Correlates of HPV vaccination and association with HPV-16 and HPV-18 DNA detection in young women

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Abstract

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Background: Human Papillomavirus (HPV) infection, primarily with high-risk (HR) types 16 and 18, is responsible for causing 17,600 cancers in women and 9,300 cancers in men in the US each year. However, the availability of the HPV vaccination series has substantially reduced the prevalence of vaccine-type HPV.

Methods: We employed a cross-sectional study design to assess factors associated with HPV vaccine uptake, the effectiveness of HPV vaccination outside of a vaccine efficacy trial, and patterns of HPV vaccination in 21-29 year old women who were eligible to receive catch-up vaccination. Data came from the HOPE (Home HPV or Pap Exam) study, a randomized controlled trial based at the University of Washington, and included self-reported demographic and HPV vaccination information and researcher-reported typing for 14 high-risk HPV types. We used multivariable logistic regression to obtain crude and adjusted prevalence odds ratios and 95% confidence intervals for our associations of interest.

Results: Of 375 subjects, 228 (60.8%) reported receipt of at least one dose of HPV vaccine at study entry, and 16 subjects (4.3%) were infected with HPV 16 and/or 18. Individuals with higher levels of education were more than four times as likely to be vaccinated than those reporting high school education or less. Among vaccinated study participants, 56.5% received their first dose of the HPV vaccination after age 18

and 68.4% after first vaginal intercourse. Unvaccinated women were somewhat more likely to have detectable HPV 16 and/or 18 (OR=2.05, 95% CI: 0.75 – 5.64). Women aged 19-26 at first HPV vaccination dose were more likely to have HPV types 16 and/or 18 compared to women who were vaccinated earlier (OR=3.2, 95% CI: 0.35 – 29.2). Similarly, women who received their first vaccination dose after first vaginal intercourse were more likely to be HPV infected (OR=1.89, 95% CI: 0.22 – 16.2).

Conclusion: Our study suggests that increased education, perhaps through targeted campaigns in less educated populations, may reduce disparities in HPV vaccination uptake and that the HPV vaccine is effective at preventing HR-HPV types 16 and 18 among women from 20 to 29 years old outside of vaccine efficacy trials. Generalizable research on patterns of HPV vaccination and vaccine efficacy among larger sample sizes of women in their twenties is needed.

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Table of Contents

Introduction:

Human Papillomavirus (HPV) is the most common sexually transmitted infection in the United States (US), infecting approximately 79 million Americans.[1] In the US, HPV is responsible for causing approximately 17,600 cancers in women and 9,300 cancers in men each year.[1] Globally, 70% of cervical, 87% of anal, 60% of oropharyngeal, and 31% of penile cancers are caused by HPV types 16 and 18, the most common high-risk types of HPV (HR-HPV). [2-3] HR-HPV types 31, 33, 45, 52, and 58 cause an additional 20% of all cervical cancer[4] and HPV types 6 and 11, although considered low-risk for developing cancer, cause 90% of genital warts.[5]

Since the HPV vaccination series became available in the US, there has been a significant reduction in the prevalence of vaccine-type HPV.[6-7] The three approved HPV vaccines in the US include Gardasil®, approved in 2006 which protects against HPV 6, 11, 16 and 18, Gardasil 9®, approved in 2014 which protects against HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58, and Cervarix®, approved in 2009 which protects against HPV types 16 and 18.[8] Current guidelines from the Centers for Disease Control and Prevention (CDC) recommend routine HPV vaccination for individuals aged 11-12 years, and vaccination up to age 26 years for women and 21 years for men who have not been adequately vaccinated.[9] The CDC considers females aged 13 years and older at vaccination to be in the vaccination catch-up phase, meaning they are outside of the ideal age group, but are still recommended to receive the vaccine.

Originally, three doses of the HPV vaccine were recommended for females, given at 0, 1-2, and 6-month increments, as vaccine efficacy trials demonstrated that the three dose series was effective.[10-14] However, as subsequent research demonstrated that two doses were equally effective at preventing vaccine-type HPV among girls[15-20] the HPV vaccine recommendations were updated. Currently, two doses of the HPV vaccine, given 6-12 months apart, are recommended for individuals who start the series before age 15 and three doses, given at 0, 1-2, and 6-month increments are recommended for those who begin the series at or after age 15 or who are immunocompromised.[9] Ongoing research is beginning to show that two doses may be equally effective at preventing HPV among females in the catch-up phase[18, 20-21] and that even one dose may be effective at preventing vaccine-type HPV.[21-22] However, more research is needed to determine if any changes to current guidelines should be made.

