# Prevalence and Correlates of Penile HPV Infection in a Clinic-Based Sample of Hispanic Males 

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Objective: The aim of this manuscript is to describe the prevalence, genotypic distribution of penile HPV infection and the behavioral risk factors associated with penile HPV infection (any HPV type, high-oncogenic-risk [HR] types, low-oncogenic-risk [LR] types, and of multiple HPV types) in a group of sexually active males who went to an STI clinic in San Juan, Puerto Rico.

Methods: After providing informed consent, the participants, underwent a detailed behavioral interview and a clinical examination. Frequency distributions and descriptive statistics were used to characterize the study samples. Prevalence estimates and 95\% confidence intervals (CI) were calculated for any type of HPV, HR types, LR types, or multiple types. Logistic regression analyses was performed to determine factors associated with each of the HPV types.

Results: Two hundred and six participants were enrolled in this study. The mean age of the participants was $37.8 \pm 13.1$ years. Close to $80 \%$ of the sample were infected with at least one HPV type; 73.5\% were infected with one or more LR-HPV types; 32.4\%, with one or more HRHPV types; and 46.0\%, with multiple HPV types. The most prevalent HR types were HPV-35, -31, and -16; the most prevalent LR types were HPV 6/11, and -84. After adjusting for age, having a high number of lifetime female sexual partners was highly associated with having multiple types of HPV infection (estimated $\mathrm{OR}=2.86 ; 95 \% \mathrm{CI}=1.41,5.80$ ).

Conclusion: HPV infection is common among sexually active males frequenting this STI clinic. HPV types not covered by the current quadrivalent HPV vaccine were identified. Multiple HPV types in the penis are significantly related to the lifetime number of female sexual partners. The high prevalence of HPV at this particular STI clinic evidences that males need to be targeted in primary care settings if the available vaccine is to be effectively promoted. In addition, opportunities for secondary prevention of HPV in STI settings are recommended, because of the burden of anal and penile cancer documented in the island. [P R Health Sci J 2015;34:128-134]

Key words: Human Papillomavirus (HPV), Men, STD Clinics, Hispanics, Puerto Rico

Human papillomavirus (HPV) is one of the most common sexually transmitted infections (STIs) and is generally asymptomatic (1). More than 100 genotypes have been identified, at least 15 of which are oncogenic, or high risk $(2,3)$. Because most HPV infections are asymptomatic or subclinical, (4) and sexually active males in particular are not routinely screened for HPV, members of this group may act as reservoirs of HPV infections and may transmit HPV to their sexual partners (5).

The prevalence of HPV infection in males varies widely, ranging from $1.3 \%$ to $77.6 \%$, worldwide (4). Although differences in sampling techniques account for much of this variability, higher penile HPV prevalence (any HPV types) has generally been observed in STI clinic populations, including $13.0 \%$ in Stockholm (Sweden) (6), 13.8\% in Hangzhou (China)
(7), $28.2 \%$ in Arizona (US) (8), $30.5 \%$ in Uppsala (Sweden) (9), $45 \%$ in Copenhagen (Denmark) (10), $72.9 \%$ in Dordrecht

[^0](the Netherlands) (11), and $77.6 \%$ in Johannesburg (South Africa) (12). Although a high burden of HPV infection has been documented, there are only a small number of studies in STI-clinic settings that describe the epidemiology by HPV type $(8,11)$. Understanding the prevalence and distribution of HPV types in this high-risk population is important to resource decision-making as well as to prevention and treatment planning. This is particularly true in relation to HPV education and vaccination decision-making.

Since 2006, when vaccines against HPV were first licensed in the United States (US), a large proportion of HPV-related diseases, including most cases of genital warts and many types of anal cancer, $(13,14)$ have become preventable. Thus, the reduction of HPV through prophylactic vaccination may reduce a substantive level of disease burden, particularly among key groups, such as men who have sex with men (MSM), HIVpositive men and men who go to STI clinics (15).

In October 2011, the Advisory Committee on Immunization Practices (ACIP) recommended the routine use of a quadrivalent HPV vaccine in men up to 21 years of age (up to 26 years if they are immunosuppressed) (16). However, uptake among individuals within the recommended age range has been low in the US (17). Also, a communication from the Vaccination Program of the PR Department of Health indicates that rates of HPV vaccination are low in the island as well. Despite the likelihood that HPV vaccination is most effective when administered before an individual's sexual debut, routine vaccination in STI clinics and other settings where high-risk populations are seen may also contribute to disease prevention among this group $(15,18)$. The current HPV vaccine that is available for males is only effective at preventing initial infections with the HPV types included in the vaccine (HPV types 6, 11, 16, and 18). Therefore, understanding the prevalence of these and other types of HPV, as well as the risk factors for prevalent HPV infections, is important for this population. For these reasons, and given the lack of data for PR, we studied the prevalence and behavioral risk factors of penile HPV infection (of any type, high-risk [HR] types, low risk [LR] types, and of multiple types) in sexually active males who were 16 years old or over who went to a specific STI clinic in San Juan, PR.

