



## Genital Human Papillomavirus Infection: Incidence and Risk Factors in a Cohort of Female University Students

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Incidence data on human papillomavirus (HPV) infection are limited, and risk factors for transmission are largely unknown. The authors followed 603 female university students in Washington State at 4-month intervals between 1990 and 2000. At each visit, a sexual and health questionnaire was completed and cervical and vulvovaginal samples were collected to detect HPV DNA. At 24 months, the cumulative incidence of first-time infection was 32.3% (95% confidence interval: 28.0, 37.1). Incidences calculated from time of new-partner acquisition were comparable for enrolled virgins and nonvirgins. Smoking, oral contraceptive use, and report of a new male sex partner—in particular, one known for less than 8 months before sex occurred or one reporting other partners—were predictive of incident infection. Always using male condoms with a new partner was not protective. Infection in virgins was rare, but any type of nonpenetrative sexual contact was associated with an increased risk. Detection of oral HPV was rare and was not associated with oral-penile contact. The data show that the incidence of HPV associated with acquisition of a new sex partner is high and that nonpenetrative sexual contact is a plausible route of transmission in virgins.

cohort studies; incidence; papillomavirus, human; sexual abstinence; sexual partners; sexually transmitted diseases

Abbreviations: CI, confidence interval; HPV, human papillomavirus; HR, hazard ratio; PCR, polymerase chain reaction.

Genital human papillomavirus (HPV) infections are the etiologic agents of genital warts and squamous intraepithelial lesions, and certain types (primarily 16, 18, 31, 33, and 45) are causally related to the development of anogenital cancers (1–3). HPV infections are highly prevalent, and current evidence suggests that at least 50 percent of sexually active women have been infected with one or more types (3). Although transmission is known to occur primarily through sexual contact, rates of acquisition and risk factors for infection are largely unknown (4). Furthermore, the potential risk of infection from nonpenetrative sexual contact remains undetermined, including the possible association between oral-penile contact and oral HPV (which is associated with oral cancer (5)). This prospective study was conducted to estimate the cumulative incidence of HPV infection in a cohort of female university students, as well as to investigate

potential characteristics of women and their sex partners that may increase the risk of infection in women.

### MATERIALS AND METHODS

#### Study population and data collection

Between September 1990 and September 1997, female students 18–20 years of age were recruited to participate in a longitudinal study of genital HPV infection. Letters of invitation were mailed to a random sample of students, and women were eligible for participation if they were Washington State residents who planned to stay in the area for at least 3 years and were able to provide written informed consent. A total of 603 women (approximately 20 percent of eligible women receiving letters) were enrolled. The

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protocol was reviewed and approved by the University of Washington Institutional Review Board.

Visits were scheduled for every 4 months. At each visit, a nurse practitioner administered a face-to-face interview and a standardized pelvic examination. Medical and sexual history information, including socioeconomic status, gynecologic and obstetric history, current and past sexual behavior, and history of genital tract infections, was collected at the first visit. At each follow-up visit, updated behavioral and medical information and information on new sex partners was collected. At every visit, separate cervical and vulvovaginal Dacron (E. I. du Pont de Nemours & Co., Inc., Wilmington, Delaware)-tipped swab specimens were collected into specimen transport media for HPV DNA analysis by a polymerase chain reaction (PCR)-based method. A subset of 529 women provided 2,640 toothbrush samples of the buccal mucosa. These samples were collected into specimen transport media and were analyzed for HPV DNA.

