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Genital and extra-genital warts increase the risk of asymptomatic genital human papillomavirus infection in men

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Abstract

Objectives—To evaluate the relationship of warts in different parts of the body and the risk of asymptomatic genital human papillomavirus (HPV) infection in men.

Methods—We examined the relationship of self-reported genital and extra-genital warts with the subsequent acquisition of asymptomatic genital HPV infection in a cohort of 331 adult men. Participants were followed at 2-month intervals for up to 4 years. Past and current presence of warts was queried at study entry. At each visit, the external genitals were sampled for HPV DNA testing.

Results—Men who reported a history of genital warts, including current warts, were at increased risk of acquisition of asymptomatic HPV infection of the penis glans/corona, penis shaft and scrotum. The magnitude of these associations was greatest for HPV 6/11 infection. History of warts on the fingers, arms and trunk of the body was also associated with increased risk of genital HPV infection. Current presence of warts on the fingers and trunk specifically increased the risk of acquisition of HPV types not typically found on the genitals.

Conclusions—Men with a history of warts on the genitals, fingers, arms and trunk may be at increased risk for acquisition of new genital HPV infections. Warts may provide an efficient reservoir for the transmission of virions to the genitals through auto-inoculation. The potential for the spread of HPV throughout the body through auto-inoculation has important implications for prevention and control of HPV infection.

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Ethics approval This study was conducted with the approval of the Committee on Human Studies of the University of Hawaii.

Contributors BYH: oversight of study, including planning, conduct, laboratory analysis, data analysis and interpretation; She was the primary author of the original and revised manuscripts. YBS: lead statistical analyses, data interpretation and assistance with manuscript revision. MTG: data interpretation. LRW: statistical analysis. PJT: data management. XZ: laboratory testing. JT: clinical examination and specimen collection. LN: study site coordination, clinical examination and specimen collection.

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INTRODUCTION

Warts are diverse manifestations of human papillomavirus (HPV) infection and may occur at mucosal and cutaneous tissue sites throughout the body. Genital warts, or condylomas, affect the genitals, anus and perianum, and are primarily caused by HPV 6 and 11.[1] Common skin warts, typically found on the fingers, hands, knees and elbows, are caused by HPV 2, 4, 7, 26, 27, 28, 29 and 57.[23] Other skin warts and their associated HPV types include deep plantar warts (HPV 1, 4) primarily found on the bottom of the feet; filiform warts (HPV 1, 2, 7) occurring on the face, mouth, lips, eyelids and nose; flat or plane warts (HPV 2, 3, 10, 26, 27, 28, 29, 41) found throughout the body, including sun-exposed areas of the face, arms, hands and knees; and endophytic, or punctate, warts (HPV 60, 63, 65).[2–4] Warts in the oral cavity are attributed to HPV 1, 2, 4, 6, 7, 11 and 13.[2] Despite the ubiquitous nature of HPV infection, there is limited knowledge of the relationship of clinical and sub-clinical HPV infection occurring in different parts of the body. In a prior study of HPV transmission in heterosexual couples, we observed that auto-inoculation was common in men and included transmission of sub-clinical HPV infection between different genital sites as well as between genital and extra-genital sites of the body.[5] To further examine the dynamics of HPV auto-inoculation, we examined the relationship of self-reported wart history to the acquisition of asymptomatic genital HPV infection in a cohort of adult men.

METHODS

Study enrolment and follow-up

This study was approved by the Committee on Human Studies of the University of Hawaii. Participants were enrolled and followed between June 2004 and February 2008. Participants were recruited from a large university community and the general public. Recruitment was facilitated through print and electronic media. All study visits were conducted at the University of Hawaii Health Services and the Cancer Research Center of Hawaii located in Honolulu, Hawaii, USA. Written informed consent was obtained from all study subjects. Eligible men were at least 18-years-old, spoke English and had no history of blood-clotting disorders. The latter criterion was related to the collection of blood for serological evaluation, which is not included in the present analysis. Participants were followed at 2-month intervals for up to 4 years.