## Materials and Methods

This was a sub-study conducted from 2009 to 2011 as part of an ongoing epidemiological investigation of patients attending a public STI/HIV screening and treatment center in San Juan, PR. The UPR-Medical Sciences Campus Institutional Review Board (IRB) previously approved this study. The design and methods of the parent epidemiological study have been described elsewhere (19). Briefly, male and female patients aged 16 years old or older were selected from the clinic waiting room and screened for eligibility (including age and capacity for consent). Participants provided written informed consent for the study
procedures and the extraction of selected clinical data from their medical charts (including current STI and HIV status).

## Genital specimen collection

For the sub-study, genital samples were collected from the male participants, as has been previously described in the literature (19). A sterilized strip of emery paper ( 2 by 4 cm ; 600A-grit Wetordry Tri-M-ite; 3M) was used with steady pressure to repeatedly abrade the entire surface of the penis. Next, a sterile Dacron swab moistened with sterile saline was used to swab the entire area. Both the emery paper and swab tip were then immersed in Sample Transport Medium (STM, QIAGEN Inc., Valencia, CA). After collection, specimens were frozen at the clinical facilities of the Puerto Rico Clinical and Translational Research Consortium (PRCTRC), where they were then stored at $-70^{\circ} \mathrm{C}$ and shipped on dry ice to the University of California, San Francisco (UCSF), for HPV typing.

## DNA extraction/HPV detection and typing

DNA was prepared from each STM sample and frozen until the specimens were batched for analysis. DNA preparation took place after the samples were thawed, they were heated at $56^{\circ} \mathrm{C}$ for 1 hour. After cooling, $25 \mu \mathrm{l}$ of $10 \mathrm{mg} / \mathrm{ml}$ proteinase K ( PK ; Invitrogen, 250 $\mu \mathrm{g} / \mathrm{ml}$ final concentration) was added. The samples were vortexed and digested overnight at $50^{\circ} \mathrm{C}$ in a waterbath and heated at $95^{\circ} \mathrm{C}$ for 10 minutes to inactivate the PK. After DNA purification, PCR was performed using a modified pool of MY09/MY11 consensus HPV L1 primers as well as primers for the amplification of the human beta-globin gene. Five microliters of sample was used for PCR amplification, using a 40-cycle protocol. After PCR, 6 $\mu \mathrm{L}$ of amplification mixture was applied to a nylon membrane and probed with a biotin-labeled HPV consensus probe mixture containing HPV $11,16,18$, and 51 L1 DNA. A separate membrane was probed with a biotin-labeled probe for the human beta-globin gene. Each specimen was also studied for the presence of specific HPV types by preparing membranes (as described above) with $6 \mu \mathrm{~L}$ of specimen. The biological specimen was considered HPV positive (any HPV) when it tested positive with the consensus probes or with 1 or more probes for specific HPV types. Specimens negative for beta-globin gene amplification were excluded from the analysis. Negative controls for each experiment consisted of the amplification of the solution containing all of the above components except for sample DNA. Positive controls included the amplification of cloned HPV DNA. The specific HPV genotypes sought included HR-HPV types (16, 18, 31, 33, 35, $39,45,51,52,53,56,58,66,68,70,73$, and 82), LR types ( $6 / 11$, $32 / 42,54,61,62,71,81,83,84+$, and $86 / 87)$ and types that are of unknown risk ( $30,34+, 57 / 2 / 27,90 / 106$, and $102 / 108$, as well as 2 separate mixtures: mix1, containing 7/13/40/43/44/55/74/91, and mix 2 , containing $3 / 10 / 28 / 29 / 77 / 78 / 94)(20)$.

## Variables of interest

After providing their informed consents, eligible males participated in a behavioral interview that collected demographic
factors (age, education, income, employment, marital status, and type of health insurance, if any); lifestyle factors such as alcohol and substance use in the last 90 days, information about sexual partnering (e.g., MSM vs. non-MSM), the individual's age of sexual initiation and lifetime number of sexual partners (female and male), and current sexual practices; and clinical factors such as circumcision status, history of health-service utilization, and self-reported STIs (HIV, syphilis, gonorrhea, chlamydia, genital warts, and herpes). HR HPV type was defined if the study participant was positive for one or more HR genotypes, whether or not it was also positive for one or more LR HPV genotypes. On the other hand, LR HPV type was defined if it was positive only for LR HPV genotypes. Finally, a combination of more than two HR or LR types was defined as having multiple types. Information on recent condom use was derived from a set of questions about practices at the last sexual event. If no condom was used in the participant's last sexual encounter and/or the participant ejaculated inside the vagina without a condom, that sexual event was coded as "no condom use." Alternately, if the participant reported condom use during his last sexual intercourse and/or he ejaculated with the condom inside the vagina, the event was coded as affirmative for "condom use."

