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INCIDENCE AND RISK FACTORS FOR HUMAN PAPILOMAVIRUS INFECTIONS IN YOUNG FEMALE ONLINE DATERS

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Abstract

Risk factors for incident HPV infections are undefined in young women who use internet dating Web sites. From 2010–2012 we followed 18–24-year-old female internet daters (N=164) triannually for a mean of one year. Women collected and returned self-collected vaginal samples for HPV genotyping and health and behavior questionnaires. We used Kaplan-Meier methods to estimate incidence of clinically-relevant HPV infection (high-risk HPV, HPV-6, or HPV-11) and generalized estimating equations and Firth logistic regression to identify associated risk factors. At enrollment, women reported a median lifetime number of 6 male sex partners, and 36% reported a history of HPV vaccination. The 12-month cumulative incidence of clinically-relevant HPV was 32.9% (95%CI:26.0%–41.0%). Reporting a recent male sex partner met via the internet versus not was not significantly associated with incident HPV (odds ratio [OR]=0.91, 95%CI:0.53–1.55). In multivariate analysis adjusted for lifetime number of partners, reporting new and/or multiple partners in the past 6 months was positively associated with incident HPV (OR=6.38, 95%CI: 1.56–26.02, compared to reporting no recent partners). In a separate model, self-reporting 1 dose of HPV vaccine was inversely associated with vaccine-type HPV (6/11/16/18) (OR=0.21, 95%CI: 0.05–0.86), but the association was attenuated and not statistically significant after adjusting for sexual history (OR=0.36, 95%CI:0.09–1.43). While recent high-risk sexual behavior was associated with incident HPV, sex with partners met via the internet was not associated with increased HPV risk in young female internet daters. Although not statistically significant after adjusting for sexual history, HPV vaccination showed substantial protection against vaccine-type HPV infection. This article is protected by copyright. All rights reserved

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Keywords

HPV; human papilloma virus; women; internet dating; incidence

INTRODUCTION

Human papillomavirus (HPV) is the most common sexually transmitted infection in the U.S., with incidence peaking in young adults 20 to 24 years of age [Satterwhite et al., 2013]. Although many risk factors for HPV acquisition have been well-described in sexually active young women [Burchell et al., 2006], the risk associated with meeting sex partners via the internet is undefined. With online dating increasing, particularly among 18- to 24-year old adults (from 10% in 2013 to 27% in 2015, according to a U.S. national survey [Smith, 2016]) determining the associated risk for HPV infection has implications for targeted HPV education and prevention efforts in populations of young female online daters.

Also of interest in this age group is the impact of prophylactic HPV vaccination on HPV incidence. Prophylactic HPV vaccines have been widely available in the U.S. since 2006, and are recommended for 11- to 12 year olds (with “catch-up” vaccination through age 26) [Markowitz et al., 2014]. While data from the National Health and Nutrition Examination Survey (NHANES) indicate that vaccination has reduced vaccine-type HPV prevalence in adolescent and young adult females [Markowitz et al., 2016], data on the impact of HPV vaccination on HPV incidence in real-world cohorts are limited.

From 2010–2012, we recruited and followed a cohort of 18- to 24-year old female online daters in a longitudinal study of HPV infections. “Online dating” was defined as using the internet to search for romantic partners, regardless of whether the result was meeting a sex partner. Study aims were to determine risk factors for HPV infection associated with online dating and other sexual behaviors, as well as to estimate the protective effect of HPV vaccination in a real-world cohort of young women actively seeking new partners. Furthermore, we sought to compare rates of and risk factors for HPV infections to those observed in a previous cohort of mid-adult (25- to 65-year old) female online daters that we recruited and followed with a similar protocol. In our mid-adult cohort, associations between online dating and HPV infection were inconsistent, with an increased likelihood of prevalent infection associated with online dating [Winer et al., 2012], but no association for incident HPV [Winer et al., 2016]. We previously reported no association between online dating and prevalent HPV infection in a cross-sectional analysis of young adult female online daters, but did report a protective effect of self-reporting 1 dose of HPV vaccine on prevalent vaccine-type HPV [Barrere et al., 2015]. In this paper, we report results from a subset of young female online daters that were followed longitudinally, including HPV incidence and associated risk and protective factors.