Prior studies have demonstrated that there are demographic differences, including differences in race,

age, insurance status, and education level between younger girls [23-28] as well as females in the vaccination catch-up population [29-32] who are and are not vaccinated, though results are inconsistent. Increased research is needed to help clarify and reduce these inconsistencies so that public health practitioners and clinicians can effectively increase HPV vaccination uptake. Furthermore, to improve utility of vaccine efficacy trial findings, research that includes data from individuals who have received HPV vaccination outside of clinical trial settings and from individuals in the HPV vaccination catch-up phase is needed. It is likely that factors related to vaccine efficacy, including age at first dose, timing between doses, and experiencing first vaginal intercourse prior to vaccination are associated with HR-HPV infection, but the rigorous methods used in vaccine efficacy trials are not representative of vaccine delivery patterns outside of clinical trial settings. This makes it difficult to assess the true effectiveness of the HPV vaccine among the general population.

There were two primary aims of this study. The first was to assess factors associated with HPV vaccine uptake among females aged 21-29 who were enrolled in a clinical trial to evaluate cervical cancer screening strategies. The second was to assess the effectiveness of HPV vaccination in 21-29 year old women who were eligible to receive catch-up vaccination. We hypothesized that there would be differences in risk factors among vaccinated and unvaccinated women and that the HPV vaccine would be effective at preventing HR-HPV 16 and/or 18 in this age group. In addition, we sought to characterize patterns related to HPV vaccination receipt, including age at first dose, timing between doses, and age at first vaginal intercourse relative to vaccine series initiation, as well as to examine whether either age at first dose or vaccination prior to first vaginal intercourse were associated with detection of HR-HPV 16 and/or 18 DNA. Finally, we aimed to examine the association between number of doses received and detection of HR-HPV 16 and/or 18 DNA, in order to add to this increasing body of research.

Methods:

Study design and data sources:

This study employed a cross-sectional study design for all study aims, using baseline enrollment data collected from the HOPE (Home HPV or Pap Exam) clinical trial.

The HOPE study was a National Cancer Institute (NCI)-funded randomized controlled trial based out of the University of Washington, with the overall aims of assessing the acceptability and effectiveness of

home-based HPV screening compared to traditional Pap-based cervical cancer screening.[33] The HOPE study enrolled 1819 women between 21-65 years of age, from two University of Washington (UW) research clinics. Study recruitment began in March 2012 and ended in December 2014. Women who were less than 21 years, received treatment for cervical dysplasia within three years, received colposcopy of the cervix within two years, received a Pap test within one year, had undergone a hysterectomy, were pregnant at time of enrollment, or who were immunocompromised were excluded from this study.[33]

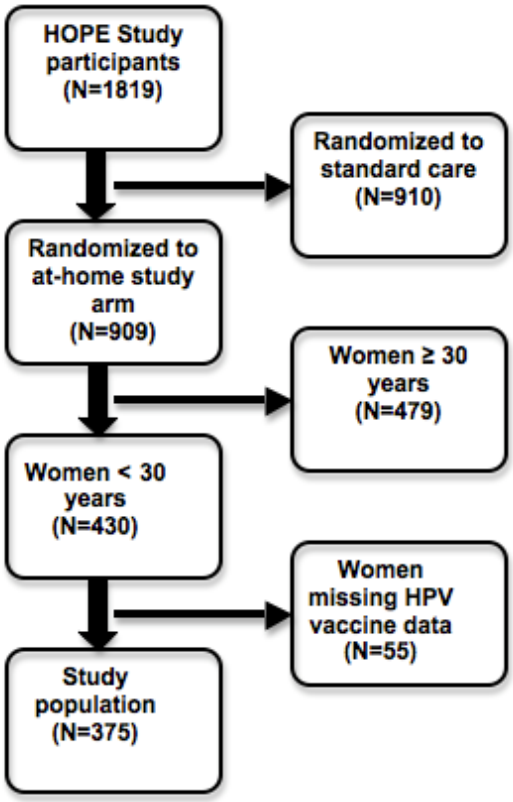
For women under 30 years old, standard care was defined as in-clinic cytology screening every three years, with HPV-based triage of women with atypical squamous cells of uncertain significance (ASCUS) and referral to colposcopy of all women with squamous intraepithelial lesion (SIL) and/or HPV+ ASCUS. For women 30 years or older, standard care was defined as screening by Pap and HPV every three years with referral to colposcopy of those who were HPV 16/18+ or with cytology > ASCUS, with retesting of those who were positive for other HR-HPV at one year. The novel approach was characterized as follows: Every three years HR-HPV testing of at home self-collected samples with in-clinic cytology of HR-HPV positive women and referral to colposcopy of women with cytology ≥ ASCUS with repeat HPV testing of HR-HPV positive but cytology negative women at one year.[33]

