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Disparities in Human Papillomavirus Vaccine Completion Among Vaccine Initiators

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Abstract

Objective—To estimate rates of completing the full three-dose prophylactic human papillomavirus (HPV) vaccination regimen in patients who initiated the series and to identify variables associated with not completing vaccination.

Methods—This single-institution review identified all patients initiating HPV vaccination at one of four affiliated clinics between January 2007 and June 2008. Vaccination “completers” were defined as patients who had completed all three vaccinations within 12 months of initiating the vaccination series. Logistic regression was used to identify factors associated with vaccine completion. Variables analyzed included age, type of insurance (private compared with public), practice location (urban compared with suburban), practice type (pediatrics, gynecology, or family practice), and race or ethnicity (white or African American and Hispanic).

Results—Of the 1,413 girls and young women who initiated HPV vaccination, 469 (33.2%) completed the vaccine series. Overall, private insurances (odds ratio 1.87, 95% confidence interval 1.26–2.76) and suburban practice locations (odds ratio 1.44, 95% confidence interval 1.04–1.98) were associated with higher vaccine completion rates. African American race was associated with lower completion rates (odds ratio 0.50, 95% confidence interval 0.38–0.65). In multivariable analyses, the combination of younger age (11–17 years) and urban practice location was associated with very low likelihood of completing HPV vaccination (22%; $P=.023$).

Conclusion—The HPV vaccine completion rate is low. When resources are limited, disparities in HPV vaccine completion should be considered when developing programs to improve vaccine utilization. Urban girls and young women should be targeted as an at-risk population.

Level of Evidence: III

Persistent infection with an oncogenic strain of human papillomavirus (HPV) is the cause of virtually every cervical cancer.¹ However, most HPV infections do not cause disease.

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Because HPV infections generally do not cause symptoms, and because most eventually resolve without intervention or clinical sequelae,² HPV exposure is essentially endemic, beginning soon after sexual debut.³ Despite an array of available screening strategies for cervical HPV disease, the American Cancer Society estimates that in 2010 there will be 4,210 cervical cancer deaths in the United States.⁴ Women who are minorities or who are in low socioeconomic groups are at two to three times higher risk of developing disease compared with those who are white or who have higher incomes.^{5–7} The costs associated with HPV-related cervical conditions to the health care system are staggering; in the United States, approximately \$4 billion are spent annually on these conditions.^{8–11}

Prophylactic vaccines protecting against infection with HPV16, 18, 6, and 11 (Gardasil or HPV4) and HPV16 and 18 (Cervarix or HPV2) have become available in the past decade. HPV4 is virtually 100% effective in preventing cervical intraepithelial neoplasia 2 or 3 associated with HPV16 and 18, the genotypes causally associated with 70% of squamous cervical cancers.^{12,13} HPV2 is also highly effective, preventing more than 90% of HPV16- and 18-associated cervical intraepithelial neoplasia 2 or 3.¹⁴ In 2007, the Centers for Disease Control Advisory Committee on Immunization Practices recommended routine vaccination of girls age 11–12 years with three doses of either HPV4 or HPV2, as well as catch-up vaccination for girls and young women age 13–26 years.¹⁵

Despite the clear effectiveness of prophylactic HPV vaccination in preventing disease, uptake of the vaccine in eligible girls and young women in the United States is low. The Centers for Disease Control reported that in 2009, only 44.3% of eligible girls (age 13–17 years) initiated HPV vaccination and only 26.7% completed the three-vaccination series.¹⁶ Other cohort studies have reported completion rates ranging from 13% to 58% among persons who initiated the vaccine series.^{17–19} Immunologic effectiveness is likely to be suboptimal with incomplete vaccination, and the societal cost of sustaining an inefficient strategy for vaccine delivery is difficult to justify. The goal of this analysis was to estimate rates of HPV vaccine completion in a cohort of girls and young women who had initiated the series and to identify variables associated with failure to complete the three-vaccination regimen within 12 months of vaccine initiation. Here, we report data reflecting vaccination completion rates in practices associated with a large academic institution.