MATERIALS AND METHODS

From October 2010 to May 2012, we enrolled 18- to 24-year-old female online daters into a longitudinal study of HPV infections. Women were recruited through advertisements posted on Craigslist.org and other free volunteer posting Web sites (described previously in our

parallel study of 25- to 65-year-old online daters [Winer et al., 2012]). Eligibility screening for all potential subjects was conducted by telephone. To be eligible, women had to report using the internet within the previous 12 months to search for partners. Women were excluded if they were pregnant, breastfeeding, or planning a pregnancy within the next 6 months, were hysterectomized, were immunocompromised, or reported no history of sex with men. Consent forms were mailed to eligible women, and women were enrolled after returning the signed consent form. The protocol for the study was reviewed and approved by the University of Washington Institutional Review Board.

Participants received up to four mailings at 4-month intervals with a kit for self-collecting vaginal samples for HPV DNA testing [Winer et al., 2012] and a survey with questions on demographics, sexual behavior, and health history (including HPV vaccination status). Vaginal samples were tested for HPV DNA using polymerase chain reaction (PCR)-based methods described previously [Winer et al., 2012]. HPV L1 consensus primers MY09, MY11, and HMB01 and β -globin primers PC04 and GH2 were used to simultaneously amplify HPV DNA and β -globin. Samples that were HPV positive by generic probe or β -globin negative were typed with the Roche Linear Array HPV genotyping test (Roche Molecular Systems, Inc, Alameda, CA) for 37 HPV types, including 21 clinically-relevant types: HPV types 6 and 11 (due to their association with genital warts [Brown et al., 1999; Greer et al., 1995]) and 19 oncogenic types classified as carcinogenic, probably carcinogenic, or possibly carcinogenic: 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82, IS39 [Bouvard et al., 2009; Munoz et al., 2003]. Samples that were β -globin negative during the initial dot blot step and HPV negative by the Roche assay were considered insufficient.

To analyze cumulative incidence of newly detected HPV infections, we conducted Kaplan-Meier analyses for individual types and the following type groups: quadrivalent vaccine-type HPV (6, 11, 16 and 18), HPV 16 and/or HPV 18, HPV 6 and/or HPV 11, oncogenic types (the 19 oncogenic types listed above), and clinically-relevant HPV types (types 6, 11, and the 19 oncogenic types). HPV types first detected during follow-up were considered incident. Time-at-risk was calculated from baseline to first detection of a specific HPV type or group of types (using the midpoint between the date of the incident positive and the previous sample), or the last sample if all samples were negative for that type or group of types. We also described the proportion of clinically-relevant HPV infections that remained positive at the subsequent follow-up visit.

To analyze risk factors for type-specific incident HPV infections, we used generalized estimating equations (GEE) with an independence working correlation structure, robust standard errors, and logit link function to estimate odds ratios (ORs) while accounting for correlation within women due to multiple outcome measurements. Separate models were constructed using clinically-relevant HPV and oncogenic HPV as the outcome. Each woman contributed an observation for each of the 21 HPV types she tested negative for at baseline. A “visit number” indicator variable was included as a time surrogate. Potential risk factors evaluated in univariate analyses included demographics, health history, and cumulative and recent sexual behaviors. Time-fixed demographic variables included race and Hispanic ethnicity, and time-varying variables included age and marital status. Time-varying health

history variables included pregnancy history, smoking history, current hormonal contraceptive use, history of an abnormal Pap test (restricted to women ≥ 21 years of age), and history of ≥ 1 dose of HPV vaccine. Time-fixed sexual behavior variables included age at first vaginal intercourse and lifetime number of male sex partners, and time-varying variables included numbers of male sex partners in the past six months and other characteristics of recent male sex partners and partnerships restricted to women reporting a male partner in the past six months (including number of partners, new partners, partners with other concurrent partners, partners met online, and condom use with male sex partners). Recent sexual behavior variables found to be statistically significant ($p < 0.10$) in univariate analyses were used to construct a time-varying composite variable to assess the overall impact of recent sexual behaviors. The variable ranged from not sexually active with male partners in the past 6 months to sexually active with one male partner with no other risk factors to sexually active with one or more male partners with at least one risk factor. The time-varying composite variable was entered into a final multivariate model with demographic, health history, and time-fixed sexual behavior variables that were statistically significant at the $p < 0.10$ level in univariate analyses.

