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# Impact of electronic health record (EHR) reminder on human papillomavirus (HPV) vaccine initiation and timely completion

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## Abstract

**Background—**Initiation and timely completion of the HPV vaccine in young women is critical. We compared initiation and completion of HPV vaccine among women in two community-based networks with electronic health records: one with a prompt and reminder system (prompted cohort) and one without (unprompted cohort).

**Methods—**Female patients aged 9–26 years seen between March 1, 2007 and January 25, 2010 were used as retrospective cohorts. Patient demographics and vaccination dates were extracted from the electronic health record.

**Results—**Patients eligible for the vaccine included 6019 from the prompted cohort and 9096 from the unprompted cohort. Mean age at initiation was 17.3 years in prompted cohort and 18.1 years at unprompted cohort with significantly more ($p<0.001$) patients initiating in the prompted cohort (34.9%) compared to the unprompted cohort (21.5%). African Americans age 9–18 years with three or more visits during the observation period were significantly more likely to initiate in the prompted cohort ($p<0.001$). Prompted cohort was significantly more ($p<0.001$) likely to complete the vaccine series timely compared to unprompted cohort.

**Conclusion—**More patients age 9–26 years initiated and timely completed the HPV vaccine series in clinics using an electronic health record system with prompts compared to clinics without prompts.

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**Conflicts of interest:** Dr. Ruffin is conducting a study funded by the National Cancer Institute and Merck provides free HPV vaccine to the study participants and pays serum assays. Merck had no role in the design, implementation or analysis of this study.

**Prior Presentation:** Early data from this study was presented at the 25th International Papillomavirus (IPV) Conference. Malmö, Sweden; May 2009 by Patel DA, Dempsey AF, Ruffin MT. HPV vaccine uptake after initiation of electronic provider prompting system.

## BACKGROUND

The Advisory Committee on Immunization Practices (ACIP) currently recommends routine vaccination of females and males aged 11 or 12 years with three doses of a HPV vaccine.[1] HPV vaccine is administered intramuscularly as three separate 0.5 ml doses, with the second dose occurring one to two months after the first dose, and the third dose occurring six months after the first dose. The vaccination series can be started beginning at age 9 years, with catch-up vaccination recommended between 13–26 years. The vaccine series was approved for males in 2010 by the Food and Drug Administration and in 2011 the Centers for Disease Control and Prevention.[2]

National estimates of HPV vaccine uptake provided by the Centers for Disease Control and Prevention's (CDC) National Immunization Survey (NIS) reported 25.1% of adolescent females aged 13–17 years initiated the vaccine series (≥1 dose) in 2007.[3] Between 2008–2012, HPV vaccine initiation increased from 37.2% to 53.8% and HPV vaccine series completion (≥3 doses) from 17.9% to 33.4% among adolescent females.[3] During the same time period of increased initiation and completion of the HPV vaccine series, there were 84% of unvaccinated girls missing one or more opportunities to get the vaccine in 2012.[3] Uptake has been substantially lower among adult women, with available data from the NIS–Adult indicating that only 10% of women ages 18–26 initiated HPV vaccination in 2007.[4] An emerging body of literature examining factors associated with HPV vaccine initiation and/or series completion has identified several significant predictors of uptake including age,[5–7] race/ethnicity,[5, 7–10] student status,[11] medical specialty,[5, 12] clinic type,[7] insurance type,[5, 7–9] urban status,[6] neighborhood education level,[9] historical health service utilization,[6, 9] receipt of meningococcal vaccine,[6] use of contraception requiring intramuscular injections every three months,[8] perceived personal importance of vaccination,[11] and strength of physician's recommendation.[11] Another critical barrier reported by parents is not receiving a health care professionals recommendation for the HPV vaccine.[13]

The few published observational studies on adherence to dosing intervals used different definitions for "on time" dosing. Tan et al. examined factors associated with on time dosing in a retrospective cohort study of female patients ages 9–26 with at least one HPV vaccine dose documented in the North Carolina Immunization Registry.[7] During the two-year study period, only 25% completed the HPV vaccine series on time as defined by the dosing window used in the quadrivalent HPV vaccine trials, with significant differences in on time series completion by age, race, ethnicity, insurance type, and clinic type. Widdice et al. examined adherence to the dosing schedule recommended by the ACIP and factors associated with series completion within 7 and 12 months in a retrospective review of health records from 9–16 year old patients who had initiated HPV vaccination at an academic medical center.[8] The authors found low adherence to ACIP-recommended intervals, with over half of doses received late and only 28% of patients completing the three-dose series by one year.