Women randomized to the at-home testing study arm were given a self-collect kit, which included two individually packed sterile Dacron tipped swabs for sample collection and one polypropylene specimen transport tube with shipping and packing materials, to obtain self-collected samples of vaginal cells. After the vaginal sample was collected using the swab and deposited into the transport tube, study participants were directed to write the date of sample collection on the tube and to enclose their tube in the provided packaging materials. They then placed the tube and their completed questionnaire into a USPS Priority Mail box and shipped their samples to the laboratory, where HR-HPV DNA of self-collected specimens was evaluated by a Hybrid Capture.[33] The Hybrid Capture provided information on whether the samples were positive for any of 13 HR-HPV types. Samples that tested positive for HR-HPV were assessed for 14 individual HR-HPV types by a Luminex-based liquid bead microarray assay (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68). [33] Of the 103 women who were found to be infected with HR-HPV at baseline, 95 were typed using Luminex-based liquid bead microarray assay and 8 samples were excluded from typing.

HOPE study participant characteristics were collected at baseline through the self-administered questionnaire that was included with the self-collect kit. Data on HR-HPV results and typing were collected and recorded by study researchers during round one of the HOPE study visits, the same round in which baseline data was collected.

This study was a secondary analysis of first visit HOPE study data. In this way, all data regarding predictors of interest and vaccination status were self-reported through the written questionnaire. Study outcome data were collected through either the written questionnaire or through laboratory recorded data. Study participants who were not randomized to the at-home HPV testing arm of the HOPE study (n=910) were excluded in this secondary analysis, as HPV testing data were not collected for these individuals. Furthermore, women who were thirty years of age or older (n=479) at baseline were excluded as these women would not have met the recommended eligibility criteria to receive HPV vaccination during any period of their lives. Finally, those for which HPV vaccination data was not collected (n=55) were also excluded. Our final study population included 375 individuals (Figure 1).

Figure 1: Study Population Flowchart



Predictors:

The predictors of interest for aim 1 of our study were race (White, Black, Asian, Pacific Islander, Native American, other), current age in years (21-23, 24-26, 27-29), highest level of education completed (high school or less, associate or technical degree, bachelor's degree, graduate school), ever use of hormonal contraception (yes, no), and age at first vaginal intercourse in years (9-15, 16-18, 19-21, 22-27) as prior research has demonstrated associations between these predictors and HPV vaccination status. [23-29, 34]

The primary predictor of interest for aim 2 of our study was self-reported HPV vaccination. Individuals who received at least one dose of the HPV vaccination series were considered vaccinated (n=228) and individuals who received no doses were considered unvaccinated (n=147). We also categorized vaccination status by doses received (0, 1, 2, 3) in order to address our sub-analysis on the association between HPV vaccination doses and HPV 16 and/or 18 DNA detection. Data regarding HPV vaccination doses received were collected through a question asking individuals if they had received the HPV vaccine (yes, no) and if so, how many doses (1, 2, 3).

To assess dosing patterns associated with HPV vaccination and our sub-analyses for study aim 2, we included age at first dose of the HPV vaccination series in years (12-18, 19-26), timing between doses in months (6 or fewer, 7-12, 13-18, 20 or more), and timing of vaccination in relation to first vaginal intercourse (prior, same year, after).

