499	1.8(1.1–2.9)	6/6111	1.0(0.4–2.2)	**2.5(1.0–6.1)**	1.8(0.7–4.6)
68	19/10960	1.7(1.1–2.7)	6/8494	0.7(0.3–1.6)	3/6128	0.5(0.2–1.5)	**3.5(1.0–12.0)**	1.4(0.4–5.8)
LR	145/7698	18.8(16.0–22.2)	57/6774	8.4(6.5–10.9)	48/5139	9.3(7.0–12.4)	**2.0(1.5–2.8)**	0.9(0.6–1.3)
6	23/10391	2.2(1.5–3.3)	7/8318	0.8(0.4–1.8)	11/5848	1.9(1.0–3.4)	1.2(0.6–2.4)	0.4(0.2–1.2)
11	10/11134	0.9(0.5–1.7)	4/8667	0.5(0.2–1.2)	1/6130	0.2(0.0–1.2)	5.5(0.7–43.0)	2.8(0.3–25.3)
26	4/11245	0.4(0.1–0.9)	1/8821	0.1(0.0–0.8)	1/6210	0.2(0.0–1.1)	2.2(0.2–19.8)	0.7(0.0–11.3)
40	13/11051	1.2(0.7–2.0)	4/8762	0.5(0.2–1.2)	2/6160	0.3(0.1–1.3)	3.6(0.8–16.1)	1.4(0.3–7.7)
42	6/11079	0.5(0.2–1.2)	5/8678	0.6(0.2–1.4)	5/6190	0.8(0.3–1.9)	0.7(0.2–2.2)	0.7(0.2–2.5)
53	32/10150	3.2(2.2–4.5)	12/8502	1.4(0.8–2.5)	4/6060	0.7(0.2–1.8)	**4.8(1.7–13.5)**	2.1(0.7–6.6)
54	16/10874	1.5(0.9–2.4)	8/8553	0.9(0.5–1.9)	5/6138	0.8(0.3–2.0)	1.8(0.7–4.9)	1.1(0.4–3.5)
55	19/10907	1.7(1.1–2.7)	5/8683	0.6(0.2–1.4)	2/6185	0.3(0.1–1.3)	**5.4(1.3–23.1)**	1.8(0.3–9.2)