### HPV DNA analysis of specimens

PCR amplification and dot-blot hybridization methods were used for HPV DNA specimen analysis. One fiftieth of each genital swab sample and oral sample was amplified in duplicate with the consensus primers MY09, MY11, and HMB01 and with human  $\beta$ -globin control primers. The products of these amplifications were then probed with a biotin-labeled generic probe designed to detect most genital HPV types. Specimens found positive by generic probe were tested with individual and mixtures of biotin-labeled, type-specific oligonucleotide probes to determine the presence of HPV types 6, 11, 16, 18, 31, 45, and 56 and the following type mixtures: 33, 35, and 39; 40, 42, 53, and 54; and 51, 52, 55, and 58. Samples hybridizing with the generic probe but not with one of the type-specific probes were classified as positive for uncharacterized genital HPV types. Unless otherwise noted, PCR test results for the cervical and vulvovaginal specimens were combined to analyze acquisition of genital HPV infection.

### Statistical analyses

The cumulative probability of acquiring an incident HPV infection was estimated by using the Kaplan-Meier method. For each subject, acquisition of an HPV infection was defined as the first positive result after having had only negative results, and time of acquisition was defined as the midpoint between the visit at which a positive result was obtained and the previous visit. In situations in which a woman tested positive, negative, and then positive for the same HPV type over three consecutive visits, the infection was considered to be persistent with an intercurrent false-negative result. We previously showed that the same HPV-16 variant was present in 100 percent of samples obtained from an individual woman, even after an intercurrent negative sample (6). Of 94 HPV infections detected by using type-specific probes, there were only 13 instances of an intercurrent false-negative result.

Women with a lifetime history of one or more sex partners at enrollment contributed at-risk time from their enrollment

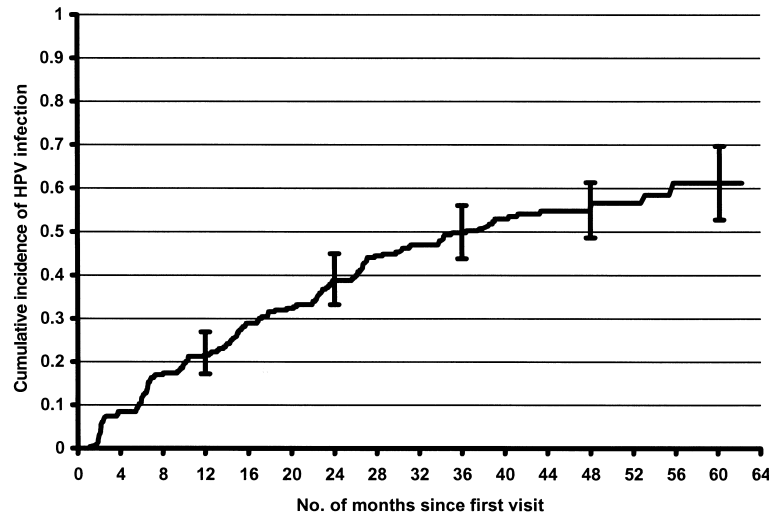
date, whereas enrolled virgins contributed at-risk time from the date of their first reported sexual intercourse. In addition, an overall cumulative incidence was calculated for all women, regardless of their sexual status, counting at-risk time from the date of enrollment. Cox proportional hazards methods were used to test whether cumulative incidences varied by enrollment year (comparing women enrolled in 1990–1993, 1994–1995, and 1996–1997).

To evaluate the risk of acquisition associated with one or more new partners among women with and without prior sexual experience, enrolled virgins contributed at-risk time as described above. Women reporting one or more partners at enrollment contributed at-risk time from the date of their first reported sexual intercourse with a new partner.

To estimate type-specific cumulative incidences, acquisition of a specific HPV type was defined as the first positive result for that type after an observed negative result for that type. To evaluate the risks from nonpenetrative sexual activity, Cox proportional hazards methods were used to determine whether oral, vulvar, or digital contact was independently associated with incident genital infection and to determine whether oral contact was associated with oral infection.