We computed four predictor variables from HOPE study data. These included age at first HPV vaccination dose, time between dose one and two, time between dose two and three, and vaccination in relation to first vaginal intercourse. To compute age at first HPV vaccination dose, we calculated the time between the study enrollment date and self-reported date of HPV vaccine dose one receipt. We then subtracted this number from baseline age, giving us the age that study participants received their first HPV vaccination dose. Categorization for this variable is defined above. We were missing a substantial amount of data for month and/or day at first dose. To address this problem, we replaced all missing month data for HPV dose one with July and all missing day data for dose one with the first of the month. In this way, participants missing both day and month were placed in the middle of the year, July 1st.

To compute time between doses one and two, we subtracted self-reported date of HPV vaccine dose one receipt from date of dose two receipt, converted time into months, and categorized the variable as

defined above. We repeated this calculation to determine the time between doses two and three. For these variables, we did not impute missing data, as the specific date was necessary to accurately characterize this information. To compute vaccination in relation to first vaginal intercourse, we used age at first vaccination dose and age at first vaginal intercourse. If age at first vaccination dose was less than age at first vaginal intercourse, then women were coded as being vaccinated prior to first vaginal intercourse; if age at first vaccination was greater than age at first vaginal intercourse, women were coded as being vaccinated after first vaginal intercourse; if these ages were the same, then women were coded as being vaccinated the same year as first vaginal intercourse.

Outcomes:

The outcome of interest for our first study aim, assessing differences in demographic characteristics between unvaccinated and vaccinated women, was self-reported HPV vaccination status (1 or more doses, no doses).

Vaccine-type HR-HPV prevalence (positive for HR-HPV 16 and/or 18, negative for HR-HPV 16 and 18), determined through Luminex-based liquid bead microarray assay, was the outcome of interest for our second study aim and sub-analyses.

Statistical Analysis:

To assess significant differences in demographics between vaccinated and unvaccinated women, we used multivariable logistic regression to obtain crude and adjusted odds ratios and 95% confidence intervals for the associations between all predictors of interest (age, race, education, use of hormonal contraception, and age at first vaginal intercourse) and HPV vaccination. Race was dichotomized as white versus other due to small sample sizes for other racial categories. Our adjusted statistical model included all predictors of interest, determined a priori, thus correcting for any potential confounding.

To evaluate the association between self-reported vaccination status and prevalence of HR-HPV 16 and/or 18 DNA, we calculated odds ratios and 95% confidence intervals using logistic regression. We repeated this analysis, replacing vaccination status with number of doses, assessed as a categorical variable, as our exposure of interest in order to examine the association between HPV vaccine doses and detection of HR-HPV 16 and/or 18 DNA.

In order to characterize age at first dose and timing between doses, we used simple counts and proportions. To evaluate our sub-analyses, assessing whether age at first dose or vaccination prior to first vaginal intercourse were associated with self-reported vaccination status and HR-HPV type detected, we calculated prevalence odds ratios and 95% confidence intervals using univariate logistic regression. We assessed both age at first dose and vaccination relative to first vaginal intercourse as separate exposures, and detection of HR-HPV 16 and/or 18 DNA as our outcome. We were unable to adjust for potential confounders in these models due to small sample sizes.

All research activities were approved by the study data safety and monitoring board, the University of Washington (No. 7489 approved July 20, 2011 and No. 9028 approved November 20, 2013) and University of Minnesota Institutional Review Boards (No. 1109M04321 approved October 5, 2011). All analyses were performed using STATA 14.[39]

Results:

Of 375 subjects, 228 (60.8%) reported receipt of at least one dose of the HPV vaccine at study entry (Table 1). Women who were vaccinated for HPV tended to be younger, were more likely to be white, and were more likely to have used hormonal contraception compared with unvaccinated women. Unvaccinated women were more likely to have high school education or less compared with vaccinated women. The greatest proportion of women were between 16-18 years at first vaginal intercourse in both vaccinated and unvaccinated groups, however unvaccinated women were more likely to be early as well as late initiators of vaginal intercourse.

In univariate analyses, we detected statistically significant differences in vaccination status by age, race, education level, and ever use of hormonal contraception (Table 2). Younger women, white women, women with higher levels of education, and women who had reported use of hormonal contraception at any point in their lives were statistically significantly more likely to be vaccinated. After adjustment for all predictors of interest, the associations between both education and vaccination status and age and vaccination status strengthened. Specifically, in our multivariable analysis, individuals with higher levels of education, reporting bachelor's or graduate level education, were more than four times as likely after adjustment to be vaccinated as those reporting high school or less as their highest level of education. In regards to age, women aged 27-29 were approximately two-thirds less likely to be vaccinated than women

aged 21-23 years. In the final multivariable model, the association between race and vaccination status became less strong, while the association between ever use of hormonal contraception and vaccination status stayed the same. However, neither of these associations were statistically significant after adjustment. There was no statistically significant evidence to support that age at first vaginal intercourse was associated with HPV vaccination status.