HPV	Brazil		Mexico		United States		Brazil vs US	Mexico vs US
	no/pmonths[a]	IR (95%CI)	no/pmonths[a]	IR (95%CI)	no/pmonths[a]	IR (95%CI)	IRR (95%CI)	IRR (95%CI)
61	25/10500	2.4(1.6–3.5)	8/8404	1.0(0.5–1.9)	2/6111	0.3(0.1–1.3)	**7.3(1.7–30.7)**	2.9(0.6–13.7)
62	33/10404	3.2(2.3–4.5)	11/8535	1.3(0.7–2.3)	4/6037	0.7(0.2–1.8)	**4.8(1.7–13.5)**	1.9(0.6–6.1)
64	4/11259	0.4(0.1–0.9)	0/8828	0.0(0.0–0.0)	0/6210	0.0(0.0–0.0)	N.E.	N.E.
66	18/10949	1.6(1.0–2.6)	5/8455	0.6(0.2–1.4)	3/6086	0.5(0.2–1.5)	3.3(0.9–11.3)	1.2(0.3–5.0)
67	4/11248	0.4(0.1–0.9)	1/8828	0.1(0.0–0.8)	2/6127	0.3(0.1–1.3)	1.1(0.2–5.9)	0.3(0.0–3.8)
69	7/11161	0.6(0.3–1.3)	1/8822	0.1(0.0–0.8)	2/6203	0.3(0.1–1.3)	1.9(0.4–9.4)	0.4(0.0–3.9)
70	18/10766	1.7(1.1–2.7)	5/8711	0.6(0.2–1.4)	2/6191	0.3(0.1–1.3)	**5.2(1.2–22.3)**	1.8(0.3–9.2)
71	7/11056	0.6(0.3–1.3)	2/8623	0.2(0.1–0.9)	1/6210	0.2(0.0–1.1)	3.9(0.5–32.0)	1.4(0.1–15.9)
72	22/10719	2.1(1.4–3.1)	3/8730	0.3(0.1–1.1)	5/6123	0.8(0.3–2.0)	2.5(0.9–6.6)	0.4(0.1–1.8)
73	20/10622	1.9(1.2–2.9)	1/8754	0.1(0.0–0.8)	3/6150	0.5(0.2–1.5)	**3.9(1.1–13.0)**	0.2(0.0–2.3)
81	17/10753	1.6(1.0–2.5)	3/8577	0.4(0.1–1.1)	4/6142	0.7(0.2–1.7)	2.4(0.8–7.2)	0.5(0.1–2.4)
82	12/11174	1.1(0.6–1.9)	2/8724	0.2(0.1–0.9)	1/6114	0.2(0.0–1.2)	6.6(0.9–50.5)	1.4(0.1–15.5)
82s[b]	9/11214	0.8(0.4–1.5)	2/8777	0.2(0.1–0.9)	0/6183	0.0(0.0–0.0)	N.E.	N.E.
83	19/10908	1.7(1.1–2.7)	2/8776	0.2(0.1–0.9)	1/6061	0.2(0.0–1.2)	**10.6(1.4–78.9)**	1.4(0.1–15.2)
84	29/10321	2.8(2.0–4.0)	12/8231	1.5(0.8–2.6)	16/5908	2.7(1.7–4.4)	1.0(0.6–1.9)	0.5(0.3–1.1)
89	30/10172	3.0(2.1–4.2)	16/8438	1.9(1.2–3.1)	4/6110	0.7(0.2–1.7)	**4.5(1.6–12.8)**	2.9(0.9–8.7)
4vHPV[c]	70/9946	7.0(5.6–8.9)	27/7997	3.4(2.3–4.9)	21/5389	3.9(2.5–6.0)	**1.8(1.1–2.9)**	0.9(0.5–1.5)
9vHPV[d]	105/9335	11.3(9.3–13.6)	42/7598	5.5(4.1–7.5)	29/5164	5.6(3.9–8.1)	**2.0(1.3–3.0)**	1.0(0.6–1.6)

Note: IR= Incidence Rates per 1000 person-months, IRR= incidence rate ratios, 95% CI= 95% Confidence Intervals, HR= High Risk HPV types, LR= Low Risk HPV types. Values in bold denote statistical significance.

[a] no/pmonths: number of men with infection / person-months

[b] HPV 82 subtype IS39

[c] 4vHPV: one or more of the 4-valent HPV vaccine types (6, 11, 16 ,18)

[d] 9vHPV: one or more of the 4-valent HPV vaccine types (6, 11, 16, 18, 31, 33, 45, 52, 58)

Table 5.