Cox proportional hazards methods were used to determine risk factors for HPV acquisition. Since information was collected every 4 months, separate models were tested by considering risk factor status at 0–4, 5–8, 9–12, and 13–16 months prior to HPV assessment; the goal was to determine which intervals (time between sex with a new partner and a scheduled visit) were associated with the highest risk of detecting incident infection. Variables considered as potential risk factors included the following: lifetime number of partners up to the beginning of the specified time interval, reporting a new partner and number of new partners during the specified time interval, current smoking (yes/no), current oral contraceptive use (yes/no), history of nongenital warts (yes/no), history of tampon use (yes/no), being delivered by cesarean section (yes/no), length of time having known a partner (<8,  $\geq$ 8 months), partner's ethnicity, partner's age (<20, 20–24, 25–29,  $\geq$ 29 years), partner's educational level (<12,  $\geq$ 12 years), partner's lifetime number of partners (none,  $\geq$ 1, unknown), partner's circumcision status (yes/no), condom use with a new partner (always/not always), whether the partner had ever had a sexually transmitted disease (yes, no, unknown), subject/partner alcohol consumption during sex (always, often, sometimes, never), and whether the woman could contact her partner again (yes/no).

Variables found to be statistically significant ( $p < 0.10$ ) in univariate analyses were tested in a multivariate model. For the final model, we collapsed risk factor status over the entire 12-month period prior to HPV assessment, since an increased risk of HPV infection was associated with risk factor status at 0–4, 5–8, and 9–12 months. We also examined the relations between the above risk factors and incident HPV-16 infection with Cox proportional hazards methods. Women who acquired an incident infection with another HPV type before acquiring HPV-16 were censored. In addition, the relations between the above risk factors and incident vulvovaginal HPV infection and incident cervical infection



**FIGURE 1.** Cumulative incidence of human papillomavirus (HPV) infection among women sexually active and HPV negative at enrollment ( $n = 296$ ) in Washington State, 1990–2000. Vertical bars, 95% confidence intervals at 12, 24, 36, 48, and 60 months.

were evaluated individually by using both Cox proportional hazards methods and McNemar's tests adjusted for multiple observations in each person. All analyses were performed by using Stata 6.0 software (7).

## RESULTS

Of 553 enrolled women for whom there were adequate samples at enrollment and follow-up, HPV DNA was detected in the genital-tract specimens of 109 (19.7 percent) at the first visit. Analyses focused on the 444 women who were HPV-DNA negative at enrollment. These women completed 4,307 visits. Their mean follow-up time was 41.2 (standard deviation, 16.3) months, the mean number of visits per person was 9.7 (standard deviation, 3.4), and the median time between visits was 4.3 months. The mean age of these women at enrollment was 19.2 (standard deviation, 0.5) years. At enrollment, 148 women were virgins. The mean lifetime number of partners of the 296 women who were sexually active at enrollment was 1.8 (standard deviation, 1.7).

Cumulative incidences were similar for enrolled nonvirgins and enrolled virgins who became sexually active by engaging in penetrative sex with a male partner (figures 1 and 2). The cumulative 24-month incidence of HPV in women who were sexually active at enrollment was 38.8 percent (95 percent confidence interval (CI): 33.3, 45.0) compared with 38.9 percent (95 percent CI: 29.4, 50.3) among virgins who initiated sexual activity. Incidences did not vary by enrollment year (Cox regression-based test;  $p = 0.53$ ). Incidences calculated from the time of acquisition of a new sex partner were not significantly different between enrolled virgins and nonvirgins (Cox regression-based test;  $p = 0.35$ ), nor was there a significant difference when comparing women reporting 0, 1–2, or 3 or more partners at enrollment (Cox regression-based test;  $p = 0.28$ ). Figure 2