## Statistical analysis

Frequency distributions and descriptive statistics were used to characterize the study samples. Prevalence estimates and $95 \%$ confidence intervals (CI) for any HPV risk types, HR, LR types, and for multiple risk types were calculated. Descriptive statistics were used to describe the prevalence of different genotypes in this sample. A p-value for trend was used to evaluate trends in HPV prevalence by age group as well as by lifetime number of female sexual partners. Chi-square analysis or Fisher's exact test was used to evaluate differences in categorical outcome measures. Factors significantly associated with HPV ( p -value<0.05) in the bivariate analysis were included in independent simple and ageadjusted multivariate logistic regression models to identify risk factors associated with penile HPV infection (any HPV, HR, LR, and multiple HPV types). First-order interactions between the significant factors of the age-adjusted model were also evaluated in the logistic regression analysis.

Statistical analyses were performed using the statistical package SPSS (Version 17.0, Chicago, IL), while $95 \%$ confidence intervals (CI) for prevalence estimations were performed using the binomial CI calculator from Stata Statistical Software (Release 11, College Station, TX).

## Results

## Participant characteristics

The demographic characteristics of the total sample ( $\mathrm{n}=206$ ) are shown in Table 1. The mean age was 37.8 years ( $\mathrm{SD}=13.1$ ). Less than a third (28\%) were visiting the STI clinic for the first time at the time of the interview. The principal reason given by the study participants for going to the clinic was to undergo
screening for an STI other than HIV (61.3\%); roughly a third had gone to the clinic for an HIV test (32.7\%) (data not shown). More than half of the participants (53.8\%) had a high school or lower education, and $61.3 \%$ were employed at the time of the interview. Approximately 20\% of the sample reported having no medical insurance. The prevalence of recent (last 90 days) tobacco and alcohol consumption was high, with more than half of the participants admitting to such use ( $55 \%$ and $62 \%$ for tobacco and alcohol, respectively). More than a third (36.7\%) of the participants reported having used drugs in the 90 days prior to the survey. Of these, the most commonly used drugs were marijuana ( $21.6 \%$ ) and cocaine ( $7.0 \%$ ). A third of the participants self-reported being circumcised (33.7\%) (data not shown).

## Sexual behaviors and other factors affecting HPV prevalence

Thirty percent of the participants had had more than 15 female sexual partners in their lifetimes, and $21.1 \%$ reported condom use at the last sexual event. Regarding sexual identity, $29.8 \%$ self-identified as MSM.

## Self-reported STIs

The prevalence of HIV in this sample was $42.2 \%$ ( $95 \%$ CI: $35.3 \%-49.4 \%$ ), and the self-reported lifetime prevalence of anogenital warts was $22.6 \%$ ( $95 \%$ CI: $17.0 \%-29.1 \%$ ). Other

Table 1. Sociodemographic characteristics of a sample of Hispanic males who went to an STI clinic in San Juan, Puerto Rico

| Variable | N | $\bar{x}$ |
| :---: | :---: | :---: |
| Sociodemographic characteristics |  |  |
| Age | 206 | 37.8 |
|  | N | \% |
| Education Level* |  |  |
| <High School | 35 | 17.6\% |
| High School | 72 | 36.2\% |
| >High School | 92 | 46.2\% |
| Employed |  |  |
| Yes | 122 | 61.3\% |
| Annual Income* |  |  |
| None | 56 | 28.1\% |
| <\$15,000 | 102 | 51.3\% |
| $\geq$ \$15,000 | 41 | 20.6\% |
| Marital Status** |  |  |
| Single, never married | 116 | 58.3\% |
| Married or cohabitating | 52 | 26.1\% |
| Separated or divorced | 30 | 15.1\% |
| Type of Health Insurance*** |  |  |
| None | 36 | 18.8\% |
| Public | 118 | 61.5\% |
| Private | 38 | 19.8\% |
| Substance Used (last 90 days) |  |  |
| Tobacco | 88 | 55\% |
| Alcohol | 99 | 62\% |
| Illicit Drug Use |  |  |
| Marihuana | 43 | 21.6\% |
| Cocaine | 14 | 7.0\% |

[^1]self-reported STIs in this study were syphilis (16.1\%; 95\% CI: $11.3 \%-21.9 \%$ ), followed by gonorrhea ( $15.6 \%$; $95 \%$ CI: $10.8 \%-21.4 \%$ ), herpes ( $14.6 \%$; $95 \%$ CI: $10.0 \%-20.3 \%$ ), and chlamydia (10.6\%; 95\% CI: 6.7\%-15.7\%).