Among study participants at baseline, the highest proportion of women (46.9%) had received three doses of the HPV vaccination series (Table 3). Among vaccinated study participants, 56.5% received their first dose of the HPV vaccination after age 18. The greatest proportion of our vaccinated study participants reported waiting 7-12 months between doses 1 and 2 as well as between 2 and 3 (42.9% and 38.2%, respectively). The majority of vaccinated study participants (68.4%) received their first dose of the HPV vaccine after first vaginal intercourse.

HPV 16 and/or 18 was detected in 16 (4.3%) women. Detection of HR-HPV 16 and/or 18 was higher among unvaccinated compared with vaccinated women (OR = 2.05, 95% CI: 0.75 – 5.64), although this association was not statistically significant (Table 4). We did not detect any statistically significant differences in detection of HR-HPV types 16 and/or 18 by number of HPV vaccination doses received, however, the odds of HR-HPV 16 and/or 18 detection was higher among those with one or no doses of the vaccine compared with two or three doses. Furthermore, although statistically insignificant, the odds of detecting HR-HPV 16 and/or 18 among women aged 19-26 at first dose was 3.2-fold higher compared with women aged 12-18. There was an 89% increase in the odds of HR-HPV 16 and/or 18-detection among women who received their first HPV vaccination dose after first vaginal intercourse, compared with women who received their first dose prior to first vaginal intercourse. Overall vaccine efficacy among our study population was 49.2%.

Discussion:

Our study demonstrates that among females aged 21-29 who were eligible for catch-up HPV vaccination, those who are younger and have received higher levels of education are more likely to be vaccinated for HPV than females who are older or have received lower levels of education. In looking at HPV dosing patterns, nearly half of our participants received all three recommended doses of the HPV vaccine. This finding may be an indication of the sampling strategy used in the HOPE study, which recruited

females who were already actively engaged in the health care system. Over two-thirds of our catch-up study population experienced first vaginal intercourse prior to HPV vaccine initiation, however, age at first vaginal intercourse was not associated with vaccination status. Moreover, most women did not receive their HPV vaccinations according to the recommended dosing schedule.

Additionally, our study suggests that the HPV vaccine is effective at preventing HR-HPV types 16 and 18 among women in the catch-up population outside of vaccine efficacy trials, especially when vaccination guidelines are followed. Although our results were statistically insignificant and vaccine efficacy was 49.2% overall, 6 of the 7 women who were vaccinated for HPV and tested positive for HR-HPV 16 and/or 18 received their first dose of the vaccine after first vaginal intercourse. Our data suggests similar protection among women who have obtained two and three doses, but a substantial decrease in protection among women who had received only one dose of the HPV vaccine.

Prior research on the association between education and HPV vaccination has focused on adolescent females, has included only parental educational status, rather than patient educational status, and has produced inconsistent findings. For instance, many studies have found no significant difference between parental education and HPV vaccination, [49-53] one study found higher vaccination prevalence among more educated parents, [26, 54] and one study found lower vaccination prevalence among more educated parents, [55] yet none of these studies include females older than 18 years. Our study adds to the literature by including females older than 18 years and demonstrating that, among this older age group, higher educational attainment is associated with higher prevalence of HPV vaccination.

Studies that have included women older than 18 have found that this age group is less likely to be vaccinated than adolescent women [25, 46] and that among females 18-26, older women are less likely to be vaccinated. [25] Moreover, prior research including the HPV vaccination catch-up population has demonstrated differences in vaccination uptake and completion by race, with white race being associated with higher uptake and completion of the series than other racial categories. [23, 28, 46] These findings are consistent with our study results.