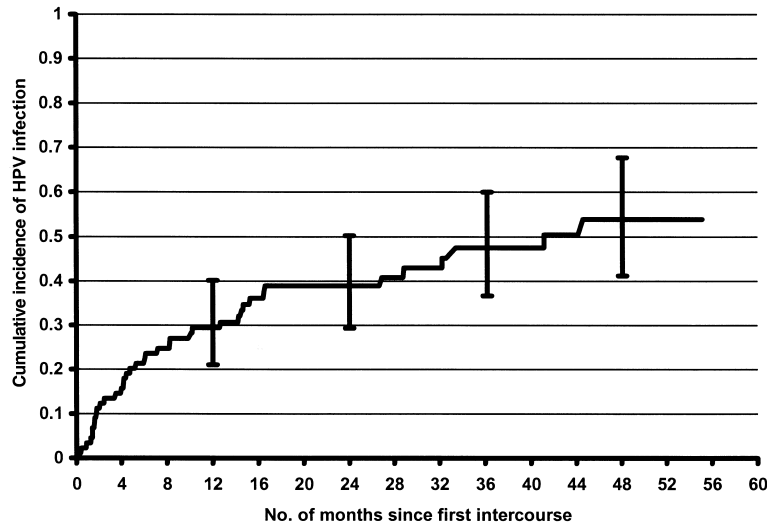
also shows that the minimum time between first sexual exposure and detection of HPV DNA was less than 1 month.

The 24-month cumulative incidences of specific HPV types among sexually active women are listed in table 1. Of four high-risk types (16, 18, 31, and 45), the incidence of type 16 was the highest (10.4 percent, 95 percent CI: 7.8, 13.8).

The most common individual types of first infections were HPV-16, -56, and -6 (figure 3). Twenty-one women (10.9 percent) were infected with multiple types. A total of 104 incident (54.2 percent) HPV infections were detected in the vulvovaginal region only, 20 (10.4 percent) in the cervix only, and 68 (35.4 percent) in both the vulvovaginal region and the cervix. HPV detected in the vulvovaginal region was more likely than HPV detected in the cervix at every time interval (McNemar's test;  $p < 0.01$ ).

Report of a new sex partner was associated with an increased risk of HPV acquisition (table 2). The greatest risk was associated with report of a new partner 5–8 months prior to the visit date (hazard ratio (HR) = 3.0, 95 percent CI: 2.1, 4.3). Similar trends were observed when we analyzed cervical and vulvovaginal HPV independently, although report of a new partner 0–4 months prior to the visit date was not associated with a significantly increased risk of cervical infection. A separate analysis of HPV-16 infection yielded results similar to those for all HPV.

No associations were observed between report of vaginal intercourse and incident infection after controlling for cumulative lifetime number of partners and report of a new partner during the specified time interval (HR at 5–8 months = 1.1, 95 percent CI: 0.8, 1.6). Furthermore, neither penile-vulvar (HR at 5–8 months = 1.2, 95 percent CI: 0.5, 3.5) nor finger-vulvar contact (HR at 5–8 months = 0.8, 95 percent CI: 0.4, 1.5) was associated with an excess risk of HPV infection after controlling for vaginal intercourse, cumulative lifetime



**FIGURE 2.** Cumulative incidence of human papillomavirus (HPV) infection from time of first sexual intercourse ( $n = 94$ ) among women in Washington State, 1990–2000. Vertical bars, 95% confidence intervals at 12, 24, 36, 48, and 60 months.

number of partners, and report of a new partner during the specified time interval.

A total of 2,640 oral specimens were tested for HPV DNA. Of 2,619 sufficient samples, only five (0.2 percent) were positive. Although the proportion of exposure was high (among sexually active women, 59.5 percent of women reporting vaginal intercourse since their last visit also reported oral-penile contact), no association was found between incident oral HPV infection and report of oral-penile contact in the past 12 months (HR = 0.5, 95 percent CI: 0.07, 3.5).

Only 13 (1.7 percent) genital-tract specimens collected during 757 visits from virgins (women who had never engaged in penetrative vaginal intercourse) were positive for HPV DNA; eight were uncharacterized types, and three were

positive for HPV-16. The 24-month cumulative incidence of infection in virginal women was 7.9 percent (95 percent CI: 3.5, 17.1). Among the 94 enrolled virgins who became sexually active (and completed at least two visits), the 24-month cumulative incidence of HPV infection before initiation of sexual intercourse was 15.3 percent (95 percent CI: 6.1, 35.2), whereas among the 54 women who remained virgins throughout the course of the study (and completed at least two visits), the 24-month cumulative incidence of infection was only 2.4 percent (95 percent CI: 0.4, 16.1).