## Penile HPV prevalence

Samples were obtained from 205 participants, and beta-globin was detected in 204 ( $99.5 \%$ ) of the specimens. Table 2 shows the prevalence of penile HPV infection among the participants with suitable samples ( $\mathrm{n}=204$ ). Overall, $79.5 \%$ ( $95 \%$ CI: 73.3-84.8) of the study participants tested positive for any type of HPV. The prevalence of HR penile HPV was $32.4 \%$ (95\% CI: 24.1-41.7). The most prevalent HR subtypes were 35 (27.9\%), 31 (16.3\%), and 16 (13.9\%). LR HPV types were found in $73.5 \%$ ( $95 \%$ CI: 64.5-81.2) of the participants, and multiple types were found in $46.0 \%$ ( $95 \%$ CI: $0.37-0.56$ ) of the sample. The most prevalent LR subtypes were 6/11 (33.3\%), 84 (24.2\%), and 61 (6.7\%). Of the HPV-infected individuals, $42.4 \%$ were positive for $6 / 11$, 16, and 18 HPV types combined (Table 2).

## Any HPV type infection

Regarding the correlates of any HPV infection, the prevalence of any HPV type decreased as age increased. However, this trend was only marginally significant ( $p$-value for trend $=0.07$ ) (Table 3). The prevalence of any type of HPV infection was significantly lower (estimated OR $=0.44$ [ $95 \%$ CI: $0.20-0.93$ ]) for 45 to 54 -year-old men than it was for 18 - to 24 -year-old men (data not shown). Participants who, at the time of the interview, reported being separated or divorced had a $56.0 \%$ lower odds of having an type HPV infection than did those who reported being single (estimated OR $=0.44$ [95\% CI: 0.19-1.02]) (Table 3). In simple logistic regression models, participants who had consumed alcohol in the last 90 days were twice as likely to be positive for any HPV type infection [estimated OR=2.05; ( $95 \%$ CI: 1.02-4.14)] than were those who had not consumed alcohol in the last 90 days (Table 3). However, after adjusting for age, neither of the predictors (marital status separated/divorced [estimated age-adjusted OR $=0.54$ ( $95 \% \mathrm{CI}: 0.22-1.34]$ ) and alcohol consumption in last 90 days (estimated age-adjusted OR $=1.75$ [ $95 \%$ CI: 0.85-3.63]) achieved statistical significance. No significant first-order interactions were observed between the predictors (marital status, alcohol consumption in the last 90 days) and age ( p -value $>0.10$ ).

## HR HPV infection

The prevalence of HR HPV infection was 22\% higher among individuals who reported having used a condom in their last sexual encounter (estimated OR $=1.22$ [ $95 \% \mathrm{CI}: 0.41-3.66]$ ) than it was among the participants who reported no such use; however, the prevalence did not achieve statistical significance in simple logistic regression analysis (Table 3). In age-adjusted models, an association was observed between employment and HR-HPV, in which those who reported being employed at the time of the interview were $56 \%$ less likely to have an HR HPV infection than

Table 2. Prevalence of penile HPV types

| HPV type | Penile $(\mathbf{n}=\mathbf{2 0 5 )}$ |
| :--- | :--- |
|  |  |
| Any HPV (95\% Cl) |  |

*HR HPV type 73 was tested, but it was not found in this sample; **Among those who could be typed ( $\mathrm{n}=113$ ); +Those that have two or more HPV types; $\ddagger$ Those who had HPV detected using the consensus probe mixture but were negative for all specific HPV genotype probes.
were those who were unemployed (estimated age-adjusted OR= 0.44 [ $95 \%$ CI: 0.20-0.97]). No significant first-order interactions between employment and age were observed ( $p$-value $>0.10$ ).

## Multiple HPV infection

The prevalence of multiple HPV infection was higher among those men who reported having had 15 or more female sexual partners (estimated OR $=2.71$ [95\% CI: 1.35-5.44]) (Table 3) than it was among those not reporting same. This association remained significant after adjusting for age (adjusted OR $=2.86$ [ $95 \%$ CI: 1.41-5.80]). No significant first-order interactions between lifetime number of female sexual partners and age were observed ( p -value $>0.10$ ).

## LR HPV infection

No factors were significantly associated with LR HPV types in this sample (all p-value >0.10).