Similar methods were used to evaluate the association between HPV vaccination history (≥ 1 dose vs. 0 doses) and incident HPV infection with vaccine types (6, 11, 16 or 18). To construct a final multivariate model with vaccine-type HPV as the outcome, we included HPV vaccination history plus all variables selected for the multivariate analysis inclusive of all clinically-relevant HPV types. Due to some zero cells in the final multivariate model, we used Firth's penalized likelihood logistic regression [Heinze and Schemper, 2002]. The Firth model provides estimates when one category of a predictor perfectly predicts the dependent variable. To account for within-subject correlation, we permuted HPV vaccine status across women (1000 permutations) to evaluate the p-value.

RESULTS

One hundred ninety-five age-eligible women were enrolled into the longitudinal study. Analyses were restricted to 164 (84%) women who returned ≥ 1 follow-up sample. At enrollment, their mean ($\pm$ standard deviation [SD]) age was 22.0 (± 1.7) years, and they reported a median lifetime number of 6 (interquartile range: 3–12) male sex partners. Fifty-eight percent reported new or multiple male sex partners within 6 months of enrollment, and 36% self-reported a history of prophylactic HPV vaccination (Table 1). Mean follow-up duration ($\pm$ SD) was 12.6 (± 3.4) months, the mean interval between sample collections was 5.3 (± 2.0) months, and 108 women (66%) returned 4 samples.

The incidence rate of clinically-relevant HPV was 36.9 per 100 women-years, with a 12-month cumulative incidence of 32.9% (26.0%–41.0%) (Table 2 and Figure 1). The individual types with the highest incidence rates were HPV-56, HPV-53, and HPV-52. The incidence rate of detecting any new vaccine-type HPV was 7.2 per 100 women years with a 12-month cumulative incidence of 8.1% (4.7%–13.9%). A total of 100 incident clinically-relevant HPV infections were detected during follow-up, including 64 that were detected prior to the last follow-up visit. Of these 64, 43 (67.2%) were re-detected at the subsequent follow-up visit.

In univariate analyses, lifetime number of male sex partners and recent sex with male partners were each positively associated with an increased likelihood of incident infections with clinically-relevant HPV types (Table 3). In analyses restricted to women reporting male partners in the past 6 months, reporting multiple sex partners and new sex partners were each associated with an increased likelihood of infection. We then created a composite variable measuring report of recent new and/or multiple male sex partners; women with at least one of these risk factors had a higher likelihood of infection than women who were not recently sexually active. Univariate results were similar in models using oncogenic HPV as the outcome (data not shown).

The multivariate analysis included the composite recent sexual behavior variable and the lifetime number of partners variable (Table 3). Associations between lifetime number of partners and incident HPV were attenuated and not statistically significant. Relative to women reporting no sex partners in the past 6 months, those reporting 1 non-new male sex partner had a non-statistically-significantly increased likelihood of incident HPV (OR=3.01, 95% CI: 0.73–12.38). Women with multiple sex partners and/or new sex partners had an OR of 6.38 (95% CI: 1.56–26.02) relative to those with no recent partners. Multivariate results were similar in models using oncogenic HPV as the outcome (data not shown).

For analyses restricted to vaccine-type HPV, history of HPV vaccination was inversely associated with incident infection (Table 4). Compared to women self-reporting no history of HPV vaccination, those reporting 1 dose had an OR of 0.21 (95% CI: 0.05–0.86) in univariate analysis. HPV vaccination was attenuated and no longer statistically significant in the multivariate analysis after adjusting for lifetime number of male sex partners and the composite recent sexual behavior variable (OR= 0.36 (95% CI: 0.09–1.43). The p-values from the Firth model and the permuted distribution were 0.148 and 0.143, respectively. The two cases of incident vaccine-type HPV detected in women reporting a history of HPV vaccination were both HPV-16. One of these women reported receiving 1 dose of the HPV vaccine, and the other reported 2 doses.

