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RESEARCH PAPER

Human papillomavirus vaccination completion rates among gynecological providers: an institutional retrospective review

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ABSTRACT

Objective: The primary aim of this study is to assess and characterize correlates of human papillomavirus (HPV) vaccine series completion among young adult women evaluated by gynecological (GYN) providers at a single institution and to measure changes over 4-y period.

Methods: At a major academic center, the medical records of 845 women administered the HPV vaccine series by a GYN provider were retrospectively reviewed from 2006 to 2010 and 2014 to 2015. Patients were grouped based on the date of vaccine initiation into "earlier" (2006–2010) and "later" (2014–2015) cohorts. Patient demographics, dates of vaccine administration, and practice locations where vaccines were administered were collected. Patients who received all 3 vaccines within 6 months were deemed "complete". Patients seen by a provider but did not receive the vaccination were deemed "missed opportunities". The primary outcome was completion of HPV vaccination according to the ACIP guidelines.

Results: The 845 patients were divided into earlier (n = 399) and later (n = 446) cohorts. There was no statistically significant difference in completion rates between the earlier-cohort compared to the later-cohort (*35.2% vs. 30.9%, p = .20*). Age at initiation were similar (*p = .61*), with the complete cohort having a significantly lower body mass index (BMI) than the incomplete cohort (*p = .0015*). There was a significant difference between the completion rates among race/ethnic groups (*p* = .036). African-American and Hispanic (*18.9% and 20.0%, respectively, p = .04)* patient-populations had the lowest completion rates and higher missed opportunities.

Conclusion: Our study found an overall low completion rate in both earlier and later cohorts. Additionally, higher BMI and African-American and Hispanic race/ethnicity were associated with low vaccine completion.

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Introduction

The human papilloma virus (HPV) is a double-stranded DNA virus and is the most common sexually transmitted infection in the United States, with an estimated 14 million people developing new infections every year[1]. HPV infections are largely self-limited and asymptomatic; however, untreated and persistent HPV infection is responsible for cervical cancer in women, and genital warts and anogenital and oropharyngeal cancers in both men and women[2]. The Center for Disease Control and Prevention estimates that approximately 11,866 new cases of HPV related cervical cancer are diagnosed each year with the highest rates among African-American and Hispanic women[2,3].

Since 2006, the Food and Drug Administration (FDA) has approved three HPV vaccinations, a quadrivalent vaccine (Gardasil, Merck & Co., Inc.), bivalent vaccine (Cervarix, GlaxoSmithKline Biologicals) and 9-valent vaccine (Gardasil-9, Merck and Co., Inc.) in 2006, 2009 and 2016 respectively[2,4]. In 2015, the Advisory Committee on Immunization Practices (ACIP) recommended routine HPV vaccination initiation at age 11–12 y for males and females or for females aged 13–26 y and males aged 13–21 y who have not completed their vaccination series previously. The current vaccination schedule for persons initiating the series prior to age 15 is a 2-dose schedule with the second dose given 6 to 12 months after the first dose. The 3-dose vaccine series is recommended for persons starting the vaccination aged 15–26 y with a schedule of 0, 1–2 and 6 months[5]. In a phase III efficacy trial by Huh and colleagues demonstrated that Gardasil-9 was found to by 96.7% effective in preventing precancerous lesions caused by HPV 31, 33, 45, 52, or 58 in the per protocol population who received completed their vaccination series[6]. In October 2018, the FDA expanded its approval of the Gardasil-9 HPV vaccine to include men and women between 27 and 45 in efforts to help prevent HPV-related diseases and cancers in a broader age range. This was supported by a study that followed women ages 27 through 45 for three and a half years and found that Gardasil was 88% effective in preventing genital warts, vulvar and vaginal and cervical precancerous lesions and HPV-related cervical cancers[7].

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Despite its efficacy, HPV vaccination has increased very slowly since its introduction, with the 2017 National Immunization Survey (NIS)-Teen demonstrating a 48.6% series completion rate among adolescents aged 13–17 y[8]. Given this low completion rate and the paucity of data regarding vaccine coverage in adult women, the primary objective of our study is to assess the HPV vaccination completion rates of young adult women seen by gynecological (GYN) providers and changes in the rates over a span of 4 y.