Reminder calls to families are, in general, effective at vaccine uptake.[14] Only three studies that have examined reminder calls or prompts for adolescent vaccination have been

published.[15–17] Only the recent study demonstrated clinician-focused intervention that included electronic health record (EHR) alerts was most effective for initiating the HPV vaccination series.[15] However, EHR alerts were part of a more resource intense intervention so one cannot determine the impact of turning on alerts.

The objectives of this study were to examine the effect of simply turning on an EHR alert for HPV vaccine initiation, series completion, and adherence to ACIP-recommended dosing intervals among eligible female patients. This less resource intense approach will be become more common in our practices. We hypothesized that the practice with EHR prompts for the HPV vaccine would have higher initiation, more timely completion of the series, and more patients completing the series.

## METHODS

### Study Design

We used a retrospective cohort design.

### Study Population

We defined two cohorts of women age 9–26 years beginning in March 1, 2007, with at least one doctor appointment between March 1, 2007 and January 25, 2010 seen in two different community-based Family Medicine practices.

### Study Setting

The exposure or prompted cohort was from patients seen in five academic community-based Family Medicine practices in the Midwest with a common institution-created EHR and electronic reminder system. The control or unprompted cohort was patients from another four academic community-based Family Medicine practices in the Midwest with a common EHR without any electronic prompting or alert system for vaccines (hereafter referred to as unprompted cohort). The two academic centers do not have overlapping catchment areas. The available characteristics of the clinics from 2007 are summarized in Table 1 by prompted and unprompted cohort. There are a wide range of full time equivalent faculty physicians, number of patient visits in 2007, and patient per full time equivalent faculty physicians between clinics within a cohort and between cohorts as highlighted in Table 1. In the prompted cohort, two of five clinics have residents while all clinics in the unprompted cohort have residents. All of the clinics have medical students. The research ethics were reviewed by human research committees and approved by an institutional review board.

### Outcomes

The primary outcome of interest was the initiation and completion of the HPV vaccine series including time between each vaccine. The covariates of interest were age, race, and number of visits during the observation period.

### Exposure and Intervention

The primary intervention was the exposure during HPV vaccine alerts during encounters with their health care providers in the prompted cohort. At the time of the patient encounter,

patients and parents, providers (including physicians, nurse practitioners, physician assistants, and medical assistants) received the HPV vaccine paper prompt produced by the EHR. These practices had been using such a system since 2000, which included alerts for preventive and chronic care services.[18] Vaccine alerts had been in place for a variety of childhood, adolescent and adult vaccines. The HPV vaccine alert was started March 2, 2007. The provider alert was a simple list of services needed. For HP V vaccine the alert was HPV followed by the vaccine needed in the series. As part of this active prompting system, providers were required to respond to the HPV vaccine prompts with one of the following options: done, ordered, patient declined, patient not eligible, discussed, or not addressed. If results indicate not addressed or if additional vaccinations are due, the prompt will return at the next following visit. Patients and parents received a brief note of services your provider will recommend for today. Reminder algorithms were developed using Cielo Clinic™ (Cielo MedSolutions, Ann Arbor, MI) to prompt providers and patients at all appointments of females eligible to initiate or complete HPV vaccination at appropriate intervals.[18] The unprompted cohort was seen in practices with an EHR without any systematic form of alerts for vaccines or other preventive services.

## Analytic Variables

**Patient characteristics—**Patient age was based on the age at the start of the observation period, and was categorized as 9–18 years or 19–26 years. Patient race was categorized as White, African American, or Other. The total number of visits during the observation period was categorized as 1–2 visits or at least 3 visits made with a clinician including medical doctors (MD), doctor of osteopathic medicine (DO), nurse practitioner (NP), or physician's assistant (PA). Visits made solely for vaccine delivery were not included in the analysis.

**HPV vaccine initiation and series completion—**Vaccine initiation was defined as receipt of at least one dose of HPV vaccine during the observation period. Series completion was defined as receipt of all three doses of HPV vaccine during the observation period. Variables were created to indicate opportunity to get subsequent HPV vaccine doses, based on the lower limits recommended by the ACIP. Patients with at least thirty weeks elapsing after their first HPV vaccine dose were considered to have had the opportunity to complete the vaccine series during the observation period. We defined the time between doses using the date of vaccine from the EHR for each dose.