## Discussion

To our knowledge, this is the first epidemiological study that reports the distribution and correlates of penile HPV infection

Table 3. Magnitude of the associations between sociodemographics, lifestyle, clinical factors and penile HPV infection

| Variable | Any HPV type |  | Low-risk types |  | High-risk types |  | Multiple types |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Prevalence (\%) | OR ${ }^{\dagger}$ (95\% CI) | Prevalence (\%) | OR ${ }^{+}$ (95\% CI) | Prevalence (\%) | OR ${ }^{\dagger}$ (95\% CI) | Prevalence (\%) | OR ${ }^{+}$ (95\% CI) |
| Sociodemographic characteristics |  |  |  |  |  |  |  |  |
| Employed |  |  |  |  |  |  |  |  |
| No | 61 (80.3) | 1.00 | 30 (35.3) | 1.00 | 16 (43.2) | 1.00 | 22 (36.1) | 1.00 |
| Yes | 97 (79.5) | 0.95 (0.47-1.95) | 55 (64.7) | 1.49 (0.63-3.51) | 21(56.8) | 0.70 (0.31-1.58) | 30 (30.9) | 0.79 (0.40-1.56) |
| Marital Status |  |  |  |  |  |  |  |  |
| Single, never married | 97 (84.3) | 1.00 | 50 (59.5) | 1.00 | 23 (62.2) | 1.00 | 31 (32.0) | 1.00 |
| Married/cohabitating | 40 (76.9) | 0.79 (0.37-1.70) | 24 (28.6) | 1.24 (0.47-3.27) | 11 (29.7) | 1.20 (0.50-2.87) | 14 (35.0) | 1.13 (0.53-2.41) |
| Separated or divorced | 20 (66.7) | 0.44 (0.19-1.02) | 10 (11.9) | 1.15 (0.29-4.52) | 3 (8.1) | 0.59 (0.15-2.29) | 7 (35.0) | 1.11 (0.42-2.98) |
| Risk Factors |  |  |  |  |  |  |  |  |
| Substance Use (last 90 days) |  |  |  |  |  |  |  |  |
| Used Tobacco |  |  |  |  |  |  |  |  |
| No | 70 (75.3) | 1.00 | 37 (43.5) | 1.00 | 14 (37.8) | 1.00 | 23 (32.9) | 1.00 |
| Yes | 88 (83.8) | 1.70 (0.84-3.43) | 48 (56.5) | 1.39 (0.59-3.23) | 23 (62.2) | 1.60 (0.72-3.56) | 29 (33.0) | 1.00 (0.52-1.96) |
| Used Alcohol |  |  |  |  |  |  |  |  |
| No | 59 (72.8) | 1.00 | 35 (41.2) | 1.00 | 17 (45.9) | 1.00 | 22 (37.3) | 1.00 |
| Yes | 99 (84.6) | 2.05 (1.02-4.14) $\ddagger$ | 50 (58.8) | 1.01 (0.42-2.37) | 20 (54.1) | 0.75 (0.34-1.65) | 30 (30.3) | 0.73 (0.37-1.44) |
| Used Condom (last sexual event) |  |  |  |  |  |  |  |  |
| No | 35 (83.3) | 1.00 | 23(53.5) | 1.00 | 9 (47.4) | 1.00 | 16 (45.7) | 1.00 |
| Yes | 46 (80.7) | 0.84 (0.29-2.38) | 20 (46.5) | 0.68 (0.21-2.14) | 10 (52.6) | 1.22 (0.41-3.66) | 15 (32.6) | 0.58 (0.23-1.42) |
| Lifetime Female |  |  |  |  |  |  |  |  |
| Sexual Partners |  |  |  |  |  |  |  |  |
| <5 partners | 48 (72.7) | 1.00 | 30 (37.0) | 1.00 | 16 (45.7) | 1.00 | 12 (25.0) | 1.00 |
| 5-14 partners | 51 (79.7) | 0.99 (0.47-2.08) | 26 (32.1) | 0.72 (0.29-1.74) | 9 (25.7) | 0.56 (0.23-1.36) | 12 (23.5) | 0.52 (0.24-1.10) |
| $\geq 15$ partners | 52 (86.7) | 1.96 (0.85-4.56) | 25 (30.9) | 0.92 (0.37-2.31) | 10 (28.6) | 0.81 (0.34-1.95) | 25 (48.1) | 2.71 (1.35-5.44) $\ddagger$ |
| P -value for trend | 0.054 |  | 0.546 |  | 0.199 |  | 0.013 |  |
| Lifetime Anal-Sex |  |  |  |  |  |  |  |  |
| Partners (Insertive |  |  |  |  |  |  |  |  |
| \& Receptive) |  |  |  |  |  |  |  |  |
| $\leq 1$ partner | 6 (85.7) | 1.00 | 4(13.8) | 1.00 | 1 (7.7) | 1.00 | 3 (50.0) | 1.00 |
| 2-9 partners | 14 (73.7) | 0.68 (0.23-2.02) | 7 (24.1) | 1.03 (0.33-3.13) | 1 (7.7) | 0.87 (0.30-2.48) | 5 (35.7) | 1.15 (0.36-3.61) |
| $\geq 10$ partners | 25 (71.4) | 0.56 (0.25-1.30) | 18 (62.1) | 1.02 (0.10-10.25) | 11 (84.6) | 0.68 (0.07-6.82) | 4 (16.0) | 0.34 (0.11-1.04) |
| P -value for trend | 0.489 |  | 0.428 |  | 0.082 |  | 0.058 |  |
| Circumcised |  |  |  |  |  |  |  |  |
| No | 104 (78.8) | 1.00 | 59 (69.4) | 1.00 | 28 (75.7) | 1.00 | 36 (34.6) | 1.00 |
| Yes | 54 (81.8) | 1.21 (0.57-2.57) | 26 (30.6) | 0.62 (0.26-1.49) | 9 (24.3) | 0.53 (0.22-1.28) | 16 (29.6) | 0.80 (0.39-1.62) |
| Sexual Identity |  |  |  |  |  |  |  |  |
| MSW | 115 (82.7) | 1.00 | 57 (67.9) | 1.00 | 24 (64.9) | 1.00 | 41 (35.7) | 1.00 |
| MSM | 42 (72.4) | 0.55 (0.27-1.13) | 27 (32.1) | 1.49 (0.57-3.91) | 13 (35.1) | 1.41 (0.61-3.29) | 10 (23.8) | 0.56 (0.25-1.26) |
| Self-reported STIs HIV |  |  |  |  |  |  |  |  |
| No | 94 (82.5) | 1.00 | 50 (58.8) | 1.00 | 16 (43.2) | 1.00 | 30 (31.9) | 1.00 |
| Yes | 64 (76.2) | 0.98 (0.42-2.28) | 35 (41.2) | 0.65 (0.28-1.52) | 21 (56.8) | 2.17 (0.98-4.82) | 22 (34.4) | 1.12 (0.57-2.19) |
| Syphilis |  |  |  |  |  |  |  |  |
| No | 133 (80.6) | 1.00 | 70 (83.3) | 1.00 | 32 (86.5) | 1.00 | 45 (33.8) | 1.00 |
| Yes | 25 (78.1) | 0.86 (0.34-2.16) | 14 (16.7) | 1.25 (0.38-4.16) | 5 (13.5) | 0.75 (0.24-2.31) | 7 (28.0) | 0.76 (0.30-1.96) |
| Health Services |  |  |  |  |  |  |  |  |
| New Patient at the STI Clinic |  |  |  |  |  |  |  |  |
| No | 113 (79.0) | 1.00 | 61 (71.8) | 1.00 | 31 (83.8) | 1.00 | 37 (32.7) | 1.00 |
| Yes | 45 (81.8) | 1.20 (0.54-2.65) | 24(28.2) | 1.23 (0.46-3.27) | 6 (16.2) | 0.40 (0.15-1.09) | 15 (33.3) | 1.03 (0.49-2.14) |