Results

Eight hundred and forty-five patients were included in this study (Earlier: n = 399 vs. Later: n = 446). The age at initiation of vaccine series were similar between the cohorts (*Earlier: 22.0 ± 3.2 y vs. Later: 22.3 ± 3.5 y, p = .16*; Table 1). The Later-cohort trended to have a slightly lower completion rate than the Earlier-cohort (*Earlier: 35.2% vs. 30.9%, p = .20*), Table 1. There were no significant differences between the cohorts in the time duration between the sequential doses, including first and second doses (*Earlier: 3.2 ± 3.4 mons vs. Later: 2.9 ± 2.4 mons, p = .18*), second and third (*Earlier: 4.9 ± 2.4 mons vs. Later: 4.7 ± 2.2 mons, p = .40*), and first and third (*Earlier: 7.6 ± 3.7 mons vs. Later: 7.2 ± 2.5 mons, p = .14*; Table 1).

Amongst complete and incomplete patients in the Later-cohort, the ages at initiation were similar between the two cohorts (*Complete: 22.2 ± 3.8 y vs Incomplete: 22.4 ± 3.3 y, p = .61*), Table 2. There was a significant difference in BMI, with the Complete-cohort having a significantly lower BMI than the incomplete cohort (*Complete: 25.42 ± 7.00 kg/m^2 vs Incomplete: 27.23 ± 7.63 kg/m^2, p = .0015*), Table 2. There was a significant difference in completion rates among the various races ($p = .04$), with African-American (18.9%) and Hispanic (20.00%) patient-populations having the lowest completion rates, Table 2. There were no significant differences in completion rates within the different type of practices patients were seen, Table 2.

There were 97 patients in the later-cohort who were incomplete and had missed opportunities, Table 3. The mean ± SD of patient age and number of visits that represented missed opportunities was 22.4 ± 3.3 y and 1.7 ± 1.2 visits, respectfully, Table 3. African-Americans (27.5%) and Hispanics (33.3%) were the most prevalent patient populations that had missed opportunities, Table 3. African-Americans and Hispanics did not have a significantly greater mean SD missed opportunities than the other races 0.44 ± 0.9 and 0.50 ± 0.8, respectively ($p = .71$; Table 3).

Table 1. Completion rates and time duration between doses of GYN patients.

Variable	Earlier (n = 399)	Later (n = 446)	P-Value
Age at Initiation (Years)	22.0 ± 3.2	22.3 ± 3.5	0.16
Completion Rate (%)	35.2	30.9	0.20
Time Duration Between Vaccines			
Dose 1 and 2	3.2 ± 3.4	2.9 ± 2.4	0.18
Dose 2 and 3	4.9 ± 2.4	4.7 ± 2.2	0.40
Dose 1 and 3	7.6 ± 3.7	7.2 ± 2.5	0.14

Table 2. Patient demographics and completion (within 6 months) of the later cohort.

Variable	Complete	Incomplete	P-Value
Age at Initiation (Years)	22.2 ± 3.8	22.4 ± 3.3	0.61
BMI (kg/m^2)	25.4 ± 7.0	27.2 ± 7.6	*<0.01**
Race			*0.04**
White (%)	34.3	65.7	
African American (%)	18.8	81.3	
Hispanic (%)	20.0	80.0	
Asian (%)	43.8	56.3	
Middle Eastern (%)	37.5	62.5	
Practice			0.21
Private (%)	36.1	63.9	
Faculty	25.8	74.2	
Resident (%)	33.5	66.5	
Affiliated-Rural (%)	24.0	76.0	
Colposcopy (%)	15.0	85.0	

Differences Between Practices

Practice	P-Value
Resident vs. Private	0.71
Resident vs. Faculty	0.29
Resident vs. Rural	0.24
Resident vs. Colposcopy	0.13
Private vs. Faculty	0.18
Private vs. Rural	0.30
Private vs. Colposcopy	0.13
Faculty vs. Rural	0.83
Faculty vs. Colposcopy	0.38
Rural vs. Colposcopy	0.54

Table 3. Number and characteristics of missed opportunities among incomplete patients in the later cohort.

Variable	Missed Opportunity (n = 97)
Age at Initiation (Years)	22.4 ± 3.3
# of Missed Opportunities	1.7 ± 1.2
Race	
White (%)	19.2
African American (%)	27.5
Hispanic (%)	33.3
Asian (%)	25.0
Middle Eastern (%)	12.5
Practice	
Private (%)	16.7
Faculty (%)	19.7
Resident (%)	20.5
Affiliated-Rural (%)	34.0
Colposcopy (%)	30.0

Comparison of # Missed Opportunities By Race and Practice

Variable	Mean #	P-Value
White	0.34 ± 0.9	
African American	0.44 ± 0.9	
Hispanic	0.50 ± 0.8	0.71
Asian	0.38 ± 0.8	
Middle Eastern	0.13 ± 0.4	
Private	0.30 ± 0.8	
Faculty	0.27 ± 0.7	
Resident	0.32 ± 0.9	0.06
Affiliated-Rural	0.68 ± 1.4	
Colposcopy	0.45 ± 0.8	

A patient who was seen in a practice that administered the HPV vaccine, but did not receive a scheduled vaccine was deemed a "Missed Opportunity". Frequency is # of missed opportunities/# white patients who are complete (n = 107).