## Statistical Analysis

Descriptive statistics on age, race, and number of vaccines received were calculated and compared between the two study cohorts using chi-square and independent samples t-tests and between clinics within cohorts using chi-square and one-way ANOVA. Multiple imputation was performed to impute values of race for subjects where race was unknown. A multinomial logistic regression model, including covariates of age, study cohort, number of visits, and number of HPV vaccines received, was used to estimate race category probabilities for observations with missing race information. These probabilities were used to multiply impute race information for a total of 10 imputed data sets. Analysis including race was performed on each imputed data set and results combined using Rubin's formula.[19]

Correlates of vaccine initiation were examined using a clustered multivariable logistic regression model predicting receipt of ≥1 HPV vaccine doses versus no vaccination during observation period. Correlates of vaccine series completion were examined in the subset of study patients who initiated the HPV vaccine series and had the opportunity to complete the series during the observation period, using a clustered multivariable logistic regression model predicting receipt of all three HPV vaccine doses versus receipt of any (i.e., 1 or 2) doses during observation period. Both models included the covariates of age, race, number of visits during the observation period, study cohort, and interactions of study cohort with all other covariates. Both models were fit using a generalized estimating equations approach with exchangeable working correlation structure to account for practice clustering. Results are presented as adjusted odds ratios and associated 95% confidence intervals (CI).

Time to subsequent vaccine dose was estimated using the Kaplan-Meier product-limit estimator for time between dose 1 and 2 and dose 1 and 3 (completion) on the subset of subjects who initiated the series, and for time between dose 2 and 3 on the subset of subjects who received a second dose during the study period. Differences in survivor functions by study cohort were tested using the log-rank test. Cox proportional hazard models were used to estimate the impact of study cohort on time to vaccination after adjusting for covariates for the same three intervals, using the same subsets of subjects as Kaplan-Meier estimates. Covariates in all three models included study cohort, patient age, patient race, and interactions between cohort and both race and age. Standard errors were calculated using a robust variance estimator method to account for practice clustering. Results are presented as hazard ratios with corresponding 95% confidence intervals. All analyses were conducted using SAS version 9.3 (SAS Institute, Inc., Cary, NC).

## Results

### Study population

During the observation period, a total of 5994 females ages 9–26 in the prompted cohort and 9027 at the unprompted cohort were seen and eligible for the HPV vaccine. The prompted population had younger patients, on average (17.8 years vs. 18.5 years, p-value <0.001). Race distribution is inconclusive given ethnic race was not self-reported and noted as “missing” in over 33% of the unprompted study patients. Descriptive data of the study population is provided in Table 2.

In Table 3, the distribution of patients eligible for HPV vaccine by clinics within each cohort by age and vaccine delivery is summarized. Within each cohort there were significant differences between clinics by age, race, and vaccine delivery. However, all of the clinics within the prompted cohort had significantly higher rates compared to the clinics in the unprompted cohort.

### HPV vaccine initiation

More vaccine-eligible females seen during the observation period initiated the series (received at least one dose) in the prompted cohort (35.0%) compared to the unprompted cohort (21.3%), overall (Table 1). Age, number of visits, and race were significantly

associated with HPV uptake. Significant interactions between cohort and each covariate indicate differences in the cohort effect on initiation for different levels of covariate values, which are illustrated in Figure 1. The prompted cohort had significantly higher odds of initiation at each level of covariates with the exception of the subset of Other race younger patients who had 3 or more visits with their PCP during the study period (OR=0.9, p-value=0.41). The highest effects were present in the older age group who had fewer visits during the study period (ORs range from 3.5 to 6.3).

### HPV vaccine series completion

There were 1936 patients who initiated and had the opportunity to complete the vaccine series in the prompted cohort and 1706 in the unprompted cohort. Age and race were significantly associated with series completion in the prompted cohort while race and number of observations were significant in the unprompted cohort. The effect of study cohort on series completion are illustrated in Figure 2, the prompted cohort had significantly higher odds of completion when compared with the unprompted for all levels of covariates, with the highest effects present for patients with fewer number of physician visits.

### Time to subsequent vaccine doses

Patients in the prompted cohort were significantly more likely ($p<0.001$) to receive all three doses on time and at shorter median intervals between each dose compared to those at the unprompted cohort per the study-defined schedule. These differences are further highlighted in Figure 3.