Materials and Methods

This single-institution retrospective study was approved by the Johns Hopkins Institutional Review Board. Participants in the analysis included all nonpregnant girls and young women age 11–26 years who initiated the HPV4 series in one of four outpatient clinics associated with the Johns Hopkins Hospital (Baltimore, MD) between January 1, 2007 and June 30, 2008. During the time frame analyzed in this study, the vaccine manufacturer recommended that the vaccination series should be completed within 12 months of initiation. In this analysis, participants who received all three vaccinations within 12 months of initiation were defined as “completers.” “Noncompleters” were defined as those who did not complete all three vaccinations within 12 months of their first vaccination. To estimate HPV4 completion rates, data were collected through June 30, 2009.

All nonimmunized, nonpregnant female patients age 11–26 years should have been offered HPV vaccine initiation during their annual preventive examination, with future appointments made for the second and third doses. Furthermore, individual providers may have offered the vaccine during other types of office visits. Because the data were collected from vaccination-based databases, data on eligible patients that were not offered the vaccine or declined to initiate the vaccine series were not obtained.

Data were collected from four ambulatory clinics associated with Johns Hopkins Hospital. The two inner-city, urban outpatient clinic sites (Johns Hopkins Outpatient Center and Johns Hopkins Bayview Medical Offices) were included. Additionally, a subset of the suburban outpatient clinic sites (Johns Hopkins White Marsh and Johns Hopkins Odenton) was included. The sociodemographic characteristics of the two suburban sites in this analysis are not significantly different from the other suburban sites in our system. The study population was drawn from the pediatric, family practice, and gynecology practices at these facilities. The data were extracted using an electronically generated search for the International Classification of Diseases, 9th Revision, Clinical Modification code for HPV vaccination (V04.89). Vaccination logs and electronic medical records were used to verify vaccination, visit dates, and clinic sites for individual participants. Additionally, socioeconomic variables, including age, race or ethnicity, and insurance type, were obtained from billing databases and from patient charts.

Analyses were segregated by age cohorts (girls age 11–17 years compared with young women age 18–26 years), type of insurance (private [private, hospital-based private, or military] compared with public [medical assistance]), practice type (pediatrics, family practice, or gynecology), and practice location (urban compared with suburban). Categorical comparisons of completion rates were performed using two-sample z tests for population proportions. For small sample sizes, comparisons were made using the Fisher exact test. The χ^2 test of homogeneity was used to compare completion rates between three or more predictors. Stepwise logistic regression was used to determine variables associated with completing the three-vaccination sequence within a 12-month period. For all analyses, statistical significance was defined as $P=.05$.

Results

A total of 1,413 nonpregnant girls and women age 11–26 were included in this analysis. Demographic characteristics of the total cohort are presented in Table 1. The three-shot HPV4 series was completed by 469 participants (33.2%) within the 12-month period after receiving the first dose. Of the remaining 944 participants, 504 (35.7%) completed two vaccinations and 440 (31.1%) received only one vaccination during the study period.

Overall univariable HPV vaccine series completion rates are presented in Table 2. Completion rates among subcohorts range from 20% to 38.3%. To account for confounding variables, multivariable logistic regression was used to determine the association of individual variables with HPV4 completion. In multivariable analyses, completers were more likely than noncompleters to have private insurance as a payer method, more likely to

be examined at a suburban clinic than an urban clinic, and more likely to be white than a minority race (Table 3).

Having private medical insurance was the strongest single predictor of completing the HPV vaccine series. Patients with private insurance had significantly higher vaccination completion rates than patients who had public insurance (odds ratio [OR] 1.87, 95% confidence interval [CI] 1.26–2.76; $P=.002$; Table 3). This differential was more pronounced in suburban clinics than in urban clinics. In suburban clinics, women with private insurance were substantially more likely to complete vaccination than those with public insurance (37.8% compared with 13.2%, OR 4.02, 95% CI 1.55–10.39; $P=.002$). In urban clinics, private insurance also was associated with higher HPV4 completion rates than public insurance (30.0% compared with 21.1%, OR 1.61, 95% CI 1.05–2.46; $P=.03$). Although private insurance patients examined in suburban offices had higher vaccine compliance than those examined in urban offices (37.8% compared with 30.0%, OR 1.42, 95% CI 1.03–1.95; $P=.03$), those patients with public insurance had similarly low HPV vaccine completion rates for both suburban and urban sites (13.2% compared with 21.1%; $P=.26$; Fig. 1A).