Statistical significance is set for $p < 0.05$.

Discussion

In this retrospective cohort study, adult women who were administered the HPV vaccine series by a GYN provider demonstrated a relatively low completion rate, with no significant difference in the patterns of vaccination over

a 4-y time period. Overall, the completion rates for the HPV vaccination series were similar to national average completion rates of approximately 30–35% at that time. In 2018, the updated Healthy People 2020 objectives include increasing HPV vaccine series completion for females aged 13–15 y to 80% by the year 2020[9]. Unfortunately, national and institutional vaccine rates fall far below this goal.

In a systematic review of 55 relevant articles, Dawn et al. found several common barriers to HPV vaccination among adolescents in the US[10] Health care professionals reported financial concerns and parental attitudes as barriers to providing HPV vaccination. Parental concerns included the vaccine's effect on sexual behavior, low perceived risk of HPV infection, social influences, irregular preventative care, and vaccine cost[9]. Since vaccine licensure in 2006, HPV vaccine coverage among females in the United States have increased over time but remains low compared with other vaccinations recommended at the same ages[10].

Low completion rates of the HPV vaccine series have been attributed to a variety of barriers with the overall lack of knowledge and education of the medical implications of HPV as the most common among young adult women. In a randomized-controlled trial of 365 women aged 19–26 y old, Unger et al. found that knowledge of HPV was highly variable with a mean HPV knowledge score of 11.0 out of 19.0 (SD = 3.3)[11]. In another survey study of 383 undergraduates, Barnard et al. showed the HPV vaccination rate in females to be 47%, and most respondents had a low perception and understanding of contraction susceptibility[12]. Similarly, Mills et al. found that knowledge gaps about HPV, cervical cancer, and vaccination, as well as ambiguous information sources were major barriers in young women aged 18–26 y old to initiating and completing the HPV vaccination[13]. However, Sanderson et al. found that provider recommendation, but not education materials, increased the likelihood of vaccine receipt at the initial clinic visit among adolescents[14]. Targeted interventions providing education to increase an overall greater understanding of the HPV vaccine, as well as transmission and susceptibility, may lead to increased vaccination rates.

Our study also suggested racial/ethnic disparities in the vaccination rates. Previous studies have identified racial disparities in HPV vaccine initiation and completion of series. In a retrospective cohort study of 9,648 adolescents and young adults, Simons et al. demonstrated an overall completion rate of 29%, with being non-Hispanic Black as a significant association with lower completion rates[15]. In a survey study of 835 college women aged 18–26 y old, Okafor et al. demonstrated in an adjusted analysis that Black women were significantly less likely to report initiation and completion (adjusted prevalence ration 0.78 and 0.64, respectively), compared to White women[16]. Similarly, in a retrospective review of 310 adolescent and young women aged 13–26 y old, Perry et al. found that Black patients had the lowest completion rate and were significantly less likely to compete the vaccination series compared to White patients (adjusted relative risk of 0.71)[17]. Hull et al. showed that African-American adolescents and their mothers overwhelmingly thought campaigns should target both girls and boys for HPV vaccination[18]. Parallel to the aforementioned studies, our study demonstrated racial/ethnic disparities in vaccine uptake, with lower HPV vaccination rates in African-American and Hispanic women compared to White women. Further studies are needed to understand implications of cultural perception of the HPV vaccine to provide more appropriate and targeted interventions.

While the prior studies have addressed patient specific influences, there have been a few studies that have investigated provider and clinic factors that may impact HPV vaccination rates. In a retrospective study of 44 providers, Henrikson et al. showed a high proportion of providers reported a lack of concern for either HPV vaccine completion or initiating the vaccine series several years past the recommended target age[19]. In a qualitative study of 61 interviews with different type of providers within the same healthcare system, Hudson et al. found that providers at medical centers with higher HPV vaccine-series completion reported a greater communication technique, cultural awareness, practical barriers to access, and supportive environment to complete the vaccine series, compared to the providers in low completion centers[20]. While our study did not identify significant differences in completion rates based on clinic setting, we found a remarkably high number of patients (n = 97) in the later-cohort who were incomplete and had missed opportunities in clinic to receive their necessary vaccination doses. Providing provider, clinic and overall practice specific interventions to reduce missed opportunities is important to better care for patients and increase HPV vaccination rates.