Results of Kaplan-Meier survival analyses and log rank tests indicated that survival functions for time to subsequent dose was significantly different between cohorts in all three time periods (dose 1 to 2, dose 2 to 3, and dose 1 to 3, p-value<0.0001 for all three). Hazard ratios, estimated using Cox proportional hazard models (Figure 4), between cohorts were significant in all situations with the exception of the comparison of prompted vs. unprompted patients who were either African American or of Other race and in the older age group on the time between dose 1 and dose 3.

## DISCUSSION

In this unique contrast of two community-based family medicine networks using retrospective cohorts, we demonstrated that clinics using an EHR with clinicians and patient HPV prompts at office appointments resulted in significantly more young women initiating and completing the vaccine in a timely fashion. Whether using prompts or not, females age 9–18 years and having three or more visits were significantly more likely to initiate the vaccine. The differences were more pronounced when contrasting the two clinical networks for these variables. African Americans in the prompted clinics were significantly more likely to initiate the HPV vaccine than Whites. The prompts to both clinicians and patients may create a common agenda that facilitates the initiation and/or minimizes the unconscious discrimination of clinicians.[20] Many reports have noted that African Americans are less likely to get the HPV vaccine.[8, 9, 21] Clinicians could be unconsciously assuming that African Americans are not interested in the HPV vaccine.[22] Therefore, the clinician does not

bring it up given all of the patient-centered competing demands during an appointment. In addition, discriminatory actions are more likely to occur when situational demands are unclear or when norms for appropriate actions are ambiguous.[23] Given the time period of this study, women presenting for a primary care visit would not have a clear medical standard to be offered HPV vaccine. Systematic systems such as cues and alerts have been shown to reduce the difference between White and African American uptake of preventive services such as colorectal cancer screening.[24] This study is the first to report an impact of alerts on vaccine uptake in young African American women.

We found having three or more visits was associated with increased rates of initiation in both cohorts. This effect however was more pronounced at the unprompted cohort. There was no correlation with number of visits to vaccination completion in the prompted cohort. Patients and providers in the prompted cohort appeared to be using the encounters to address HPV vaccine in addition to the primary reason for the visit. As a result, fewer appointments were needed which led to more efficiency. This highlights the promise of an electronic prompting system in improving vaccination uptake without increasing visits.

As hypothesized, timeliness of vaccination was also demonstrated to be superior at the prompted cohort compared to unprompted cohort across all three doses of the HPV vaccine series. The prompts may reflect completion at subsequent visits for reasons other than vaccination only. Or the clinics with the prompts may have other systems in place to assure appointments just to complete the vaccine are scheduled. We are not aware of any systematic protocols in any of the five clinics using the prompts during the observation time period. We did not count appointments for vaccination only with a nurse or medical assistants. The visits counted were with a clinician.

There are limitations to this study. This was not a randomized control trial allocating clinics to HPV vaccine prompt and no prompts. This was a retrospective cohort study observation of two different clinical networks during the same time period. There could be other factors that may account for the differences noted in initiation, completion and interval between vaccines other than the EHR vaccine alert for HPV. These other factors could be community or population acceptance of the vaccine, insurance coverage, access to healthcare, competing health issues, clinician attitude about the vaccine, and office organization. We do not have data to examine these and other variables. The prompted clinics were also seeing alerts for other childhood, teen, and adult vaccines. The HPV vaccine was not the only vaccine prompt; therefore, unique focus of clinics and clinicians to HPV vaccine in the alerts was unlikely. We only focused on female patients given that the vaccine was only approved for women during the study time period. We are not able to comment on the impact of male patients' uptake and completion of HPV vaccine. Finally, the observation period was early in the rollout of the HPV vaccine. Other environmental and cognitive factors that have been linked to preventive uptake and completion of preventive services may be different now.[24] Therefore, uptake and completion of HPV vaccines may be different now. However, our initiation and completion rates were higher than a recently published trial of an intervention done in 2010–2011.[15] Given the recent data on alternative number of shots and schedules for HPV vaccine, striving for completion of the three-dose HPV vaccine series at these intervals may not be critical.[25–27]