Compared with prior studies evaluating HPV vaccination and dosing patterns outside of clinical trials that have included women in the catch-up population, women in our study had a similar prevalence of vaccine series completion but a lower prevalence of on-time series completion. [43, 46, 48] Similar to our study,

many of these studies recruited participants from university-based clinical settings and included women in their twenties.[43, 44, 48] However, unlike our study, most of these studies include adolescent participants.[43, 44, 48] When compared to studies that utilize non-university-based sampling frames, we still observe comparable results. [7, 45-47] Our findings suggesting that older age and receipt of the first dose of the HPV vaccine series after first vaginal intercourse are associated with higher detection of HR-HPV 16 and/or 18 are consistent with findings from clinical trials that include the catch-up population, [57-60] however, these associations are understudied outside of trial settings.

This study adds to the increasing body of research that demonstrates differences between females who are and are not vaccinated. Moreover, although prior research has demonstrated the effectiveness of the HPV vaccine, few studies have assessed HPV vaccine effectiveness among women outside of efficacy trials. [7, 40-42] Additionally, the research methods and participant demographics vary greatly between these existing studies, making them difficult to compare. For instance, although our findings suggesting vaccine effectiveness are consistent with prior studies, of these studies, two use data from CDC's National Health and Nutrition Examination Survey [7, 41], one includes females recruited via the internet, [40] and one includes only inner-city adolescent females. [42] Among the limited existing research, our vaccine effectiveness results are lower, with one study finding effectiveness as high as 82% with only one dose of the HPV vaccine.[7] Similar to our study, this study relied on self-report data, however, this effectiveness estimate included adolescent women, who we know to have different risk factors than women in the catch-up population.

The use of self-report data in this study was a strength in that we were able to obtain rich data on past sexual and reproductive health experiences, which can be difficult to obtain through clinical databases alone. Through a combination of baseline self-report data and laboratory acquired clinical testing results, we were able to assess the association between detection of HR-HPV 16 and/or 18 and receipt of the first dose of the HPV vaccine series after first vaginal intercourse, which prior observational studies have been unable to assess. Furthermore, unlike those in vaccine efficacy trials, the HPV dosing patterns of women in this study are indicative of HPV dosing patterns of women in their twenties presenting to a health clinic for cervical cancer screening.

A primary limitation of this study is its cross-sectional design, which prevents us from being able to assess protection against incident HR-HPV. Furthermore, our small sample size of women who tested

positive for HPV 16 and/or 18 made us underpowered to generate statistically significant associations related to HR-HPV 16 or 18-detection. Although use of self-report data was necessary for us to collect the data we needed on prior sexual experiences and HPV vaccination dosing patterns, self-report data is subject to both recall [61] and social desirability biases.[62] Specifically, reliance on self-report data led to a substantial amount of missing data, and potentially misreported data, on the number and date of HPV vaccination doses. Even after imputing data on month and day of vaccination doses, we were still missing 46.7% of data for the date of first vaccine dose among our study population. The proportion of missing data differed between those with and without HR-HPV 16 and/or 18-detection, which may have led to misclassification of these exposures. Finally, the majority of our study participants were white and a large proportion of our non-white study participants were Asian. Although this distribution is reflective of the racial distribution in Seattle and King County, we were unable to assess the influence of particular racial categories on vaccination status as prior studies have demonstrated.

Our study shows that there is significant potential to increase protection from HPV among females who are less educated or greater than 21 years old. Nearly 40% of our study population was unvaccinated for HPV at baseline, even though most were still under 26 years old, meaning that they were within CDC's recommended vaccination age group. Targeted HPV vaccination campaigns are needed to prevent vaccine-type HPV and subsequent cancer among these groups of women.

Our findings further imply that targeting females prior to sexual debut is necessary for protection from vaccine-type HPV. Among vaccinated study participants, we only detected HPV 16 and/or 18 for one individual who was vaccinated prior to first vaginal intercourse. However, the majority of our vaccinated study population, 68.4%, received their first dose of the HPV vaccine after first vaginal intercourse. Although opportunistic vaccination among the catch-up population is common and lends itself to imperfect vaccination circumstances, improving outreach efforts for HPV vaccination among females before they experience sexual debut has the potential to decrease vaccine-type HPV infection.

In addition, our findings indicate that many women who begin the HPV vaccination series are only obtaining one or two vaccine doses in the series, rather than completing the full series. This was true for approximately a quarter of our vaccinated study participants and is a further indication of widespread opportunistic vaccination among this older age group. Completing the dosing schedule is important for

vaccine-type HPV protection and clinicians should be diligent in subsequent visits to ensure full vaccine series completion among their patients. Reliance on opportunistic vaccination alone is not sufficient. More research is needed to assess whether one dose will adequately protect individuals from vaccine-type HPV, especially among catch-up phase populations outside of vaccine efficacy trials, in which many individuals may not be able to comply with vaccination guidelines as demonstrated in this study.