DISCUSSION

In this study, we followed a cohort of young adult female online daters in a longitudinal study of incident HPV infections, taking into consideration sexual behaviors and HPV vaccination history. At enrollment, women reported a median lifetime number of male sex partners (6) that was considerably higher than those reported by similarly-aged women in the population-based 2006–2008 National Survey of Family Growth (1.4 and 2.6 among 15 to 19 year old and 20 to 24 year old women, respectively) [Chandra et al., 2011]. The incidence of oncogenic HPV was 34.4 per 100 person-years (36.9 for any clinically-relevant HPV type), slightly higher than the incidence of oncogenic HPV in our previous study of mid-adult (25- to 65-year-old) female online daters (29.5 per 100 person-years) [Winer et al., 2016]. Thirty-six percent of our cohort self-reported a history of HPV vaccination. We did not collect data on timing of vaccination in relation to sexual debut, and note that given the timing of the study (2010–2012) in relation to introduction of the HPV vaccine in the U.S. (2006), vaccinated members of our cohort would have been vaccinated under “catch up” recommendations for females 13 years of age and older [Markowitz et al., 2014].

Nonetheless, using the baseline data from this high-risk young adult cohort, we previously reported a statistically-significant 61% reduction in vaccine-type HPV prevalence for self-reporting 1 versus no doses of HPV vaccine [Barrere et al., 2015]. We similarly observed a high level of protection against incident vaccine-type HPV in our longitudinal data (79% reduction for 1 versus no doses in univariate analysis), albeit attenuated (64% reduction) and not statistically significant after adjusting for lifetime number of partners and recent sexual behavior. Our findings align with published findings on HPV vaccine effectiveness. Among 15- to 25-year old women included in the intent-to-treat analysis of the bivalent HPV vaccine trial, vaccine effectiveness against incident HPV-16 or HPV-18 was 68% [Harper et al., 2004]. Among 14- to 24-year old females participating in the 2009–2012 NHANES, self-reported history HPV vaccination (1 dose) was associated with a reduction in vaccine-type HPV prevalence (16, 18, 6, 11) of 89% [Markowitz et al., 2016]. In a recent longitudinal study of sexually-active adolescent females (aged 13 to 21 years) in a U.S. inner city, there was a 78% reduction in quadrivalent vaccine-type HPV incidence associated with being fully vaccinated versus unvaccinated [Schlecht et al., 2016]. We also note that the incidence of vaccine-type HPV in our partially-vaccinated cohort was lower than in 15- to 25-year old women enrolled in the placebo arms of HPV vaccine trials. For example, whereas the incidence of HPV-16 was 4.4 per 100 person-years in our study, placebo-arm incidence of HPV-16 was 5.9 per 100 person-years in the quadrivalent vaccine trial [Insinga et al., 2010] and 5.0 per 100 person-years in the bivalent vaccine trial [Ramanakumar et al., 2016].

We did not find evidence that sex with partners met online, per se, increases the risk of HPV infection for young women. While reporting recent new or multiple male sex partners was associated with increased infection risk (similar to results in our mid-adult cohort [Winer et al., 2016]), whether or not a partner was met online was unassociated. Similarly, in our previous analysis of the baseline data from this cohort, meeting partners online was not associated with prevalent oncogenic HPV [Barrere et al., 2015]. Furthermore, in our previous study of 25- to 65-year-old women, online dating was associated with prevalent but not incident HPV [Winer et al., 2016; Winer et al., 2012]. Other studies on the associations between online sex partner seeking and STI risk have been equivocal [Al-Tayyib et al., 2009; McFarlane et al., 2000; Ross et al., 2008]. As we noted previously [Barrere et al., 2015], broad and varying definitions of online dating and continually evolving modes of seeking partners online complicate studying and interpreting effects on STI risk. Furthermore, with online partner seeking becoming increasingly common and mainstream (particularly in young adults) [Smith, 2016], meeting partners online may not in and of itself be indicative of high-risk sexual behavior.

While lifetime number of male sex partners (a measure inclusive of both past and recent partners) was positively associated with incident HPV, the observed associations were not statistically significant. As for other sexual behavior risk factors, we note that there was a positive association between inconsistent condom use and incident HPV infection. While not statistically significant, the direction and magnitude of effect aligns with our previous finding of a significant association between inconsistent condom use and prevalent oncogenic HPV infection in our cross-sectional analysis of young female online daters [Barrere et al., 2015].