Incidence rates of anal HPV by country and sexual history

HPV	MSM/MSWM					MSW				
	Brazil IR (95%CI)	Mexico IR (95%CI)	US IR (95%CI)	BZ vs US IRR (95%CI)	MX vs US IRR (95%CI)	Brazil IR (95%CI)	Mexico IR (95%CI)	US IR (95%CI)	BZ vs US IRR (95%CI)	MX vs US IRR (95%CI)
Any	33.1(27.6–39.6)	24.3(16.3–36.3)	23.4(15.1–36.2)	1.4(0.9–2.3)	1.0(0.6–1.9)	7.2(4.5–11.4)	8.3(5.9–11.5)	5(3.1–8.2)	1.4(0.7–2.8)	1.7(0.9–3.0)
HR	19.1(15.7–23.2)	17.7(11.9–26.2)	10.8(6.1–19.0)	1.8(0.9–3.2)	1.6(0.8–3.3)	4.2(2.4–7.3)	5.4(3.8–7.9)	3.3(1.9–5.8)	1.3(0.6–2.8)	1.6(0.8–3.2)
16	3.8(2.6–5.7)	3.9(1.8–8.1)	2.9(1.1–7.6)	1.3(0.5–3.9)	1.4(0.4–4.6)	0.0(0.0–0.0)	1.4(0.7–2.8)	1.1(0.4–2.8)	NE	1.3(0.4–4.4)
18	2.9(1.8–4.5)	2.1(0.8–5.5)	2.2(0.7–6.8)	1.3(0.4–4.4)	0.9(0.2–4.2)	1.6(0.6–3.7)	0.3(0.1–1.4)	0.5(0.1–2.0)	3.2(0.6–16.4)	0.7(0.1–5.0)
31	1.0(0.5–2.1)	1.0(0.3–4.0)	2.0(0.7–6.3)	0.5(0.1–1.9)	0.5(0.1–3.0)	0.0(0.0–0.0)	0.2(0.0–1.2)	0.2(0.0–1.7)	NE	0.7(0.0–11.2)
33	0.7(0.3–1.7)	1.6(0.5–5.0)	1.4(0.3–5.6)	0.5(0.1–2.6)	1.2(0.2–7.0)	0.3(0.0–2.2)	0.2(0.0–1.2)	0.0(0.0–0.0)	NE	NE
35	1.5(0.8–2.8)	0.5(0.1–3.7)	1.4(0.3–5.4)	1.1(0.2–5.0)	0.4(0.0–4.2)	0.0(0.0–0.0)	0.2(0.0–1.2)	0.0(0.0–0.0)	NE	NE
39	1.6(0.9–2.9)	0.5(0.1–3.8)	0.7(0.1–5.0)	2.3(0.3–17.5)	0.8(0.0–12.1)	0.3(0.0–2.2)	0.5(0.2–1.6)	1.0(0.4–2.6)	0.3(0.0–2.8)	0.5(0.1–2.4)
45	2.7(1.7–4.3)	3.7(1.8–7.8)	1.5(0.4–5.9)	1.8(0.4–7.8)	2.5(0.5–12.2)	0.3(0.0–2.2)	0.3(0.1–1.4)	0.7(0.2–2.3)	0.4(0.0–4.0)	0.5(0.1–2.8)
51	3.2(2.1–4.9)	2.2(0.8–5.7)	3.8(1.6–9.0)	0.9(0.3–2.3)	0.6(0.2–2.1)	1.0(0.3–3)	1.3(0.6–2.6)	1.0(0.4–2.6)	1.0(0.2–4.5)	1.3(0.4–4.4)
52	1.5(0.8–2.7)	3.4(1.5–7.5)	1.4(0.3–5.6)	1.0(0.2–4.8)	2.4(0.5–12.0)	0.9(0.3–2.9)	0.9(0.4–2.1)	0.5(0.1–1.9)	1.9(0.3–11.4)	1.8(0.3–9.2)