testimated OR with $95 \% \mathrm{Cl}$; $\ddagger$ statistically significant $p$-value<0.05; MSW = Men who have sex with women; MSM = Men who have sex with men
in Puerto Rican males. As expected, given that the setting of this study was in an STI clinic, any types of HPV infection were common (79.5\%), which is very similar to what was reported by an STI clinic in South Africa (78\%) (12), but which is higher than what was reported by studies performed at STI clinics in Greenland, Denmark (10), the US (8), Sweden (9), and the Netherlands (11). Similar prevalence estimates of any penile HPV infection might have been found because of the high prevalence of HIV infection both in the members of our study (42.2\%) and in those of the South African study (49.5\%).

In our study sample, HPV types not currently in the quadrivalent HPV vaccine were identified. HR HPV type 35 was the most prevalent followed by HPV type 31 and 16. Despite the high prevalence of any HPV infection in this sample, $42.4 \%$ of the infected participants were positive for either HPV 6/11, 16, or 18 , which are the types that are targeted by the quadrivalent HPV vaccine.

Given that our study was composed of a population in which high-risk sexual practices are prevalent, the capacity of the study to detect significant associations between well-known risk factors might have been affected. For example, although a higher prevalence of any type HPV was observed in HIV-positive males taking part in this study, this association was not significant ( p -value 0.971 ), which might be because of the high prevalence of HPV infection in the HIV-negative group. Another factor that has been shown, which confers a protective effect against HPV infection, is circumcision $(21,22)$. In this study, although lower odds of penile HPV were observed in men who reported being circumcised, this association was not significant in the bivariate analysis. On the other hand, the only factor significantly associated with multiple-risk HPV infection was having 15 or more lifetime female sexual partners. This latter indicator is a consistent risk factor associated with detecting HPV and has been found to be so by other studies (4).