Among young adults (age 18–26 years), HPV4 completion rates in urban and suburban practices were very similar (31.0% compared with 31.8%; $P=.85$). However, we found that in girls age 11–17 years, completion rates were very different depending on practice location. In urban practices, female children and adolescents were much less likely than young adults to complete vaccination (22% compared with 31.8%, OR 0.60, 95% CI 0.39–0.93; $P=.023$; Fig. 1B). Conversely, in suburban practices, female children and adolescents were more likely to complete vaccination than young adults (44.9% compared with 31.0%, OR 1.82, 95% CI 1.39–2.37; $P<.001$; Fig. 1B). In analyses segregated by practice types, we found that differences in HPV4 completion were also strongly associated with practice location. Pediatric patients seen in suburban practices were more than twice as likely as pediatric patients seen in urban practices to complete vaccination (47.7% compared with 19.7%, OR 2.71, 95% CI 2.51–5.48; $P<.001$; Fig. 1C). This finding is consistent with the rates of completion analyzed by age cohorts. In gynecology practices, we found no difference in completion rates between suburban and urban clinics (38.2% compared with 36.4%; $P=.7$). Because 58% of the pediatric patients were examined in urban clinic settings as compared with only 28% of the gynecology patients, overall pediatric HPV4 completion rates were lower than overall gynecology completion rates (31.5% compared with 37.7%, OR 0.76, 95% CI 0.59–0.98; $P=.03$). These findings suggest that girls and young women examined in urban clinics face significant barriers that hamper their ability to undergo the complete preventive vaccination regimen. This is of concern because they are arguably a cohort at high risk for HPV disease.

Discussion

Although it is generally appreciated that prophylactic HPV vaccines are underutilized, less is known about specific factors that can be used to predict noncompletion of the three-dose vaccine regimen. Here, we report on vaccine completion rates in a multisite, multipractice academic setting. Similar to other cohort studies,^{16–19} our cohort had low rates of vaccine

completion; only one-third of patients who initiated the series received all three shots within the recommended 12 months. This analysis identifies the combination of young patient age and urban practice location as a predictor of failure to complete three HPV vaccinations in patients who had obtained an initial vaccination.

Only HPV vaccine doses administered at one of four outpatient clinic sites were captured. Any other doses administered by any other provider were not included in the analysis. Whereas this limitation could potentially skew our analysis toward underestimation of vaccine completion rates, our electronic medical record system does include visits to all institution- related practice sites. The likelihood that girls and young women would obtain booster vaccinations with outside providers, without documentation, is low, based on the cost of vaccination. Another potential limitation of our analysis is that all patients were seen in clinics affiliated with a single academic institution. Although this cohort comprises a significant diversity of patients in terms of types of insurance, practice locations, and patient age and race or ethnicity, these findings may not be generalizable to nonacademic practice settings.

In our cohort, overall, patients seen in pediatric practices had lower HPV vaccine completion rates than patients seen in gynecology practices. This finding was unexpected and differs from other reports.²⁰ Providers in pediatrics practices are more accustomed than providers in gynecology practices in counseling and administration of preventive vaccinations. Moreover, pediatric practices have established office infrastructure to track vaccine delivery. Completion rates for other recommended pediatric and adolescent multidose vaccinations, including measles, mumps, and rubella and hepatitis B, are nearly 90% in girls age 11- 17 years.¹⁶

This unexpectedly low pediatric vaccine completion rate may be attributable to a skewed sociodemographic distribution between urban and suburban practices in our study. Most of the young or pediatric patients in our analysis received their care in urban practice settings. In our cohort, these patients had much lower rates of HPV4 completion than girls and young women receiving care in suburban practice settings. HPV completion rates in our older patient population and among the patients seen in gynecology outpatient clinics did not differ by clinic location. This finding suggests that clinic location is linked to the likelihood of vaccine completion in our younger patients. In contrast, clinic location is not associated with differences in completion in our older patients. Further research is needed to identify the barriers that prevent young patients in the urban setting from completing vaccination. Because most of the financial burden should be alleviated through the Federal Vaccine for Children program, other barriers must still be preventing compliance with the three-shot HPV series in this subpopulation. The disparities in HPV4 compliance in the younger population could be a consequence of several factors, including differences in access to care, in cultural attitudes toward vaccination, or in the ability to provide adequate counseling.