Whereas nonpenetrative sexual contact was not associated with an increased risk of infection among sexually active women, any type of nonpenetrative sexual contact (finger-vulvar, penile-vulvar, or oral-penile) was associated with an increased risk of genital infection in virgins. Of 72 virginal

**TABLE 1.** Cumulative incidence of human papillomavirus types in a population of women in Washington State, 1990–2000

HPV* type(s)	Cumulative incidence at 24 months (%)	95% CI*	No. with infection/ person-years at risk
16	10.4	7.8, 13.8	44/802
18	4.1	2.6, 6.4	18/855
31	4.8	3.1, 7.3	21/861
45	1.3	0.6, 3.0	6/879
51, 52, 55, 58	8.8	6.5, 11.9	38/840
56	8.1	5.9, 11.0	36/852
33, 35, 39	11.3	8.6, 14.7	49/822
6/11†	9.4	5.3, 10.0	41/821
6	7.5	7.0, 12.6	33/839
11	0.9	0.3, 2.3	4/883
40, 42, 53, 54	8.0	5.8, 11.0	35/847

\* HPV, human papillomavirus; CI, confidence interval.

† Not all HPV-6/11 specimens were individually tested for HPV-6 and -11 separately.

**TABLE 2. Hazard ratios for the association between incident human papillomavirus infection and acquisition of a new sex partner at varying time intervals prior to assessment of human papillomavirus status in a population of women in Washington State, 1990–2000**

Time interval (months) of new partner report	All HPV*			HPV 16			Cervical HPV			Vulvovaginal HPV		
	Adjusted† HR*	95% CI*	Infections/ person-years at risk	Adjusted† HR	95% CI	Infections/ person-years at risk	Adjusted† HR	95% CI	Infections/ person-years at risk	Adjusted† HR	95% CI	Infections/ person-years at risk
0–4												
Yes	2.2	1.5, 3.3	70/171	1.9	0.7, 4.8	14/155	1.4	0.9, 2.1	48/197	2.5	1.7, 3.8	66/172
No	1.0		123/903	1.0		24/874	1.0		102/982	1.0		107/907
5–8												
Yes	3.0	2.1, 4.3	64/129	4.9	2.3, 10.7	15/120	2.7	1.9, 4.1	49/156	3.4	2.3, 5.0	63/132
No	1.0		129/945	1.0		23/910	1.0		101/1,022	1.0		110/947
8–12												
Yes	2.4	1.6, 3.5	40/98	3.5	1.5, 8.1	10/94	3.5	2.3, 5.1	48/129	2.4	1.6, 3.5	36/98
No	1.0		124/806	1.0		26/775	1.0		88/882	1.0		110/809
13–16												
Yes	1.5	0.9, 2.3	25/76	2.6	1.1, 6.4	8/73	1.3	0.8, 2.2	22/100	1.4	0.9, 2.3	22/77
No	1.0		105/680	1.0		19/653	1.0		93/757	1.0		94/681