56	1.9(1.1–3.3)	0.5(0.1–3.8)	0.7(0.1–4.7)	2.8(0.4–21.7)	0.8(0.1–12.8)	0.0(0.0–0.0)	0.0(0.0–0.0)	0.2(0.0–1.7)	NE	NE
58	1.6(0.9–2.9)	1.6(0.5–5.0)	1.4(0.3–5.5)	1.1(0.3–5.2)	1.2(0.2–6.9)	1.3(0.5–3.3)	0.2(0.0–1.2)	0.2(0.0–1.7)	5.1(0.6–46.0)	0.7(0.0–11.2)
59	3.5(2.4–5.3)	4.9(2.6–9.5)	1.4(0.3–5.5)	2.6(0.6–11.0)	3.6(0.8–16.7)	0.3(0.0–2.2)	0.9(0.4–2.1)	1.0(0.4–2.6)	0.3(0.0–2.8)	0.9(0.2–3.3)
68	2.6(1.7–4.2)	2.8(1.2–6.7)	1.4(0.3–5.5)	1.9(0.4–8.2)	2.0(0.4–10.3)	0.0(0.0–0.0)	0.2(0.0–1.2)	0.0(0.0–0.0)	NE	NE
LR	27.5(22.9–32.9)	18.0(11.9–27.4)	24.4(16.6–35.8)	1.1(0.7–1.7)	0.7(0.4–1.3)	7.6(4.9–11.6)	6.2(4.3–8.9)	5.0(3.2–8.0)	1.5(0.8–2.8)	1.2(0.7–2.2)
6	3.0(1.9–4.7)	3.5(1.6–7.8)	5.1(2.4–10.7)	0.6(0.2–1.4)	0.7(0.2–2.1)	0.6(0.2–2.5)	0.2(0.0–1.3)	1.0(0.4–2.7)	0.6(0.1–3.4)	0.2(0.0–1.5)
11	1.3(0.7–2.5)	2.1(0.8–5.7)	0.7(0.1–5.0)	1.8(0.2–14.4)	3.0(0.3–27.1)	0.3(0.0–2.2)	0.0(0.0–0.0)	0.0(0.0–0.0)	NE	NE
26	0.6(0.2–1.5)	0.0(0.0–0.0)	0.7(0.1–4.7)	0.8(0.1–7.6)		0.0(0.0–0.0)	0.0(0.0–0.0)	0.0(0.0–0.0)	NE	NE
40	1.6(0.9–2.8)	1.6(0.5–4.8)	0.7(0.1–4.7)	2.4(0.3–18.3)	2.3(0.2–22.3)	0.3(0.0–2.2)	0.2(0.0–1.2)	0.2(0.0–1.7)	1.3(0.1–20.2)	0.7(0.0–11.2)
42	0.9(0.4–1.9)	1.6(0.5–5.0)	2.7(1.0–7.2)	0.3(0.1–1.1)	0.6(0.1–2.7)	0.0(0.0–0.0)	0.3(0.1–1.4)	0.2(0.0–1.7)	NE	1.4(0.1–15.6)
53	4.2(2.9–6.2)	2.2(0.8–5.9)	1.4(0.3–5.6)	3.0(0.7–12.7)	1.6(0.3–8.7)	1.0(0.3–2.9)	1.4(0.7–2.8)	0.5(0.1–2.0)	1.9(0.3–11.6)	2.8(0.6–13.3)
54	1.9(1.1–3.3)	3.3(1.5–7.3)	2.7(1–7.2)	0.7(0.2–2.2)	1.2(0.3–4.3)	0.6(0.2–2.5)	0.4(0.1–1.4)	0.2(0.0–1.7)	2.5(0.2–28.1)	1.4(0.1–15.6)
55	1.8(1–3.1)	0.5(0.1–3.6)	0.0(0.0–0.0)	NE	NE	1.2(0.5–3.3)	0.5(0.2–1.6)	0.2(0.0–1.7)	5.1(0.6–45.5)	2.1(0.2–20.5)
61	3.5(2.3–5.3)	2.2(0.8–5.9)	0.7(0.1–4.8)	5.2(0.7–38.5)	3.3(0.4–29.3)	0.0(0.0–0.0)	0.7(0.3–1.9)	0.3(0.0–1.7)	NE	2.9(0.3–25.7)