Our findings need to be interpreted with caution. Since this study was done in an STI setting, our findings are not be generalizable to the general male population of Puerto Rico. In addition, since not enough variability regarding sexual practices was observed, the lack of identification of well-known predictors of HPV infection (such as HIV infection) was not observed in this sample.

## Conclusion

In summary, this study has allowed us to confirm that penile HPV infection in a sample of sexually active males, 16 years old or older frequenting a specific STI clinic in PR , is common. HPV types not currently covered by the HPV vaccines were found in some of the study participants. Because of the low vaccination rates indicated by the Vaccination Program from the PR Department of Health among males 16 years old or older in PR, future studies need to target this population for primary prevention. However, since penile cancer disparities have been observed in males in PR, where higher incidence and mortality
rates of this type of cancer have been reported in this population compared to what has been seen in other racial/ethnic groups in the US $(23,24)$ and with the burden of anal cancer documented on the island (25,26), increasing the opportunities for secondary prevention in STI settings are recommended.

## Resumen

Objetivo: El objetivo de este estudio es describir la prevalencia, distribución genotípica del virus del Papiloma Humano (VPH) en el área genital y los factores de riesgo que están asociados con cualquier tipo, tipos de alto riesgo (AR), bajo riesgo ( BR ), y múltiples infecciones de VPH, en los hombres que asisten a una clínica de Infección de Transmisión Sexual (ITS). Métodos: Después de proveer consentimiento para participar en el estudio, los participantes llevaron a cabo una entrevista y un examen clínico, que incluyó la toma de muestras del área del pene. Distribuciones de frecuencia y estadísticas descriptivas fueron utilizadas para caracterizar la muestra del estudio. Se estimó la prevalencia e intervalos de confianza (IC) al 95\% para cualquier tipo de VPH, AR, BR, y para múltiples tipos. Se realizaron análisis de regresión logística para determinar los factores asociados con los tipos de VPH. Resultados: Doscientos seis participantes fueron reclutados en el estudio. El promedio de edad fue $37.8 \pm 13.1$ años. Cerca de un $80 \%$ de los hombres (79.5\%) estaba infectado con algún tipo de VPH, el 73.5\% estaba infectado con tipos de VPH BR, $32.4 \%$ con VPH AR y $46.0 \%$ con múltiples tipos de VPH. Los tipos más prevalentes de AR fueron VPH-35, -31 y -16 , mientras que los tipos de BR más prevalentes fueron HPV-6/-11 y -84. Luego de ajustar por edad, el tener un mayor número de parejas sexuales femeninas se asoció significativamente con la infección de múltiples tipos de VPH (estimador del OR=2.86; IC $95 \%=1.41,5.80$ ). Conclusión: La infección de VPH es común entre los hombres sexualmente activos que asisten a la clínica de ITS. Se identificaron tipos de VPH no incluidos en la vacuna actual. La detección de múltiples tipos de VPH en este estudio se relaciona significativamente con el número de parejas sexuales femeninas. Dado a la alta prevalencia de VPH en la clínica de ITS, futuros esfuerzos para la promoción de la vacuna deben dirigirse a los hombres jóvenes que asisten a los centros de atención primaria. Por otro lado, se recomienda incluir oportunidades para la prevención secundaria de VPH en las clínicas de ITS dado a la carga que posee en el cáncer de pene y ano documentado en la isla.