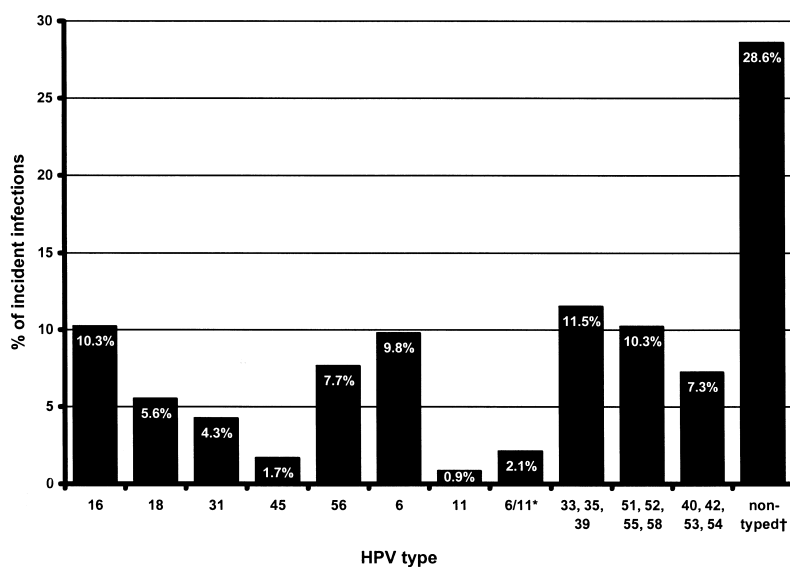
\* HPV, human papillomavirus; HR, hazard ratio; CI, confidence interval.

† Adjusted for current smoking, current use of oral contraceptives, lifetime number of partners at enrollment, and all other time intervals in which a new partner was reported.

women reporting nonpenetrative sexual contact (and completing at least two visits), seven tested positive for HPV DNA (9.7 percent) whereas only one of 76 women (1.3 percent) reporting no such contact (and completing at least two visits) tested positive.

Among sexually active women who were HPV negative at enrollment, current smoking, current oral contraceptive use, increasing cumulative number of sex partners and male partners' number of prior sex partners, and knowing a partner for less than 8 months before engaging in sexual intercourse were all significant predictors of infection (table 3). Other

characteristics of the partner (age, race, educational level, circumcision status, sexually transmitted disease history) and the partnership (condom use and alcohol consumption) were not associated with incident infection. Additional factors unrelated to the risk of acquisition were tampon use, cesarean delivery, and nongenital warts. Although condom use did not show a significant protective effect, we included it in the final model because it is of particular public health interest. When the analysis was restricted to women whose first incident infection was with HPV-16, similar trends were observed.



**FIGURE 3.** Type-specific distribution of first-time incident human papillomavirus (HPV) infection ( $n = 232$ ) among 192 women in Washington State, 1990–2000. \*Includes only 6/11 infections that could not be individually tested for HPV-6 and -11. †Positive with the generic probe, negative with type-specific probes.

**TABLE 3. Hazard ratios for the association between incident human papillomavirus infection and behavioral risk factors during the past 12 months in a population of women in Washington State, 1990–2000**

Risk factor	Adjusted* HR†	95% CI†	Infections/person-years at risk
Cumulative sex partners (continuous)	1.1	1.03, 1.1	168/1,056
Condom use with new partners			
Always	0.8	0.5, 1.2	144/938
Not always	1.0		24/118
Sex partner's no. of other partners‡			
None	1.0		79/790
≥1	5.2	1.3, 21.2	80/250
Unknown	8.0	1.8, 36.5	9/18
Time having known partner before sex (months)			
≥8	1.0		58/151
<8	1.8	1.2, 2.7	110/906
Current smoker			
No	1.0		135/931
Yes	1.5	1.0, 2.3	33/126
Currently using oral contraceptives			
No	1.0		76/553
Yes	1.4	1.01, 1.8	92/503

\* Each adjusted for whether a new partner was reported in the last 12 months (yes/no) and for all other variables in the table.

† HR, hazard ratio; CI, confidence interval.

‡ Based on female subject's report.

## DISCUSSION

The overall cumulative incidence of genital HPV infection among women who were HPV-DNA negative at enrollment was comparable to those reported in three previous studies, one conducted among a similar population of female university students in New Jersey; one among females aged 13–21 years attending family planning clinics in San Francisco, California; and one among women aged 15–19 years in the United Kingdom (4, 8, 9). Of the individual HPV types tested, 16 was the most common, with a 24-month incidence of 10.4 percent. This finding is similar to the incidences reported in previous studies (4, 9) and is significant given that HPV-16 is the type most strongly associated with cervical cancer (1–3). Risk factors for incident HPV-16 infection were similar to those for all HPV.