Data and specimen collection

Structured questionnaires were administered by trained interviewers at each study visit. The baseline questionnaire covered demographic information and medical, sexual and reproductive history. History of warts was queried: ‘Have you ever had warts on any of the following parts of your body?’ (yes/no) and ‘If yes, do you currently have warts here’ (yes/no). Wart sites were individually listed as follows: fingers, hands (including wrists), arms (including elbows), trunk (back, chest, abdomen), genitals, anus, legs (including knees), feet (including ankles), toes, head/face/or neck and mouth.

At each study visit, trained clinicians collected exfoliated cell samples from the external genitals using textured paper and saline-moistened swabs—a procedure that has been

previously described elsewhere.[67] Separate specimens were collected from each of the penis subsites (glans/coronal sulcus, shaft, inner foreskin) and scrotum for HPV DNA testing and genotyping. Disposable gloves worn by clinicians were changed between the sampling of each site to minimise the risk of contamination between sites. Visible warts and lesions were noted but avoided in sampling the genitals.

HPV testing and genotyping

DNA was extracted from specimens using commercial reagents (Qiagen Inc., Valencia, CA, USA). The PCR used PGMY09/PGMY11 primers to amplify a 450-base pair region of the L1 HPV genome. HPV positive specimens were subsequently genotyped using a reverse line blot detection method for 37 HPV types (Roche Molecular Systems, Alameda, CA, USA). HPV positive specimens that were subsequently found to be negative by the genotyping assay were considered to be untyped HPV positive specimens. All specimens were also tested using GH20 and PC04 primers to amplify a 268 base pair region of the human β-globin gene as an internal control for sample sufficiency. Specimens testing negative for β-globin were considered to be insufficient and were excluded from the analyses.

Statistical analyses

HPV DNA results were evaluated by individual genital subsites—penis glans/coronal sulcus, penis shaft and scrotum. Foreskin specimens were excluded in the analyses as no comparable specimens were available from circumcised men. HPV status was grouped as follows: any HPV; oncogenic HPV (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68)[8]; and non-oncogenic HPV (HPV 6, 11, 26, 40, 42, 53–55, 61, 62, 64, 66, 67, 69–73, 81–84, IS39 (subtype HPV-82), and CP6109 (HPV-89)). HPV DNA-positive specimens that were not positive for any of the 37 types detected by the genotyping assay were classified as untyped HPV. HPV 6 and/or 11 and untyped HPV were also evaluated separately.

Incident HPV infections were defined as the presence of a HPV genotype not identified during a previous visit. The association between HPV acquisition and history of warts was modelled through Cox regression using the number of days of HPV-negative status as the time metric. HRs and 95% CIs were used as measures of association for the comparison of men with and without a history of warts for each wart site. Factors associated with past and/or present warts were included in the initial models of risk estimation. Factors changing the parameter estimates by more than 10% or resulting in a significantly better fit according to the likelihood ratio test were retained in the models. Covariates included in the final regression models were age (continuous), monthly household income (<$1500, $1500–$2999 and ≥$3000), lifetime number of female sex partners (continuous), frequency of sexual intercourse with female partner(s) per month (0, 1–9 and ≥10), history of sex with men (yes/no) and history of genital warts in a sexual partner (yes/no).

Separate infection paths were assigned to each HPV genotype detected. For infections with multiple genotype, every genotype was considered a separate infection. Because multiple type infections contributed more than once to the analyses, we used a robust sandwich variance estimate[9] aggregated over subjects to prevent artificially deflated SEs and CI estimates. Estimation of risk associated with oncogenic types included specimens

concurrently positive for other types. Likewise, risk estimation for non-oncogenic HPV included specimens concurrently positive for oncogenic types. All p values were 2-sided; differences were considered to be statistically significant at $p<0.05$ with Bonferroni correction for multiple comparisons.