Through targeted interventions and increased research among populations outside of clinical trials, we have the potential to increase vaccine-type HPV protection among females most at-risk for acquiring HR-HPV. Furthermore, if research demonstrates that fewer doses are needed to obtain similar protection from acquiring HR-HPV, we may be able to increase access to HPV vaccination and subsequent vaccine-type HPV protection at a lower cost and burden for both healthcare consumers and providers.

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Tables

Table 1: Baseline characteristics of females 21-29 years old who were enrolled in the HOPE Study, 2012-2014

Characteristics	Vaccinated [a]		Unvaccinated	
N=375	**n=228**	**60.8%**	**n=147**	**39.2%**
Age, years				
21-23	92	40.4	46	31.3
24-26	89	39.0	52	35.4
27-29	47	20.6	49	33.3
Race				
White	169	74.5	93	63.3
Black	8	3.5	9	6.1
Asian	29	12.8	26	17.7
Pacific Islander	1	0.4	4	2.7
Native American	1	0.4	0	0
Other [b]	19	8.4	15	10.2
Hispanic	23	10.3	16	11.1
Education				
High School or Less	10	4.4	18	12.2
Associate or Technical Degree	75	32.9	52	35.4
Bachelor's Degree	77	33.8	38	25.9
Graduate School	66	29.0	39	26.5
Annual Household Income, $				
<10,000	60	36.1	45	42.1
10,000-24,999	39	23.5	25	23.4
25,000-49,999	39	23.5	21	19.6
50,000 or more	28	16.9	16	15.0
Age at 1st Vaginal Intercourse, years				
9-15	35	16.3	32	22.9
16-18	119	55.4	58	41.4
19-21	47	21.9	30	21.4
22-27	14	6.5	20	14.3
History of Sexually and Non-sexually Transmitted Infections (STI), ever	98	43.2	66	44.9
History of STI, ever	21	14.0	17	17.4
History of Yeast Vaginitis, ever	50	23.0	24	17.4
History of Bacterial Vaginosis, ever	29	13.7	20	14.6
Use of Hormonal Contraception, ever	192	84.2	111	75.5
Age at 1st Pap, years				
12-15	18	7.9	12	8.2
16-18	74	32.5	49	33.3
19-21	92	40.4	38	25.9
22-26	44	19.3	48	32.7

*Data may not add up to entire sample size due to missing data. Missing data includes: Race (0.3%), Latina (1.9%), household income (27.2%), age at 1st vaginal intercourse (5.3%), history of sexually or non-sexually transmitted infection (0.27%), history of sexually transmitted infection (33.9%), history of Yeast Vaginitis (5.3%), history of Bacterial Vaginosis (6.9%) and use of hormonal contraception (0.8%).

[a] Vaccinated is defined as having received at least one dose of the HPV vaccine.

[b] Other category includes those who self-reported race as Hispanic, Middle Eastern, Russian, Caribbean, Filipina, and Unknown

Table 2: Odds ratios (OR) and 95% confidence intervals (CI) for associations between risk factors and HPV vaccination status among females aged 21-29

Risk Factor	Vaccinated [a]		Total	Crude OR	95% CI	Adjusted OR [b, c]	95% CI
N=375	N=228	60.8%	N				
Age, years [d]							
21-23	92	66.7	138	1.0	Ref	1.0	Ref
24-26	89	63.1	141	0.86	0.52 – 1.40	0.59	0.32 – 1.09
27-29	47	49.0	96	0.48	0.28 – 0.82	0.33	0.17 – 0.64
Race [e]							
White	169	64.5	262	1.0	Ref	1.0	Ref
Other	58	51.8	112	0.59	0.38 – 0.93	0.79	0.48 – 1.30
Education [d]							
High School or Less	10	35.7	28	1.0	Ref	1.0	Ref
Associate or Technical Degree	75	59.1	127	2.60	1.11 – 6.07	2.08	0.81 – 5.34
Bachelor's Degree	77	67.0	115	3.65	1.54 – 8.66	4.15	1.53 – 11.26
Graduate School	66	62.9	105	3.05	1.28 – 7.26	4.44	1.54 – 12.82
Age at 1st Vaginal Intercourse, years							
9-15	35	52.2	67	1.0	Ref	1.0	Ref
16-18	119	67.2	177	1.88	1.06 – 3.33	1.45	0.77 – 2.72
19-21	47	61.0	77	1.43	0.74 – 2.78	1.14	0.55 – 2.39
22-27	14	41.2	34	0.64	0.28 – 1.47	0.52	0.16 – 1.50
Ever use of Hormonal Contraception							
No	34	49.3	69	1.0	Ref	1.0	Ref
Yes	192	63.4	303	1.78	1.05 – 3.01	1.78	0.94 – 3.37