The discussion of preventive HPV vaccination currently is structured around sexual behavior that presents risk, a subject that may be unsettling for some parents and time-consuming for providers. In addition, the current strategy for preventive HPV vaccination is predominantly sex-based. Lessons should be learned from the history of the implementation

of the rubella vaccine. Initial sex-based efforts to start vaccinations were spectacularly ineffective, and it was not until rubella prevention was presented in the context of reducing risk of congenital disease to unborn children that it became school-mandated and near-herd immunity was achieved.²¹ It may be that if prophylactic HPV vaccines were presented as a means to prevent cancer, instead of a means to prevent an infection associated with sexual contact, that uptake would increase.

Finally, the logistic and financial difficulties presented by clinic-based vaccine administration are consistent with the vaccine completion rates in our cohort. The three-shot series requires an office tracking system, a positive attitude about the vaccine by both provider and patient, and three vaccination appointments that are billed as procedures. In other developed high-resource settings in which preventive HPV vaccine administration is school-based, vaccination uptake and completion rates are significantly higher than in the United States. For example, in the United Kingdom, HPV vaccine is administered through a school-based program with an opt-out; vaccine coverage is 80.1%.²² In Australia, which also has instituted a school-based HPV vaccination program, vaccine coverage is 86%.²³ Mandatory, school-based vaccination, even with an opt-out, is controversial in the United States.^{24,25}

Studies to date provide evidence that barriers to vaccination include cost, access to health care, cultural beliefs, lack of vaccine awareness, and misperceptions about vaccination.^{7,26} Studies also indicate that minority women and women receiving care in inner city clinics have low rates of both initiation and completion of the vaccine regimen.^{18,20,27,28} Our results also support these findings. Additionally, inner city youths were also at significant risk for not completing the HPV4 series. Because these cohorts have low rates of screening and high rates of disease, investigation into the reasons for these disparities deserves focused attention.^{5,6} Strategies to improve preventive HPV vaccination compliance should target this at-risk population of young urban patients.

Short of a complete overhaul of reimbursement for preventive counseling and approach to vaccine delivery, initiatives to enhance vaccine completion rates in urban pediatric cohorts in the United States could involve communication-based interventions such as text message reminders the day before vaccination appointments. Because this type of intervention is being evaluated as a strategy to enhance compliance with daily oral contraceptive pill use in young women,²⁹ it is conceivable that HPV vaccination could benefit from this approach. Furthermore, developing and instituting an electronic medical record system that can automatically send reminders to a patient or provider whenever a patient has missed the HPV vaccine dose would also help increase compliance. In the end, although survey data in the United States suggest that knowledge³⁰ and acceptability⁷ of the HPV vaccine is high, we and others report that even among girls and young women who start the vaccination series, rates of completion are surprisingly low. Preventive HPV vaccines are an opportunity to reduce the incidence of HPV-associated disease and costs associated with current primary prevention strategies. Research is needed to identify reasons why persons who start HPV vaccination do not complete the series, and research is needed to develop and evaluate strategies to achieve more successful rates of HPV vaccine completion.

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Fig. 1.

Multivariable factors associated with human papillomavirus vaccine (HPV) completion rates. **A.** Privately insured patients are more likely to complete vaccinations than are patients with public insurance. **B.** Female children and adolescents in the urban clinic settings are less likely to complete HPV vaccinations than young adults in urban clinics. **C.** Pediatric patients in inner city practices are less likely than pediatric patients in suburban practices to complete HPV vaccinations.