RESULTS

A total of 445 men were initially enrolled into the study. Men who completed only the initial study visit were excluded from the present evaluation, which focused on the acquisition of new infections. In addition, as the present analysis was interested in the natural history of infection in healthy populations, we also excluded men who self-reported positivity for HIV, which has a strong confounding effect on HPV infection.[10] A total of 331 adult men were followed at 2-month intervals for an average of 418 days (range 38–1262).

Male cohort participants were predominantly young (mean 28 y), White (58%), born in the USA (81%), single/never married (83%) with at least some college education (97%). In total, 81% of men were circumcised and 82% were exclusively heterosexual (table 1). Over two-thirds of men reported a history of warts at one or more sites. The most commonly reported sites were the fingers (35%) followed by the hands (23%). Altogether, 9% of men reported a history of genital warts. A total of 20% of men reported currently having warts at one or more sites.

In order to provide some measure of the validity of self-report, wart history was compared among men with clinically documented genital warts at study entry. Of the 13 men who were found to have genital warts upon baseline clinical examination, 11 (85%) had reported ever having genital warts and 9 (69%) had reported currently having genital warts.

Men with and without a history of warts were compared for the identification of factors that may confound the association of wart history with risk of genital HPV. Compared to those with no history, men reporting ever having warts at any site were more likely to be circumcised (74.1% vs 85.5%, $p=0.01$), US-born (69.8% vs 87.4%, $p<0.0001$), have higher household income levels (≥$3000 US dollars/month; 12.2% vs 25.7%, $p=0.02$) and have a current or past female sex partner with genital warts (2.1% vs 10.3%, $p=0.01$). Compared to men without warts, men reporting currently having warts at any site were more likely to have a current or past female sex partner with genital warts (4.3% vs 18.0%, $p<0.001$) and more frequent sexual intercourse with their current female sex partner (≥10 times/week; 32.2% vs 47.2%, $p=0.05$). Men with and without a history of warts were comparable with respect to other demographic and sexual characteristics.

Baseline genital HPV status was compared by wart history. A total of 67% (147/220) of men with a history of warts had genital HPV infection at baseline compared to 52% (54/107) of men with no history. Among HPV-positive men with a wart history, a total of 31 different HPV genotypes were detected; 39% (58/147) of genital infections were of a single HPV type and 61% (89/147) were either infections with multiple types or untyped HPVs. By comparison, of HPV-positive men with no wart history, a total of 29 different HPV genotypes were observed and the majority of infections (59%, 32/54) were of a single type.

A history of genital warts increased the risk of asymptomatic genital HPV infection (any, oncogenic, non-oncogenic HPV, HPV 6 or 11) (table 2). These relationships were generally consistent for the penis glans/corona, penis shaft and scrotum. Across genital sites, the magnitude of the association was greatest for HPV 6/11 infection. Specifically, genital wart history increased the risk of genital HPV 6 and/or 11 infection of the glans/corona (adjusted HR 12.86, 95% CI 4.54 to 36.46), penis shaft (adjusted HR 8.33, 95% CI 2.44 to 28.40) and scrotum (adjusted HR 6.09, 95% CI 2.22 to 16.71). Current presence of warts also increased the risk of HPV 6 and/or 11 infection of the glans/corona (adjusted HR 10.18, 95% CI 3.09 to 33.51), shaft (adjusted HR 4.72, 95% CI 1.18 to 18.92) and scrotum (adjusted HR 4.62, 95% CI 1.40 to 15.27).

History of warts on the fingers was associated with increased risk of penile HPV infection (any, oncogenic, non-oncogenic): glans/corona (adjusted HR 1.49, 95% CI 1.16 to 1.91) and shaft (adjusted HR 1.31, 95% CI 1.06 to 1.61) for any HPV. Current presence of finger warts also increased the risk of any genital HPV infection: glans/corona (adjusted HR 1.86, 95% CI 1.32 to 2.61), shaft (adjusted HR 1.43, 95% CI 1.04 to 1.96) and scrotum (adjusted HR 1.45, 95% CI 1.02 to 2.05). Current presence of finger warts also increased the risk of penile shaft infection with untyped HPVs (adjusted HR 2.42, 95% CI 1.22 to 4.83).