In summary, in our cohort of young women, incident HPV was common and associated with recent high-risk sexual behavior, though not online dating per se. Furthermore, although not statistically significant after adjusting for sexual history, self-reported history of HPV vaccination showed substantial protection against acquiring vaccine-type HPV. Study limitations should be noted. The sample size was relatively small, and thus power was limited for analyses of certain risk factors. Furthermore, our study was a convenience sample of 18- to 24-year-old female online daters in the United States followed from 2010–2012. Results may not generalize to all young female online daters, especially given evolving technologies for seeking sex partners online and changing usage patterns over time. Future studies should aim to capture more detailed information on the technologies and patterns of seeking sex partners online to more completely evaluate impact on HPV incidence.

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Figure 1. Cumulative incidence of detecting new type-specific HPV infections not present at baseline, including any clinically-relevant HPV type (thick black line), any oncogenic HPV type (thin black line), and any vaccine HPV type (grey line). Data are for 164 women aged 18–24 years. Error bars represent 95% confidence intervals.

Table 1

Demographic, health, and sexual history characteristics of 18- to 24-year-old female online daters (N=164)

Characteristic	n ^a (%)
Age at first visit, years	
18–19	16 (9.8)
20–21	43 (26.2)
22–23	67 (40.9)
24–25 ^b	38 (23.2)
Race	
African American	35 (21.9)
Asian	15 (9.4)
White	85 (53.1)
Other ^c	25 (15.6)
Hispanic ethnicity	
No	136 (87.7)
Yes	19 (12.3)
Geographic region ^d	
Midwest	42 (25.8)
Northeast	40 (24.5)
South	28 (17.2)
West	53 (32.5)
Highest level of education completed	
Some postsecondary education or less	110 (67.9)
Bachelor's degree or higher	52 (32.1)
Current marital status	
Unmarried / Separated	121 (75.6)
Married / Unmarried, living with a partner	39 (24.4)
Ever pregnant	
Yes	38 (23.5)
No	124 (76.5)
Smoking status	
Current	28 (17.2)
Former	18 (11.0)
Never	117 (71.8)
Currently using hormonal contraceptives	
Yes	50 (30.9)
No	112 (69.1)
History of an abnormal Pap test result ^e	
Yes	33 (27.3)
No	88 (72.7)
History of genital warts	

Characteristic	n ^a (%)
Yes	8 (4.9)
No	154 (95.1)
History of HPV vaccination	
No	104 (64.2)
Yes	58 (35.8)
Number of doses ^f	
1 dose	7 (13.2)
2 doses	11 (20.8)
3 doses	35 (66.0)
Age at first intercourse, years ^g	
15	50 (30.9)
16–17	54 (33.3)
18	58 (35.8)
Lifetime number of male sex partners ^h	
1–2	29 (18.0)
3–5	39 (24.2)
6–7	30 (18.6)
8–14	30 (18.6)
15	33 (20.5)
Male sex partners in last 6 months	
0 male partners	11 (6.8)
1 male partner, non-new	56 (34.8)
new male partner(s) or multiple partners	94 (58.4)
Oncogenic HPV positive ⁱ	
Yes	53 (32.3)
No	111 (67.7)
Clinically-relevant HPV positive ^j	
Yes	53 (32.3)
No	111 (67.7)
Vaccine-type HPV positive ^k	
Yes	18 (11.0)
No	146 (89.0)

^a164 (84% of 195) women returned a baseline self-collected sample and 1 follow-up sample that were sufficient for HPV DNA testing; numbers may not add up to totals due to missing data.

^b5 women turned 25 years-old between screening and the first visit.

^cIncludes individuals reporting other races (American Indian, Alaska Native, Native Hawaiian, other Pacific Islander) or multiple races.

^dNortheast includes states: CT, MA, NJ, NY, PA, RI; Midwest includes states: IL, IN, KS, MI, MN, MO, ND, OH, WI; South includes states: AR, FL, GA, MD, MS, OK, TN, TX, and DC; West includes states: AZ, CA, CO, OR, WA, WY.

^eRestricted to women 21 years of age or older at the first visit.

^f 5 women who self-reported a history of HPV vaccination (8.6%) did not answer the question on number of doses received.

^g Approximate tertiles.

^h Approximate quintiles.

ⁱ Positive for any of the following 19 carcinogenic, probably carcinogenic, or possibly carcinogenic types: 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82, IS39.

^j Positive for any of the following clinically-relevant HPV types: 6, 11, 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82, IS39.

^k Positive for any of the following quadrivalent vaccine HPV types: 6, 11, 16, 18.