Table 1

Demographics of Study Cohort

	n (%)	Received 1 Shot	Received 2 Shots	Completer	Noncompleter
n	1,413	440 (31.1%±2.4%)	504 (35.7%±2.5%)	469 (33.2%±2.5%)	944
Age (y)					
11–17	701 (49.6)	188 (42.7%±4.6%)	266 (52.8%±4.4%)	247 (52.7%±4.5%)	454 (48.1%±3.2%)
18–26	712 (50.4)	252 (57.3%±4.6%)	238 (47.2%±4.4%)	222 (47.3%±4.5%)	490 (51.9%±3.2%)
Insurance type					
Public	275 (19.5)	111 (25.2%±4.1%)	109 (21.6%±3.6%)	55 (11.7%±2.9%)	220 (23.3%±2.7%)
Private	1,138(80.5)	329 (74.8%±4.1%)	395 (78.4%±3.6%)	414 (88.3%±2.9%)	724 (76.7%±2.7%)
Practice location					
Suburban	963 (68.2)	272 (61.8%±4.6%)	336 (66.7%±4.1%)	355 (75.7%±3.9%)	608 (64.4%±3.1%)
Urban	450 (31.8)	168 (38.2%±4.6%)	168 (33.3%±4.1%)	114 (24.3%±3.9%)	336 (35.6%±3.1%)
Practice type					
Pediatrics	515 (36.4)	153 (34.8%±4.4%)	200 (39.7%±4.3%)	162 (34.5%±4.3%)	353 (37.4%±3.1%)
Family practice	365 (25.8)	117 (26.6%±4.1%)	142 (28.2%±3.9%)	106 (22.6%±3.8%)	259 (27.4%±2.9%)
Gynecology	533 (37.7)	170 (38.6%±4.6%)	162 (32.1%±4.1%)	201(42.9%±4.4%)	332 (35.2%±3%)
Race or ethnicity					
White	732 (51.8)	201 (45.7%±4.6%)	251 (49.8%±4.4%)	280 (59.7%±4.4%)	452 (47.9%±3.2%)
Minority	495 (35.0)	181 (41.1%±4.6%)	192 (38.1%±4.2%)	122 (26%±4%)	373 (39.5%±3.1%)
African American	443 (31.4)	167 (37.9%±4.6%)	171 (33.9%±4.1%)	105 (22.4%±3.8%)	338 (35.8%±3.1%)
Hispanic	52 (3.7)	14 (3.2%±1.6%)	21 (4.2%±1.7%)	17 (3.6%±1.7%)	35 (3.7%±1.2%)
Other	61 (4.3)	18 (4.1%±1.8%)	26 (5.2%±1.9%)	17 (3.6%±1.7%)	44 (4.7%±1.3%)
Unknown	125 (8.8)	40 (9.1%±2.7%)	35 (6.9%±2.2%)	50 (9.9%±2.6%)	75 (7.9%±1.8%)

The data is presented as mean i±standard deviation.

Table 2
Human Papillomavirus Vaccination Completion Rates, Univariable Analysis (N = 1,413)

Variable	n	Completed 3 Vaccinations in 12 Mo (%)	OR (95% CI)	P
Age (y)				
18–26	712	222 (31.2)	1.0	
11–17	701	247 (35.2)	1.2 (0.96–1.5)	.11
Insurance type				
Public	275	55 (20)	1.0	
Private	1,138	414 (36.4)	2.29 (1.66–3.15)	<.001
Private payer	723	253 (35)	2.15 (1.54–3.0)	<.001
Hospital-based	84	39 (46.4)	3.47 (2.06–5.84)	<.001
Military	331	122 (36.9)	2.33 (1.61–3.38)	<.001
Practice location				
Urban	450	114 (25.3)	1.0	
Suburban	963	355 (36.9)	1.72 (1.34–2.21)	<.001
Practice type				
Pediatrics	515	162 (31.5)	1.0	
Family practice	365	106 (29.0)	0.89 (0.67–1.2)	.44
Gynecology	533	201 (37.7)	1.32 (1.02–1.7)	.03
Race or ethnicity				
White	732	280 (38.3)	1.0	
Minority	495	122 (24.6)	0.53 (0.41–0.68)	<.001
African American	443	105 (23.7)	0.50 (0.38–0.65)	<.001
Hispanic	52	17 (32.7)	0.78 (0.43–1.43)	.42

OR, odds ratio; CI, confidence interval.

Table 3
Multivariable Logistic Regression Analysis of Predictors of Human Papillomavirus Vaccine Completion

Characteristic	OR (95% CI)	P
Age (y)		
18–26	Ref (1.0)	
11–17	1.71 (1.26–2.33)	.001
Insurance type		
Public	Ref (1.0)	
Private	1.87 (1.26–2.76)	.002
Practice location		
Urban	Ref (1.0)	
Suburban	1.44 (1.04–1.98)	.027
Practice type		
Pediatrics	Ref (1.0)	
Family practice	0.78 (0.54–1.14)	.20
Gynecology	1.43 (0.99–2.06)	.053
Race or ethnicity		
White	Ref (1.0)	
African American or Hispanic	0.64 (0.49–0.83)	.001

OR, odds ratio; CI, confidence interval; Ref, reference.