History of warts on the arms was associated with increased risk of genital HPV infection (any, non-oncogenic): glans/corona (adjusted HR 1.67, 95% CI 1.23 to 2.27), shaft (adjusted HR 1.38, 95% CI 1.04 to 1.83) and scrotum (adjusted HR 1.51, 95% CI 1.13 to 2.02) for any HPV. The magnitude of the association was greatest for current arm warts and was consistent across genital sites: glans/corona (adjusted HR 3.15, 95% CI 1.59 to 6.26), shaft (adjusted HR 3.18, 95% CI 1.72 to 5.88) and scrotum (adjusted HR 2.34, 95% CI 1.15 to 4.74) for non-oncogenic HPV. History of arm warts was specifically associated with increased risk of HPV 6/11 infection of the glans/corona (adjusted HR 3.74, 95% CI 1.26 to 11.12).

History of warts on the trunk of the body was associated with increased risk of penile infection with untyped HPVs: glans/corona (HR 5.41, 95% CI 1.54 to 18.98) and shaft (adjusted HR 5.74, 95% 1.73 to 19.10).

History of warts on the anus, head, face, neck, legs and feet was not associated with increased risk of genital HPV infection.

DISCUSSION

We examined the relationship of warts located at different sites of the body and subsequent acquisition of asymptomatic genital HPV infection. Warts were very common in our population of healthy men with over two-thirds reporting a history of warts and one in five men reporting the current presence of warts. Warts on the fingers and arms were most common. Altogether, 5% of men reported the current presence of genital warts. This is higher than the estimated 1% prevalence of genital warts among sexually active adolescents and adults in the USA.[11]

We observed that a history of genital warts was associated with increased risk of acquisition of asymptomatic genital HPV infection. This relationship was observed for both oncogenic and non-oncogenic HPV types. The magnitude of the association was greatest for HPV 6 and 11, which are responsible for approximately 90% of genital warts.[1] The association of genital warts with risk of HPV 6/11 infection was consistent for any history of genital warts as well as current genital warts.

Our results provide evidence that genital warts may serve as a reservoir of infection whereby virions remain on the skin or mucosa even after the visible lesion is no longer present. This is consistent with the high rate of recurrence of genital warts.[12] It is also possible that asymptomatic HPV infection serves as a reservoir for clinically apparent infection. In a recent report on a cohort of young adult US men, genital warts frequently developed within 2 years of detection of asymptomatic genital HPV 6 or 11 infection.[13]

An unexpected finding was the observation that warts on the fingers, arms and trunk (including the back, chest and abdomen) increased the risk of genital HPV. We previously observed that auto-inoculation was common, particularly in men, and included transmission of sub-clinical HPV infection from the genitals to the hands.[5] In an early study, concurrent genital condyloma and oral warts were common[14] underscoring the possibility of oral-genital auto-inoculation. We found that the presence of warts on the fingers and trunk was specifically associated with increased risk of penile infection with untyped HPVs. Common skin and flat warts found on extra-genital sites are caused by any of a number of HPV types, including HPV 2, 3, 4, 7, 10, 27, 28, 29, 41 and 57,[23] all of which are not detected by our genotyping assay. Our PCR assay amplifies a conserved region of the HPV L1 genome. Therefore, it is possible that untyped HPVs—that is, those testing HPV DNA-positive based on L1 PCR but not positive for any of the 37 genotypes detected by our assay, included some of these cutaneous HPV types.

Our findings also suggest that other HPV types, including HPV 6 and 11, and other mucosal genital HPVs may co-occur in cutaneous warts such that they can be transmitted to genital sites. It has been shown that HPV 6- and 11-associated genital warts often contain other HPV types, including oncogenic types such as HPV 16 and 18.[1516] Similarly, different types of warts can occur together at the same site, including mixtures of common and flat warts[4] as well as anogenital warts and flat warts.[17] In our cohort, baseline genital HPV infection with multiple types and untyped HPVs was more common among men with a history of warts. This further reinforces the evidence that warts serve as an efficient source of viral transmission.