Table 2

Type-specific incidence rates of newly detected HPV in 18- to 24-year-old female online daters (N=164)

HPV Type(s)	No. of Women with Incident Detection	No. of Person-Years at Risk	Incidence Rate per 100 Person-Years (95% CI)
Any clinically-relevant HPV ^a	100	3456	36.9 (28.0–48.5)
Any vaccine-type HPV ^b	15	661	7.2 (4.1–12.8)
HPV 16 and/or HPV 18	9	325	4.2 (2.0–8.8)
HPV 6 and/or HPV 11	6	335	3.6 (1.6–7.9)
Any oncogenic HPV ^c	94	3210	34.4 (25.9–45.6)
HPV 6	6	163	3.7 (1.7–8.2)
HPV 11	0	172	0
HPV 16	7	158	4.4 (2.1–9.3)
HPV 18	2	168	1.2 (0.3–4.8)
HPV 26	0	172	0
HPV 31	5	156	3.2 (1.3–7.7)
HPV 33	1	172	0.6 (0.1–4.1)
HPV 35	4	168	2.4 (0.9–6.4)
HPV 39	8	159	5.0 (2.5–10.1)
HPV 45	1	171	0.6 (0.1–4.1)
HPV 51	6	160	3.8 (1.7–8.4)
HPV 52	9	163	5.5 (2.9–10.6)
HPV 53	9	161	5.6 (2.9–10.8)
HPV 56	9	158	5.7 (3.0–11.0)
HPV 58	6	164	3.7 (1.6–8.1)
HPV 59	6	161	3.7 (1.7–8.3)
HPV 66	7	157	4.5 (2.1–9.4)
HPV 68	5	163	3.1 (1.3–7.4)
HPV 73	3	169	1.8 (0.6–5.5)
HPV 82	5	170	2.9 (1.2–7.1)
HPV IS39	1	172	0.6 (0.1–4.1)

^aPositive for any of the following clinically-relevant HPV types: 6, 11, 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82, IS39.^bPositive for any of the following vaccine-type HPV: 6, 11, 16, 18.^cPositive for any of the following 19 carcinogenic, probably carcinogenic, or possibly carcinogenic HPV types: 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82, IS39.

Table 3

Odds Ratios (ORs) for associations between risk factors and incidence of clinically-relevant HPV in 18- to 24-year-old female online daters (N=3,347 women-types)

	No. of Incident Detections ^a	n ^b	Univariate OR (95% CI)	Multivariate OR (95% CI) ^c
Age, years				
18–19	8	246	Ref (1.0)	
20–21	18	890	0.51 (0.23–1.10)	
22–23	32	1,422	0.55 (0.21–1.45)	
24–26	42	1,513	0.58 (0.22–1.54)	
Race				
African American	18	733	Ref (1.0)	
Asian	12	303	1.70 (0.56–5.21)	
White	52	1,739	1.23 (0.55–2.76)	
Other ^d	15	489	1.25 (0.51–3.01)	
Hispanic ethnicity				
No	87	2,801	Ref (1.0)	
Yes	6	361	0.54 (0.25–1.17)	
Age at first intercourse, years				
15	30	1,015	Ref (1.0)	
16–17	39	1,088	1.16 (0.60–2.21)	
18	31	1,202	0.82 (0.39–1.71)	
Marital status				
Unmarried / Separated	70	2,733	Ref (1.0)	
Married / Unmarried, living with a partner	30	1,257	1.11 (0.62–1.99)	
Lifetime number of male sex partners at baseline				
1–2	8	599	Ref (1.0)	Ref (1.0)
3–5	23	797	2.30 (0.59–9.00)	1.77 (0.45–7.01)
6	68	1,890	3.03 (0.83–11.09)	2.39 (0.65–8.77)
Ever pregnant				
No	74	2,437	Ref (1.0)	
Yes	26	1,012	0.97 (0.54–1.76)	
Currently using hormonal contraceptives				
No	74	2,569	Ref (1.0)	
Yes	26	1,075	1.00 (0.53–1.88)	
Smoking status				
Never	62	2,240	Ref (1.0)	
Former	24	789	1.37 (0.69–2.73)	
Current	14	678	1.07 (0.43–2.68)	
Ever had an abnormal Pap test ^e				
No	49	1,823	Ref (1.0)	
Yes	26	860	1.18 (0.65–2.12)	

