Knowledge about Human Papillomavirus and Time to Complete Vaccination among Vulnerable Female Youth

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Objective To examine the association of knowledge about human papillomavirus (HPV) on the time to completion of the 3-dose quadrivalent vaccine series in an inner-city population of adolescent female subjects at high risk for infection.

Study design We prospectively followed 139 female subjects aged 14-20 years enrolled in a vaccine surveillance study in New York City during a period of at least 24 months. Participants were given a 30-item true or false survey on HPV at enrollment and ranked according to the number of correct responses. Multivariate Cox regression was used to examine the association between level of knowledge about HPV and time to completion (in days) of vaccine dose 1-3, dose 1-2, and dose 2-3.

Results Overall time to completion of the 3-dose vaccine ranged from 158 days to 1114 days. Participants in the high knowledge group (top quartile) were significantly more likely to complete the 3-dose series earlier (hazard ratio 1.69, 95% CI 1.03-2.77; $P = .04$), in particular doses 2-3 (hazard ratio 1.71, 95% CI 1.02-2.89; $P = .04$), than those with low-to-moderate knowledge (bottom 3 quartiles).

Conclusions These findings suggest that knowledge of HPV is associated with shorter time to complete the 3-dose HPV vaccine series. Educational campaigns at time of vaccination may be important to improve vaccine adherence. *(J Pediatr 2016;171:122-7)*.

The quadrivalent human papillomavirus vaccine (types 6, 11, 16, and 18; qHPV; Gardasil, Merck & Co, Inc, New Jersey) is highly effective in preventing anogenital infection with human papillomavirus vaccine (HPV), warts, and precancerous lesions in female patients who test negative for the HPV types targeted by the vaccine and are highly compliant with the 3-dose vaccination schedule.[1-3] Since the approval of the vaccine in 2006, coverage with ≥1 dose of any HPV vaccine among adolescent girls has remained low, with only 57% of girls ages 13-17 years receiving the vaccine and 38% completing all 3 doses.[4] Although a number of countries have approved reduced-dose schedules for HPV vaccination in adolescents, it is unlikely this will be adopted in the US soon while both the quadrivalent and bivalent vaccines remain licensed for 3 doses. Moreover, per the recent World Health Organization Report from the Global Advisory Committee on Vaccine Safety,[5] the 3-dose schedule remains necessary if immunization is initiated after the 15th birthday.

Additional studies, however, are needed to further determine the effectiveness of alternate dosing schedules and regimens for different age groups. Until a long-term immunologic threshold of disease protection is well established, full and timely completion of the series continues to be a desirable public health goal. A recent article compared geometric mean antibody titer levels in girls age 9-13 years and found they were greater in those receiving 3 vs 2 doses, suggesting that completion may be advantageous.[6] On the other hand, evidence from trials indicate that vaccine efficacy is maintained after just 2 doses[7] and after longer intervals of up to 24 months for a 3-dose regimen.[8,9]

Vaccine-completion rates for the 3 recommended doses among those who already have received the first dose are lower among black and Hispanic populations compared with white populations nationally,[10] with even greater disparities observed among the uninsured and disadvantaged. After controlling for insurance type, the authors of a study of 8069 young women attending an urban clinic between 2006 and 2010 found black teenagers ages 14-17 years who initiated the qHPV series were less likely to complete it than white or other ethnicity teenagers,[11] suggesting that removing financial barriers among uninsured teens of ethnic minority background is only a first step in achieving vaccine adherence.

Diffusion theory applied to newly approved vaccination programs proposes that initiation is a focus at early stages of vaccine uptake, with full and on-schedule completion (ie, by 7 months) subsequently becoming an important

HPV	Human papillomavirus
SES	Socioeconomic status
qHPV	Quadrivalent human papillomavirus vaccine (types 6, 11, 16, and 18)

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focus as programs expand and gain acceptance.[12] As nationwide vaccination efforts advance from initiation to completion, it is critical to identify modifiable factors that may facilitate completion in clinical settings serving vulnerable teens. This identification is important because, even though evidence from trials supports moving to a 2-dose vaccine schedule, which would improve compliance, little is known about the long-term consequences of partial or delayed adherence on vaccine effectiveness.[6,7]

Research to date has focused primarily on vaccine initiation, with a few studies observing significant associations between limited knowledge of HPV and decreased acceptability of the vaccine.[13-18] In an effort to expand current literature, we assessed level of knowledge about HPV transmission, treatment, consequences, vaccine efficacy, and prevention in prospectively followed ethnic minority adolescents receiving the 3-dose qHPV vaccine at a large urban adolescent health center in New York City.