It is interesting that the association of warts to subsequent acquisition of genital infection was not limited to warts currently present on the body. This underscores the possibility that HPV virions remain on the skin surface even after a wart has regressed or been removed through treatment.

We speculate that HPV may be transmitted from one site of the body to another through auto-inoculation. Nonetheless, our study methodology did not allow us to definitively prove autoinoculation. Detection of the same HPV type in wart samples from the genitals, fingers,

arms and trunk, and the subsequent genital infection would provide much stronger evidence of auto-inoculation.

An alternative explanation to our findings is the possibility that some individuals have a general susceptibility to symptomatic and asymptomatic HPV infection. Although the present analysis was limited to HIV-negative healthy adult men, it is possible that some individuals had other immune suppressive conditions that may have increased their risk of HPV. It is also possible that self-reported HIV status was under-reported.

Nonetheless, if our results were explained by general susceptibility to HPV in some individuals, we would have expected to observe associations of warts and incident genital HPV infection to extend to all wart sites, including the anus, head/face/neck, legs and feet. In addition, we would not have expected to observe associations specific to HPV 6/11 and untyped HPVs.

Misclassification of wart history was possible as measurement was based on self-report. While we do not expect that a history of warts would be over-reported by our cohort of adult men, under-reporting was possible due to embarrassment. In addition, warts located on sites readily visible to an individual—such as the face, fingers and arms—were more likely to be reported than those on locations not readily observed. Nonetheless, the validity of self-report was, to some extent, supported by our findings that a large proportion of men for whom genital warts were clinically documented at study entry had reported having a wart during their study interview.

It is possible that treatment of warts may affect the extent to which warts are a source of productive HPV infections whereby virions are actively released. Nonetheless, we did not assess whether warts occurring in the past were treated or regressed on their own.

Our study suggests that that men with a history of warts at genital and extra-genital sites may be at increased risk for acquisition of new genital HPV infections. Warts may provide an efficient reservoir for the direct transmission of virions from proximate and distant sites to the genitals via auto-inoculation. The potential for the spread of HPV throughout the body via auto-inoculation has important implications for prevention and control of HPV infection.

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Competing interests BYH has received consultation and research funds from the Merck Corporation—manufacturer of the quadrivalent HPV vaccine, Gardasil. The research funds were for a project unrelated to the study described in this manuscript.

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Key messages

- Men with a history of warts on the genitals, fingers, arms and trunk may be at increased risk for acquisition of genital human papillomavirus (HPV) infection.
- Warts may provide an efficient reservoir for the transmission of virions to the genitals via auto-inoculation.
- HPV auto-inoculation should be considered in overall strategies to prevent and control infection.

Table 1

Hawaii Male Cohort*, 2004–2006 (n=331)

Characteristic		
Number of visits, mean, (range)	6.9 (2–19)	
Length of follow-up, mean (range)	418 (38–1262) days	
Age, median (range)	24.0 (18–79) years	
Race		
White	190	57.4%
Non-white†	141	42.6%
Birthplace		
USA	268	81.0%
Non-USA‡	63	19.0%
Marital status§		
Single (never married)	275	83.3%
Ever married	55	16.7%
Education (y)		
No college	11	3.3%
Some college	216	65.3%
College degree or postgraduate	104	31.4%
Circumcised	269	81.3%
Sexual history¶		
Sex with women only	268	81.5%
Sex with men	52	15.8%
No sex	9	2.7%
Condom use with female within past 4 months**	173	69%
History of warts		
Any site(s)		
Ever	221	66.8%
Current	72	21.8%
Genitals		
Ever	29	8.8%
Current	17	5.2%
Anus		
Ever	6	1.8%
Current	0	–
Head/face/neck		
Ever	9	2.7%
Current	4	1.2%
Mouth		
Ever	3	0.9%
Current	2	0.6%