The cumulative incidences observed among virgins from the date of first reported intercourse and among sexually active women from the date of report of a new sex partner were similar, suggesting that, in this population of female university students, the risk of infection associated with new partner acquisition is independent of prior sexual experience. In addition, report of vaginal intercourse during a given time interval was not associated with an increased risk of infection after controlling for new partner acquisition during the same time interval. This finding suggests that an increased risk of incident HPV infection is more strongly associated with sex with a new partner than with sex with ongoing partners.

Report of a new partner was associated most strongly with incident HPV infection when the new partner was acquired 5–8 months before assessment of HPV status. Similar, but slightly attenuated associations were observed for report of a new partner within the past 0–4 and 9–12 months, less so at 13–16 months. If it is assumed that exposure to HPV infection is associated with a new partner, these data suggest that the critical time for detecting infection is likely to be 0–12 months after exposure.

Although vulvovaginal HPV infection was strongly associated with report of a new partner within the past 0–4 months, cervical HPV infection was not significantly associated with report of a new partner until the new partner was reported at least 5 months prior to HPV assessment. To our knowledge, these are the first data to suggest that HPV DNA may be detected in vulvovaginal sites before it is detected in the cervix.

We detected a significant association between current smoking and incident HPV infection, even after adjustment for variables that may be related to both smoking and infection (including oral contraceptive use, acquisition of a new partner and lifetime number of partners, and condom use with new partners). The majority of previous studies have failed to find an association between smoking and detection of HPV DNA (10–25), including a recent prospective study by Moscicki et al. (8). A few studies found an association between smoking and HPV prevalence (13, 17, 26), but these associations tended to diminish after adjustment for sexual

behavior variables (13, 26). Although we attempted to control for sexual behavior, it is possible that residual confounding by unmeasured sexual behavior may account for the observed association between current smoking and detection of HPV DNA. It is also possible that the relevant measure is current smoking and that by examining and interviewing women every 4 months, we were able to capture recent smoking history more accurately than was possible in previous cohort studies.

We also observed a significant association between current oral contraceptive use and incident HPV infection. Even though the majority of previous studies reported no association between oral contraceptive use and detection of HPV DNA (10–14, 16, 17, 19–21) and Moscicki et al. (8) found a significant protective effect of using oral contraceptives, a handful of other studies reported a positive relation between oral contraceptive use and detection of HPV DNA (26–28). While our results may support the hypothesis that oral contraceptives enhance detection of HPV DNA, it is also possible that use of oral contraceptives is a surrogate marker for other sexual behaviors for which we could not control.

Having known a new partner for less than 8 months before having vaginal intercourse was associated with an increased risk of HPV infection. This variable may be a proxy measure for the time between starting an exclusive partnership and engaging in sexual intercourse. If HPV infection tends to clear or to become less contagious after several months, a woman's risk of infection would be expected to be reduced if she has sex with partners who have had no other partners in the past several months.

Reporting a new sex partner who has had one or more or an unknown number of prior female sex partners was also a significant predictor of incident HPV infection. Although it is possible that women underestimate their partners' prior sexual experience, such a phenomenon would result in a dilution of the true risk of having a new partner with prior sexual experience, and we would conclude that the true risk is even greater than that observed in our data. Furthermore, note that lack of knowledge of a partner's prior sexual experience was associated with an even greater risk of HPV infection than having a new partner with one or more prior partners. This result, in conjunction with the observed protective effect associated with having known a new partner for more than 8 months before intercourse, seems to suggest that the better and longer a woman knows her partner before intercourse, the less her risk of becoming infected with HPV.