	No. of Incident Detections ^a	n ^b	Univariate OR (95% CI)	Multivariate OR (95% CI) ^c
History of HPV vaccinations ^f				
No	65	1,977	Ref (1.0)	
Yes	35	1,467	0.75 (0.42–1.34)	
Number of male sex partners in the past 6 months				
0 male partner	2	430	Ref (1.0)	
1 male sex partner	98	3,139	5.61 (1.40–22.43)	
<i>For women with 1 male sex partner in the past 6 months^g</i>				
Number of male sex partners				
1 male sex partner	39	2,280	Ref (1.0)	
2 male sex partner	59	1,880	2.09 (1.23–3.56)	
New sex partners				
0 new male partner	28	2,090	Ref (1.0)	
1 new male partner	70	2,174	2.32 (1.32–4.05)	
Male sex partners				
w/concurrent partnership				
0 male sex partners	40	1,704	Ref (1.0)	
w/concurrent partnership				
1 male sex partners	47	1,472	1.46 (0.83–2.59)	
w/concurrent partnership				
Unknown concurrent partnership status	11	1,017	0.60 (0.23–1.56)	
Male sex partners met online				
0 male sex partners met online	58	2,082	Ref (1.0)	
1 male sex partners met online	40	1,663	0.91 (0.53–1.55)	
Condom use ^h				
Always	17	1,043	Ref (1.0)	
Not always	81	2,520	1.73 (0.83–3.58)	
<i>Composite variable for women with sexual behavior in the past 6 months for multivariate analysis</i>				
Sexual behavior with male partners				
0 sex partners	2	430	Ref (1.0)	Ref (1.0)
1 partner (not new)	24	1,887	3.28 (0.78–13.82)	3.01 (0.73–12.38)
New and/or multiple partners	74	2,416	7.39 (1.83–29.95)	6.38 (1.56–26.02)

^aClinically-relevant HPV types (6, 11, 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82, IS39).

^bThe 164 women contributed an observation for each type for which they tested negative at baseline, or N=3,347 women-types. However, women-types could change categories throughout follow-up for time-dependent variables; therefore the number of women-types at risk (n) may exceed total N for time-dependent variables.

^cMultivariate analysis with all women included, with a composite variable replacing individual risky sexual behaviors.

^dIncludes individuals reporting other race or multiple races.

^eRestricted to women 21 years or older at the first visit.

^fCoded “no” if self-reported no history of HPV vaccination and “yes” if self-reported at least 1 dose HPV vaccine.

^gRestricted to women reporting a male sex partner in the past 6 months

^hThe variable was coded as “always” if the subject reported always using condoms with all male partners during the past 6 months. If a subject reported not always using condoms with at least 1 male partner, the variable was coded as “not always.” Otherwise, if condom use data were missing for at least 1 partner, the variable was set to missing. a

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Table 4

Odds ratios (ORs) for associations between self-reported HPV vaccination and incidence of vaccine-type HPV in 18- to 24-year-old female online daters (N=635 women-types)

	No. of Incident Detections ^a	n ^b	Univariate OR (95% CI)	Multivariate OR (95% CI) ^d
History of HPV vaccination ^c				
No	13	373	Ref (1.0)	Ref (1.0)
Yes	2	279	0.21 (0.05–0.86)	0.36 (0.09–1.43)

^aVaccine-type HPV (6, 11, 16, and 18)

^bThe 164 women contributed an observation for each vaccine-type for which they tested negative at baseline, or N=635 women-types. Women-types could change categories throughout follow-up for time-dependent variables; therefore the number of women-types at risk (n) may exceed total N for time-dependent variable.

^cCoded “no” if self-reported no history of HPV vaccination and “yes” if self-reported at least 1 dose HPV vaccine.

^dThe multivariate model was adjusted for lifetime number of male sex partners at baseline and a composite sexual behavior variable reflecting sexual behavior in the past 6 months: no male sex partner, 1 non-new partner, new and/or multiple male partners. Due to some zero-cells, we used Firth's penalized likelihood logistic regression to estimate the odds ratio. To account for within-subject correlation, we permuted HPV vaccine status across women (1000 permutations) to evaluate the p-value. The p-values from the Firth model and the permuted distribution were 0.148 and 0.143, respectively.