Characteristic		
Trunk (including back, chest, abdomen)		
Ever	10	3.0%
Current	4	1.2%
Arms (including elbows)		
Ever	31	9.4%
Current	6	1.8%
Hands (including wrists)		
Ever	76	23.1%
Current	12	3.6%
Fingers		
Ever	114	34.6%
Current	27	8.2%
Legs (including knees)		
Ever	29	8.8%
Current	9	2.7%
Feet (including ankles)		
Ever	48	14.6%
Current	13	4.0%
Toes		
Ever	32	9.7%
Current	4	1.2%

[*] Excludes HIV+ individuals.

[†] Includes Native Hawaiians, Japanese, Chinese, Filipinos and other race/ethnic groups.

[‡] Includes individuals born in US-affiliated areas of American Samoa, Federated States of Micronesia, Marshall Islands, Palau and Guam.

[§] One participant did not provide a valid response.

[¶] Two subjects declined to respond.

[**] Excludes men who have sex with men exclusively and men with no history of sex.

Table 2

History of warts and risk of anogenital human papillomavirus (HPV) acquisition in men*

		Adjusted HR and 95% CI†‡				
Site of wart§	**Site of incident HPV infection**	**Any HPV¶ HR (95% CI)**	**Oncogenic¶ HR (95% CI)**	**Non-oncogenic¶ HR (95% CI)**	**HPV 6 or 11 HR (95% CI)**	**Untyped HPV¶ HR (95% CI)**
Genitals						
	Penis glans/corona					
Ever		**1.67 (1.21 to 2.30)****	**2.02 (1.21 to 3.39)**	1.49 (0.99 to 2.25)	**12.86 (4.54 to 36.46)****	0.81 (0.28 to 2.28)
Current		1.41 (0.90 to 2.22)	1.89 (0.95 to 3.74)	1.18 (0.64 to 2.15)	**10.18 (3.09 to 33.51)****	0.98 (0.23 to 4.15)
	Penis shaft					
Ever		**1.68 (1.29 to 2.20)****	**1.78 (1.17 to 2.72)****	**1.64 (1.16 to 2.32)****	**8.33 (2.44 to 28.40)****	1.02 (0.42 to 2.52)
Current		1.03 (0.68 to 1.56)	1.20 (0.63 to 2.27)	0.94 (0.54 to 1.63)	**4.72 (1.18 to 18.92)**	–
	Scrotum					
Ever		**1.74 (1.31 to 2.31)****	**2.24 (1.39 to 3.59)****	**1.52 (1.06 to 2.16)****	**6.09 (2.22 to 16.71)****	0.94 (0.43 to 2.04)
Current		1.36 (0.90 to 2.04)	**2.29 (1.23 to 4.24)**	0.95 (0.53 to 1.67)	**4.62 (1.40 to 15.27)****	0.55 (0.13 to 2.22)
Fingers						
	Penis glans/corona					
Ever		**1.49 (1.16 to 1.91)****	**1.67 (1.09 to 2.55)**	**1.42 (1.04 to 1.92)**	2.63 (0.88 to 7.85)	1.03 (0.56 to 1.88)
Current		**1.86 (1.32 to 2.61)****	1.71 (0.93 to 3.15)	**1.92 (1.28 to 2.89)****	2.48 (0.69 to 8.83)	2.06 (0.91 to 4.68)
	Penis shaft					
Ever		**1.31 (1.06 to 1.61)**	**1.54 (1.08 to 2.20)**	1.18 (0.91 to 1.55)	2.48 (0.85 to 7.23)	0.82 (0.46 to 1.45)
Current		**1.43 (1.04 to 1.96)**	1.38 (0.81 to 2.35)	1.46 (0.98 to 2.18)	1.67 (0.36 to 7.65)	**2.42 (1.22 to 4.83)**
	Scrotum					
Ever		1.28 (1.01 to 1.61)	**1.65 (1.09 to 2.48)**	1.14 (0.86 to 1.51)	2.63 (0.94 to 7.45)	0.95 (0.57 to 1.59)
Current		**1.45 (1.02 to 2.05)**	**1.93 (1.11 to 3.37)**	1.22 (0.78 to 1.91)	1.27 (0.28 to 5.78)	1.27 (0.56 to 2.87)
Arms						
	Penis glans/corona					
Ever		**1.67 (1.23 to 2.27)****	**1.81 (1.06 to 3.08)**	**1.60 (1.10 to 2.33)**	**3.74 (1.26 to 11.12)**	1.39 (0.62 to 3.08)
Current		**2.96 (1.65 to 5.28)****	2.64 (0.89 to 7.83)	**3.15 (1.59 to 6.26)****	4.07 (0.55 to 30.18)	2.01 (0.41 to 9.73)