Consistent with previous studies (4, 7, 11, 17, 29, 30), we observed no protective effect associated with condom use. Although report of always using condoms with a new partner showed a protective trend against incident HPV infection, this trend was not significant. Improper condom use by the women in this cohort or biased reporting (e.g., women may be overestimating their condom use with new partners) are possibilities and would be expected to dilute any true protective effect of condom use. It is also possible that since HPV is transmitted presumably through skin-to-skin contact, condoms may not protect against HPV because the virus can be transmitted through nonpenetrative sexual contact.

Another possibility is that condoms may be more effective in preventing female-to-male transmission than male-to-female transmission (31).

Although vaginal intercourse is clearly the predominant mode of genital HPV transmission, our data show that genital HPV is also transmissible through modes other than nonpenetrative sexual contact. The 24-month cumulative incidence of HPV in virginal women was a considerable 7.9 percent, but detection of HPV DNA in genital samples from virginal women was rare (1.7 percent). This finding is consistent with the results of a study by Rylander et al. (32) that found a 1.8 percent positivity rate in cervical samples collected from virginal women. Whereas neither penile-vulvar nor finger-vulvar contact was associated with an excess risk of HPV infection in sexually active women, any type of nonpenetrative sexual contact was associated with an increased risk of HPV infection in virgins. Enrolled virgins who initiated sexual intercourse with a male partner during the course of the study had a greater 24-month cumulative incidence of HPV infection before initiation of sexual intercourse (15.3 percent) than did women who remained virgins throughout the course of the study (2.4 percent). This finding may reflect varying patterns in nonpenetrative sexual behavior between women who did and those who did not remain virgins. Furthermore, the incident infections observed in virginal women within 1 month of initiating vaginal intercourse are likely to reflect infections acquired from nonpenetrative sexual contact prior to initiation of intercourse, and these women did in fact report some form of nonpenetrative sexual contact prior to their date of first intercourse. These results support the role of nonpenetrative sexual contact as a primary mode of genital HPV infection in virginal women.

Despite a high frequency of oral-penile contact among study participants, the prevalence of oral HPV was low, and no association between oral-penile contact and oral HPV was observed. Although oral HPV infection has been clearly documented (33), our results suggest that transmission is uncommon and not clearly associated with oral-penile contact. This finding is reassuring given recent reports in the popular press that oral sex has become widespread among adolescents (34). However, an alternative explanation is that our test and/or sampling method lacks sensitivity for detecting oral HPV DNA. If this explanation were true, our ability to detect a true association between oral-penile contact and oral HPV would be compromised.

One potential limitation of our study is that only about 20 percent of eligible women randomly selected for participation chose to enroll. Clinic-based studies achieve higher participation rates (4, 8, 9) but must contend with the fact that young women attending such clinics often do so because of signs or symptoms of a genital tract infection. The comparability of HPV incidences reported in recent studies of young women, including the present study, suggest that method of cohort recruitment has not been an important source of bias (4, 8, 9). Another limitation is that we were unable to capture all potential forms of nonpenetrative sexual contact. Furthermore, there is the potential for reporting bias, in that women may have been reluctant to disclose sexual behavior information. Recall bias is another

possibility since women were asked to report information from the past 4 months. We were also unable to capture frequency of sexual exposures or concurrent partnership information. This information is being captured in a current study. Note also that PCR-based methods for HPV DNA detection have improved during the last decade. Consensus primers now detect a wider range of HPV types, and multiple assays are no longer required for identifying individual HPV types. Finally, our results may not generalize to other populations of women, including those that are older, have human immunodeficiency virus infection, or have high rates of sex-partner change.

In conclusion, the present study showed that the incidence of genital HPV associated with acquisition of a new sex partner is high and that risk of infection is especially high if a partner has been known for less than 8 months and if a partner reports having had sex with other partners. Oral HPV infection is rare and not clearly associated with oral-penile contact. Genital HPV infection in virginal women seems to be rare, but nonpenetrative sexual contact is a plausible route of transmission.

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