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## References

1. Vardas E, Giuliano AR, Goldstone S, et al. External genital human papillomavirus prevalence and associated factors among heterosexual men on 5 continents. J Infect Dis 2011;203:58-65.
2. Giuliano AR, Tortolero-Luna G, Ferrer E, et al. Epidemiology of human papillomavirus infection in men, cancers other than cervical and benign conditions. Vaccine 2008;26(suppl 10):K17-K28.
3. Grahovac B, Dorić A, HruškarŽ, HadžisejdićI, Grahovac M. Human Papillomavirus Infection in Croatian Men: Prevalence and HPV Type Distribution. Available at: http://cdn.intechopen.com/pdfs/33069/ InTech-Human_papillomavirus_infection_in_croatian_men_prevalence_and_hpv_type_distribution.pdf.Accessed October 10, 2013.
4. Dunne EF, Nielson CM, Stone KM, Markowitz LE, Giuliano AR. Prevalence of HPV infection among men: A systematic review of the literature. J Infect Dis 2006;194:1044-1057.
5. Castellsagué X, Bosch FX, Muñoz N. The male role in cervical cancer. Salud Publica Mex 2003;45(suppl 3):S345-S353.
6. Wikström A, Popescu C, Forslund O. Asymptomatic penile HPV infection: a prospective study. Int J STD AIDS 2000;11:80-84.
7. Tang X, Xu AE, Dong XP, Sun XK, Shen H, Liu JF. Epidemiological investigation of human papillomavirus infection in men attending a sexually transmitted disease clinic in Hangzhou area. Biomed Environ Sci 2006;19:153-157.
8. Baldwin SB, Wallace DR, Papenfuss MR, et al. Human papillomavirus infection in men attending a sexually transmitted disease clinic. J Infect Dis 2003;187:1064-1070.
9. Strand A, Rylander E, Evander M, Wadell G. Genital human papillomavirus infection among patients attending an STD clinic. Genitourin Med 1993;69:446-449.
10. Svare EI, Kjaer SK, Worm AM, Osterlind A, Meijer CJ, van den Brule AJ. Risk factors for genital HPV DNA in men resemble those found in women: a study of male attendees at a Danish STD clinic. Sex Transm Infect 2002;78:215-218.
11. Bleeker MC, Hogewoning CJ, Berkhof J, et al. Concordance of specific human papillomavirus types in sex partners is more prevalent than would be expected by chance and is associated with increased viral loads. Clin Infect Dis 2005;41:612-620.
12. Müller EE, Chirwa TF, Lewis DA. Human papillomavirus (HPV) infection in heterosexual South African men attending sexual health services: associations between HPV and HIV serostatus. Sex Transm Infect 2010;86:175-180.
13. Markowitz LE, Dunne EF, Saraiya M, Lawson HW, Chesson H, Unger ER; Centers for Disease Control and Prevention (CDC); Advisory Committee on Immunization Practices (ACIP). Quadrivalent human papillomavirus vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2007;56:1-24.
14. Kane MA. Preventing cancer with vaccines: progress in the global control of cancer. Cancer Prev Res (Phila) 2012;5:24-29.
15. Meites E, Llata E, Hariri S, et al. HPV vaccine implementation in STD clinics-STD Surveillance Network. Sex Transm Dis 2012; 39:32-34.
16. Centers for Disease Control and Prevention (CDC). Recommendations on the use of quadrivalent human papillomavirus vaccine in males--Advisory Committee on Immunization Practices (ACIP), 2011. MMWR 2011;60:1705-1708.
17. Stupiansky NW, Alexander AB, Zimet GD. Human papillomavirus vaccine and men: what are the obstacles and challenges. Curr Opin Infect Dis 2012;25:86-91.
18. Clatts MC, Rodríguez-Díaz CE, García H, et al. Sexually transmitted infections clinics as strategic venues for targeting high-risk populations for HIV research and sexual health interventions. P R Health Sci J 2011;30:101-108.
19. Weaver BA, Feng Q, Holmes KK, et al. Evaluation of genital sites and sampling techniques for detection of human papillomavirus DNA in men. J Infect Dis 2004;189:677-685.
20. IARC (2012). Human papillomaviruses. IARC Monogr Eval Carcinog Risks Hum, Vol 100B. Available at: Url: http://monographs. iarc.fr/ENG/Monographs/vol100B/mono100B-11.pdf. Accessed October 15, 2013.
21. Wilson LE, Gravitt P, Tobian AA, et al. Male circumcision reduces penile high-risk human papillomavirus viral load in a randomised clinical trial in Rakai, Uganda. Sex Transm Infect 2013;89:262-266.
22. Albero G, Castellsagué X, Giuliano AR, Bosch FX. Male circumcision and genital human papillomavirus: a systematic review and meta-analysis. Sex Transm Dis 2012;39:104-113.
23. Colón-López V, Ortiz AP, Soto-Salgado M, et al. Penile cancer disparities in Puerto Rican men as compared to the United States population. Int Braz J Urol 2012;38:728-738.
24. Ortiz AP, Pérez-Irizarry J, Soto-Salgado M, et al. Human papillomavirusrelated cancers among people living with AIDS in Puerto Rico. Prev Chronic Dis 2014;11:E80.
25. Colon-Lopez V, Ortiz AP, Soto-Salgado M, et al. Survival from anal cancer among Hispanics-Puerto Rico, 2000-2007. J Gastrointest Cancer 2014;45:234-238.
26. Ortiz AP, Ortiz-Ortiz KJ, Traverso-Ortiz M, Ríos MY, Colón-López V, Palefsky JM. Anal cancer trends in Puerto Rico from 1985 to 2005: the potential impact of the AIDS epidemic. AIDS Patient Care STDS 2014;28:165-167.

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[^1]:    *missing values, $\mathrm{n}=7$; ** missing values, $\mathrm{n}=8$; *** missing values, $\mathrm{n}=14$