There have been efforts to increase HPV vaccine initiation and completion rates by implementing various programs and initiatives across adolescents and young adults. In a multifactorial intervention consisting of provider and staff education, feedback on vaccine coverage, patient reminders and provider recall notifications, McLean et al. demonstrated an increase in HPV vaccine coverage from 41% to 59% in the departments receiving the intervention compared to a 32–45% coverage rate in the control groups[21]. Additionally, other countries, such as Australia, have implemented national publicly funded HPV programs resulting in vaccination rates as high as 78.6% for girls and 72.9% for boys. With these vaccinations rates, Australia has predicted that cervical cancer would be eliminated as public health problem, with fewer than 1 death per 100,000 women per year by 2034[22]. Our study highlights the need to explore barriers and initiatives to improve these vaccination rates.

This study has limitations with possible implications for its interpretation. The data was retrospectively analyzed for the purposes of this study and are subject to the inherent weaknesses of retrospective analyses. Socioeconomic status was not collected and may have an influence on access to vaccination completion. Provider details including education, credentials, and time of experience were not collected and may have implications on our findings. The practice type for the early cohort was not collected and comparison to the later cohort may provide more information regarding the trends of HPV completion rates in specific practice settings. Reasons for HPV vaccine series discontinuation, including side-effects, were not evaluated and may have contributed to incomplete vaccination series. Reasons for missed opportunities were not

evaluated and may have an impact on vaccination completion. Despite these limitations, our analysis highlights a relatively low completion rate that has not significant changed over a 4-y period. BMI was associated with lower HPV vaccination completion. Further studies are needed to explore this association. Additionally, African-American and Hispanic race/ethnicity had lower vaccine completion despite the higher rate of HPV related cervical cancer in those populations. Because HPV vaccination is now indicated in men and women up to age 45,[7] our study suggests an opportunity to expand interventions for HPV vaccination in adults.

Materials & methods

The medical records of 845 adult women (≥18 y old) who were administered the HPV vaccine series by a GYN provider affiliated with a major academic institution from 2006 to 2010 and 2014 to 2015 were retrospectively reviewed. Institutional Review Board approval was obtained prior to study initiation. Patients were grouped based on date of vaccine initiation, January 2006–December 2010 (Earlier: n = 399) versus January 2014–December 2015 (Later: n = 446). The later cohort reflects the period after an institutional initiative to increase provider awareness for HPV vaccine initiation and completion. Women who completed any part of the vaccination series outside of the institution and no documentation of vaccination were excluded from the study.

Baseline characteristics and demographic variables included patient Age, Body Mass Index (BMI), and Race/Ethnicity: White, African American, Hispanic, Asian, and Middle Eastern. Other variables collected included dates of vaccinations and type of practice where the patients were seen: Private Practice, Faculty Practice, Resident Practice, Affiliated-Rural Practice, and Colposcopy clinic.

Patients who successfully received all three vaccines within six months of vaccine series initiation date were deemed "complete" in line with guidelines at the time. Patients who were seen by a GYN provider during the 6-month period after vaccine series initiation date and did not receive the sequential vaccine were considered "missed opportunities". The primary outcome investigated in this study was completion rate of patients with missed opportunities. The secondary analysis investigated characteristics of patients and providers that were associated with increased completion.

Parametric data were expressed as means ± standard deviation (SD) and compared using the Student's t-test. Nominal data were compared with the Chi-square test. All tests were two sided and were statistically significant if the *p*-value was less than 0.05. Statistical analysis was performed using JMP®, Version *12*. SAS Institute Inc., Cary, NC, 1989–2007.

Conclusion

Our study found an overall low HPV vaccine completion rate by gynecologic providers that does not significantly change over a 4-y period. Additionally, higher BMI and African-American and Hispanic race/ethnicity were associated with low vaccine completion. Further studies are needed to identify effective, cost-efficient interventions to increase HPV vaccination initiation and completion rates among young adults and ultimately reduce the burden on HPV-related cancers in the United States. Moreover, targeted intervention based on practice setting and patient population is necessary to better serve patients and decreases barriers of access.

Disclosure of potential conflicts of interest

The authors whose names are listed immediately below certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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