This study demonstrated that simply alerting patients and clinicians at an office appointment with women age 9–26 years increases the uptake and completion of the HPV vaccine series. The other study of prompts for HPV vaccine was not just an intervention of EHR generated alerts. The intervention included (1) HPV vaccine alerts, (2) a 1-hour presentation about the alerts and review of practice-based HPV vaccine rates, and (3) quarterly performance feedback about HPV vaccine rates.[15] This intervention increased vaccination rates by 9, 8 and 13 percentage points for each HPV dose and accelerated vaccination by 151, 68, and 93 days.[15] This was a much more resource intense intervention compared to turning on a new vaccine alert. The prompted clinics had 15-percentage point increase in HPV vaccine completion. The vaccine dosing was accelerated on average by 60, 30, and 70 days between dose 1 and 2, dose 2 and 3, and dose 1 and 3 compared to the unprompted clinics. Our less resource intense intervention had similar improvements. All EHRs should have functionality of vaccine alerts as a core component. Further refinements of this process needs to be examined to push the uptake and timely completion of HPV vaccine higher. We also need to examine outreach that moves beyond the patient clinician encounter that may have even greater impact.

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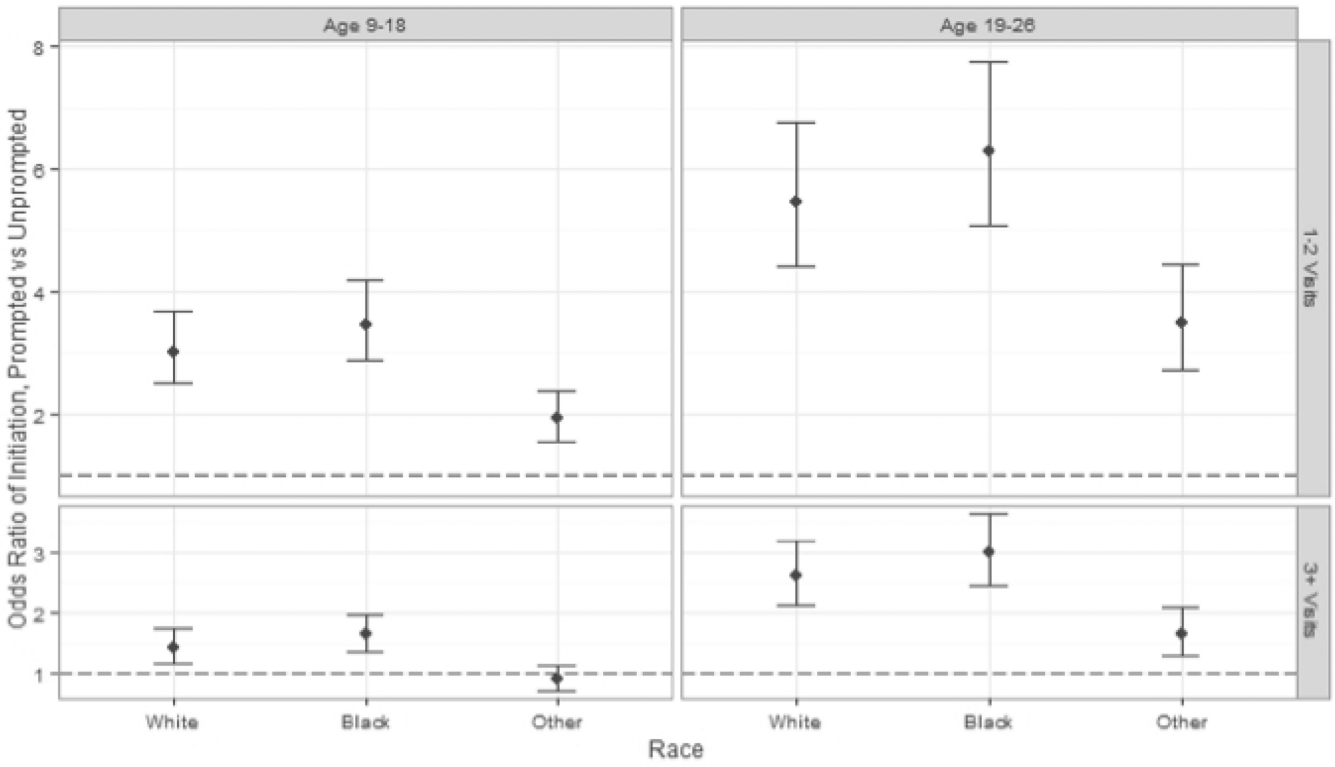


**Figure 1.**

Odds Ratioa (95% Confidence Interval) of series initiation, Prompted Site vs Unprompted Site, at levels of covariates

[a] Odds ratios from clustered logistic regression predicting receipt ≥1 HPV doses versus no vaccination during observation, including age, race, number of visits and interaction of all variables with study site. Analysis also adjusted for practice clustering using GEE with exchangeable working correlation structure.