*Data may not add up to entire sample size due to missing data. Missing data includes: Race (0.3%), age at 1st vaginal intercourse (5.3%), and use of hormonal contraception (0.8%).
[a] Vaccination is defined as having at least one dose of the HPV vaccination series.
[b] The Adjusted model excludes 24 observations because of missing data.
[c] Model is adjusted for all predictors of interest including: age, race, education, ever use of hormonal contraception and age at first vaginal intercourse
[d] Statistically significant odds ratios after adjustment for at least one category.
[e] Strata were collapsed to increase power.

Table 3: Vaccine-related characteristics of females 21-29 years old who were enrolled in the HOPE Study, 2012-2014

Characteristics N=375	n	%
Number of Doses Received		
0	147	39.2
1	18	4.8
2	34	9.1
3	176	46.9
Age at 1st Dose, years [a]		
12-15	19	9.5
16-18	68	34.0
19-21	57	28.5
22-26	56	28.0
Months Between Dose 1 and 2 [a]		
6 or fewer	32	26.9

7-12	51	42.9
13-19	22	18.5
20 or more	14	11.8
Months Between Dose 2 and 3 [a]		
6 or fewer	14	13.7
7-12	39	38.2
13-19	31	30.4
20 or more	18	17.7
Receipt of Dose 1 Relative to 1st Vaginal Intercourse [a]		
Prior	45	20.9
Same Year	23	10.7
After	147	68.4

*Data may not add up to entire sample size due to missing data. Missing data includes: Age at 1st Dose (12.3%), months between dose 1 and 2 (39.9%), months between dose 2 and 3 (32.5%), receipt of dose 1 relative to first vaginal intercourse (5.7%).
*Missing data for months between dose 1 and 2 and months between dose 2 and 3 excludes women who did not receive a second or third dose respectively
[a] Includes only those who were vaccinated for HPV (N=228)

Table 4: Odds ratios (OR) and 95% Confidence Intervals (CI) for detection of HR-HPV Types 16 or 18, among vaccinated and unvaccinated women aged 21-29

N = 364	16 or 18 Detected		Total	Crude OR	95% CI
Exposure	**n=16**	**%**	**N**		
HPV Vaccination Status					
Vaccinated [a]	7	3.2	221	1.0	Ref
Not Vaccinated	9	6.3	143	2.05	0.75 – 5.64
# Doses					
0	9	6.3	143	2.23	0.73 – 6.81
1	1	5.6	18	1.95	0.22 – 17.7
2	1	3.1	32	1.07	0.12 – 9.48
3	5	2.9	171	1.0	Ref
Age at Dose 1, years [b, e]					
12-18	1	1.2	85	1.0	Ref
19-26	4	3.7	109	3.2	0.35 – 29.2
Receipt of Dose 1 Relative to 1st Vaginal Intercourse [b, e]					
Prior	1	2.3	44	1.0	Ref
Same Year	0	0	23	---	---
After	6	4.2	142	1.89	0.22 – 16.2

*Data may not add up to entire sample size due to missing data. Missing data includes: Age at 1st Dose (46.7%) and receipt of dose 1 relative to first vaginal intercourse (42.6%).
[a] Vaccinated is defined as having received at least one dose of the HPV vaccine.
[b] Includes only those who were vaccinated for HPV (N=221).
[c] Adjusted model excluded 34 observations due to missing data.
[d] Model is adjusted for all predictors of interest including: age, race, education, ever use of hormonal contraception and age at first vaginal intercourse.
[e] Sample size too small to adjust for multivariable assessment