Methods

The current study included 139 participants between 14 and 20 years of age enrolled in a longitudinal HPV vaccine surveillance study[19,20] at the Mount Sinai Adolescent Health Center in New York City from October 2007 to February 2012. Mount Sinai Adolescent Health Center is an urban health center that provides comprehensive care that is confidential and free of charge, including administration of the qHPV vaccine. Women eligible for the main study: (1) were between 12 and 19 years of age at time of consent; (2) had ever engaged in vaginal intercourse; and (3) intended to get or had already received the qHPV vaccine. At time of analysis, 709 participants had enrolled in the main study, of which the majority already had initiated or completed the vaccine series. Because this study focused on the time course of vaccine completion, only participants receiving the first vaccine dose at the time of the baseline visit (ie, vaccine-naïve) were included. Participants who were pregnant, or those who had terminated a pregnancy within 4 weeks of enrollment, were excluded. One vaccine-naïve participant was later excluded because she was vaccinated erroneously earlier than the minimum recommended schedule.

Participants were informed about the study by research staff, and written informed consent was collected from all participants before enrollment. The study was approved by the Institutional Review Board of the Icahn School of Medicine at Mount Sinai. Before receiving the vaccine, participants completed a self-administered paper-and-pencil questionnaire consisting of multiple items that assessed demographic characteristics, risk behaviors for HPV acquisition, and knowledge about HPV. At the conclusion of the baseline visits, or shortly thereafter at a subsequent visit, dose 1 of the vaccine was given and the vaccination receipt date was recorded in the electronic medical record. Participants were scheduled to receive dose 2 and dose 3 according to the intervals recommended by the US Advisory Committee on Immunization Practices at the time of the study: dose 1-2 = 28 days, dose 2-3 = 84 days, and dose 1-3 = 168 days. Vaccines were still administered, however, at the shortest-recommended intervals if participants presented to the clinic outside of study visits. The study took place under optimum vaccination conditions, including appointment reminders, follow-up of participants to reschedule missed appointments via a phone call, and approaching them during clinic appointments outside of study visits.

The primary outcomes of this analysis were time (in days) to completion of doses 1-3, 1-2, and 2-3 of the qHPV vaccination series after the administration of dose 1. Subjects were followed until they completed the 3-dose series or withdrew from the study. For those subjects who were lost to follow-up before vaccine completion, a participating physician (J.N.) reviewed the New York Citywide Immunization Registry and recorded dates for vaccine doses that were received elsewhere.

Assessment of Knowledge about HPV

A self-administered HPV knowledge survey comprising 30 items was scored as true/false/not sure covering general aspects of HPV transmission, treatment, consequences, vaccine efficacy, and prevention. Questions included were similar to those found in a recently validated general knowledge about HPV scale.[21] Responses to items were dichotomized into either correct or incorrect/not sure: participants were given 1 point for a correct response and 0 for an incorrect/not sure response. The total knowledge score (ranging from 0 to 30) reflects the number of correct responses (Cronbach $\alpha = 0.89$). Participants with missing data in 4 items or fewer were given a zero for that individual item (n = 11). Those missing more than four items were excluded from the main analyses (n = 4).

Covariates

Information regarding demographics and sexual practices also was assessed by self-report questionnaire. Demographic characteristics included: (1) age measured in years (range 12-20 years); (2) ethnicity/race categorized by use of The National Longitudinal Study of Adolescent Health (ie, Add Health) guidelines (http://cpc.unc.edu/projects/addhealth/data/code/race), which integrate ethnicity and race into 3 ethnic/race groups: Hispanic, Non-Hispanic black/African American, and other (white, Asian, Native American, other); (3) socioeconomic status (SES), dichotomized by assigning participants a score of one (low SES) if they responded positively to ever receiving any of the following: welfare assistance, food stamps, Medicaid, Women, Infants and Children (ie, WIC), free lunch, or those who reported "often not having enough to eat" in the past year or 0 for all other participants (not low SES); and (4) current school attendance (yes/no).

Sexual practices assessed included: (1) age at vaginal, anal, or oral sexual debut (11-14, 15, and ≥16 years); (2) recent (in the past 6 months) number of sexual partners (0-1, 2, and ≥3