HPV	MSM/MSWM					MSW				
	Brazil IR (95%CI)	Mexico IR (95%CI)	US IR (95%CI)	BZ vs US IRR (95%CI)	MX vs US IRR (95%CI)	Brazil IR (95%CI)	Mexico IR (95%CI)	US IR (95%CI)	BZ vs US IRR (95%CI)	MX vs US IRR (95%CI)
62	4.2(2.9–6.1)	1.1(0.3–4.2)	0.0(0.0–0.0)	NE	NE	0.6(0.2–2.5)	1.2(0.6–2.6)	1.0(0.4–2.6)	0.6(0.1–3.5)	1.2(0.4–4.2)
64	0.3(0.1–1.1)	0.0(0.0–0.0)	0.0(0.0–0.0)	NE	NE	0.3(0.0–2.2)	0.0(0.0–0.0)	0.0(0.0–0.0)	NE	NE
66	2.3(1.4–3.8)	1.1(0.3–4.3)	1.4(0.3–5.6)	1.7(0.4–7.3)	0.8(0.1–5.5)	0.3(0.0–2.2)	0.5(0.2–1.7)	0.2(0.0–1.7)	1.3(0.1–20.1)	2.2(0.2–20.9)
67	0.6(0.2–1.5)	0.5(0.1–3.5)	0.0(0.0–0.0)	NE	NE	0.0(0.0–0.0)	0.0(0.0–0.0)	0.5(0.1–1.9)	NE	NE
69	0.9(0.4–1.9)	0.5(0.1–3.6)	0.7(0.1–4.7)	1.3(0.2–10.6)	0.8(0.0–12.0)	0.3(0.0–2.2)	0.0(0.0–0.0)	0.2(0.0–1.7)	1.3(0.1–20.4)	NE
70	2.7(1.7–4.3)	1.6(0.5–4.9)	0.7(0.1–4.8)	4.0(0.5–30.0)	2.3(0.2–22.4)	0.0(0.0–0.0)	0.3(0.1–1.4)	0.0(0.0–0.0)	NE	NE
71	0.9(0.4–1.9)	0.5(0.1–3.8)	0.0(0.0–0.0)	NE	NE	0.3(0.0–2.2)	0.0(0.0–0.0)	0.0(0.0–0.0)	NE	NE
72	2.8(1.8–4.4)	1.6(0.5–4.8)	3.5(1.5–8.5)	0.8(0.3–2.1)	0.4(0.1–1.9)	0.3(0.0–2.2)	0.0(0.0–0.0)	0.0(0.0–0.0)	NE	NE
73	2.7(1.7–4.3)	0.5(0.1–3.6)	1.4(0.3–5.5)	2.0(0.5–8.6)	0.4(0.0–4.1)	0.6(0.2–2.5)	0.0(0.0–0.0)	0.2(0.0–1.7)	2.6(0.2–28.3)	NE
81	2.3(1.4–3.7)	0.0(0.0–0.0)	2.1(0.7–6.4)	1.1(0.3–3.8)	0.4(0.0–4.1)	0.3(0.0–2.2)	0.4(0.1–1.4)	0.0(0.0–0.0)	NE	NE
82	1.6(0.9–2.8)	0.5(0.1–3.6)	0.7(0.1–5)	2.2(0.3–17.1)	0.7(0.0–11.6)	0.3(0.0–2.2)	0.2(0–1.2)	0.0(0.0–0.0)	NE	NE
82s[a]	1.1(0.6–2.2)	1.0(0.3–4.1)	0.0(0.0–0.0)	NE	NE	0.0(0.0–0.0)	0.0(0.0–0.0)	0.0(0.0–0.0)	NE	NE
83	2.2(1.3–3.6)	0.5(0.1–3.6)	0.7(0.1–5)	3.1(0.4–23.4)	0.7(0.0–11.3)	1.2(0.5–3.3)	0.20(0.0–1.2)	0.0(0.0–0.0)	NE	NE
84	3.7(2.4–5.5)	2.3(0.9–6.2)	6.9(3.6–13.3)	0.5(0.2–1.1)	0.3(0.1–1.1)	1.3(0.5–3.3)	1.40(0.7–2.9)	1.5(0.7–3.3)	0.9(0.2–3)	1(0.3–2.8)
89	4.3(2.9–6.2)	7.2(4.2–12.4)	2.1(0.7–6.5)	2.0(0.6–6.8)	3.4(1.0–12.1)	0.7(0.2–2.6)	0.40(0.1–1.4)	0.2(0.0–1.7)	2.7(0.2–29.4)	1.4(0.1–15.9)
4vHPV[b]	9.5(7.3–12.3)	9.3(5.6–15.4)	8.9(4.9–16.1)	1.1(0.6–2.0)	1.0(0.5–2.3)	2.6(1.3–5.3)	2(1.1–3.6)	2.5(1.3–4.8)	1.1(0.4–2.7)	0.8(0.3–2.0)
9vHPV[c]	15.0(12.1–18.6)	14.6(9.4–22.5)	15.9(9.9–25.5)	0.9(0.6–1.6)	0.9(0.5–1.7)	4.7(2.8–7.9)	3.8(2.4–5.9)	3.1(1.7–5.6)	1.5(0.7–3.4)	1.2(0.6–2.6)

Note: MSM=Men who have sex with only men, MSWM= Men who have sex with men and women, MSW= Men who have sex with only women, US= United States, BZ=Brazil, MX=Mexico, IR= Incidence Rates per 1000 person-months, IRR= incidence rate ratios, 95% CI= 95% Confidence Intervals, HR= High Risk HPV types, LR= Low Risk HPV types. Values in bold denote statistical significance.

[a] HPV 82 subtype IS39

[b] 4vHPV: one or more of the 4-valent HPV vaccine types (6, 11, 16, 18)

[c] 9vHPV: one or more of the 4-valent HPV vaccine types (6, 11, 16, 18, 31, 33, 45, 52, 58)