Adjusted HR and 95% CI[†‡]						
Site of wart[§]	**Site of incident HPV infection**	**Any HPV[¶] HR (95% CI)**	**Oncogenic[¶] HR (95% CI)**	**Non-oncogenic[¶] HR (95% CI)**	**HPV 6 or 11 HR (95% CI)**	**Untyped HPV[¶] HR (95% CI)**
	Penis shaft					
Ever		**1.38 (1.04 to 1.83)**	1.58 (0.99 to 2.53)	1.27 (0.89 to 1.81)	1.61 (0.39 to 6.66)	1.21 (0.62 to 2.38)
Current		**3.01 (1.80 to 5.02)****	**2.83 (1.10 to 7.27)**	**3.18 (1.72 to 5.88)****	4.25 (0.57 to 31.50)	3.25 (0.83 to 12.69)
	Scrotum					
Ever		**1.51 (1.13 to 2.02)****	1.44 (0.84 to 2.48)	**1.55 (1.10 to 2.18)**	1.54 (0.40 to 5.96)	1.06 (0.54 to 2.06)
Current		**2.21 (1.20 to 4.08)****	1.97 (0.59 to 6.52)	**2.34 (1.15 to 4.74)****	3.44 (0.25 to 47.79)	1.60 (0.36 to 7.13)
Trunk (including back, chest, abdomen)						
	Penis glans/corona					
Ever		0.92 (0.41 to 2.09)	0.43 (0.06 to 3.25)	1.21 (0.50 to 2.95)	–	**5.41 (1.54 to 18.98)**
Current		0.73 (0.23 to 2.32)	–	1.14 (0.36 to 3.68)	–	8.76 (0.93 to 82.53)
	Penis shaft					
Ever		1.41 (0.81 to 1.84)	0.87 (0.28 to 2.70)	1.75 (0.93 to 3.32)	–	**5.74 (1.73 to 19.10)**
Current		0.60 (0.19 to 1.89)	–	0.96 (0.31 to 3.03)	–	–
	Scrotum					
Ever		1.06 (0.52 to 2.15)	0.78 (0.19 to 3.20)	1.21 (0.54 to 2.73)	–	1.48 (0.35 to 6.27)
Current		0.52 (0.13 to 2.09)	–	0.77 (0.19 to 3.12)	–	–

[*] Excludes HIV positive individuals.

[†] Adjusted for age, income, lifetime number of female sexual partners, frequency of sexual intercourse, men who have sex with men history and history of warts in a current/past sexual partner.

[‡] Statistically significant HRs are in bold.

[§] HRs for warts of the anus, head/face/neck, legs and feet were not significant and are not included.

[¶] Any HPV include any of the 37 HPV genotypes detected in the assay, including oncogenic HPV (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68), non-oncogenic HPV (6, 11, 26, 40, 42, 53–55, 61, 62, 64, 66, 67, 69–73, 81–84, IS39 (subtype HPV-82) and CP6109 (HPV-89)) and untyped HPV (HPV DNA positive specimens that were not positive for any of the 37 genotypes detected by our assay).

[**] HR remained significant after Bonferroni correction.