Dotted line represents an odds ratio of 1, which would indicate no significant site effect.

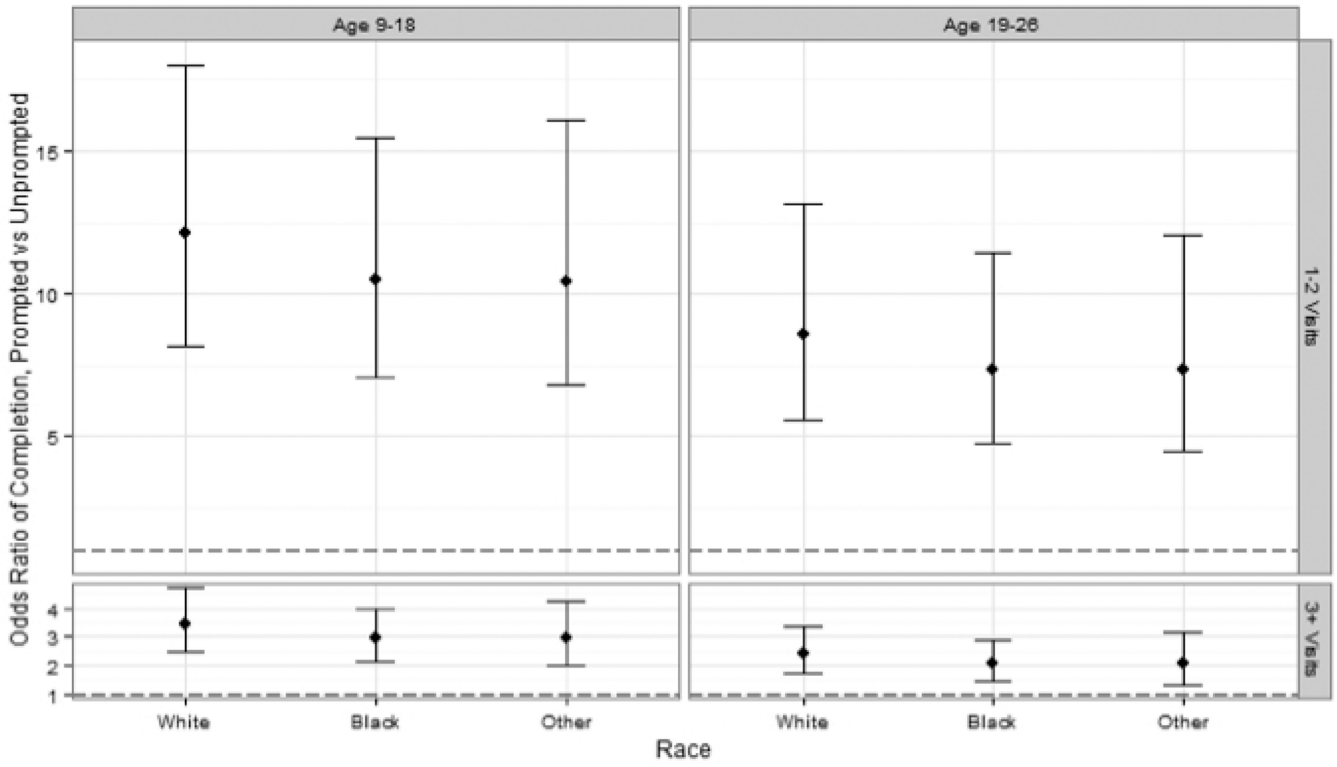


**Figure 2.**

Odds Ratioa (95% Confidence Interval) of series completion, Prompted Site vs Unprompted Site, at levels of covariates among patients who initiated the HPV vaccine series and had the opportunity to complete the series during the observation periodb

[a] Odds ratios from clustered logistic regression predicting receipt of all three vaccination doses vs any (i.e. 1 or 2) doses during observation, including age, race, number of visits and interaction of all variables with study site. Analysis also adjusted for practice clustering using GEE with exchangeable working correlation structure.

[b] 1936 patients with opportunity to complete series at Prompted site and 1706 at Unprompted site Dotted line represents an odds ratio of 1, which would indicate no significant site effect.

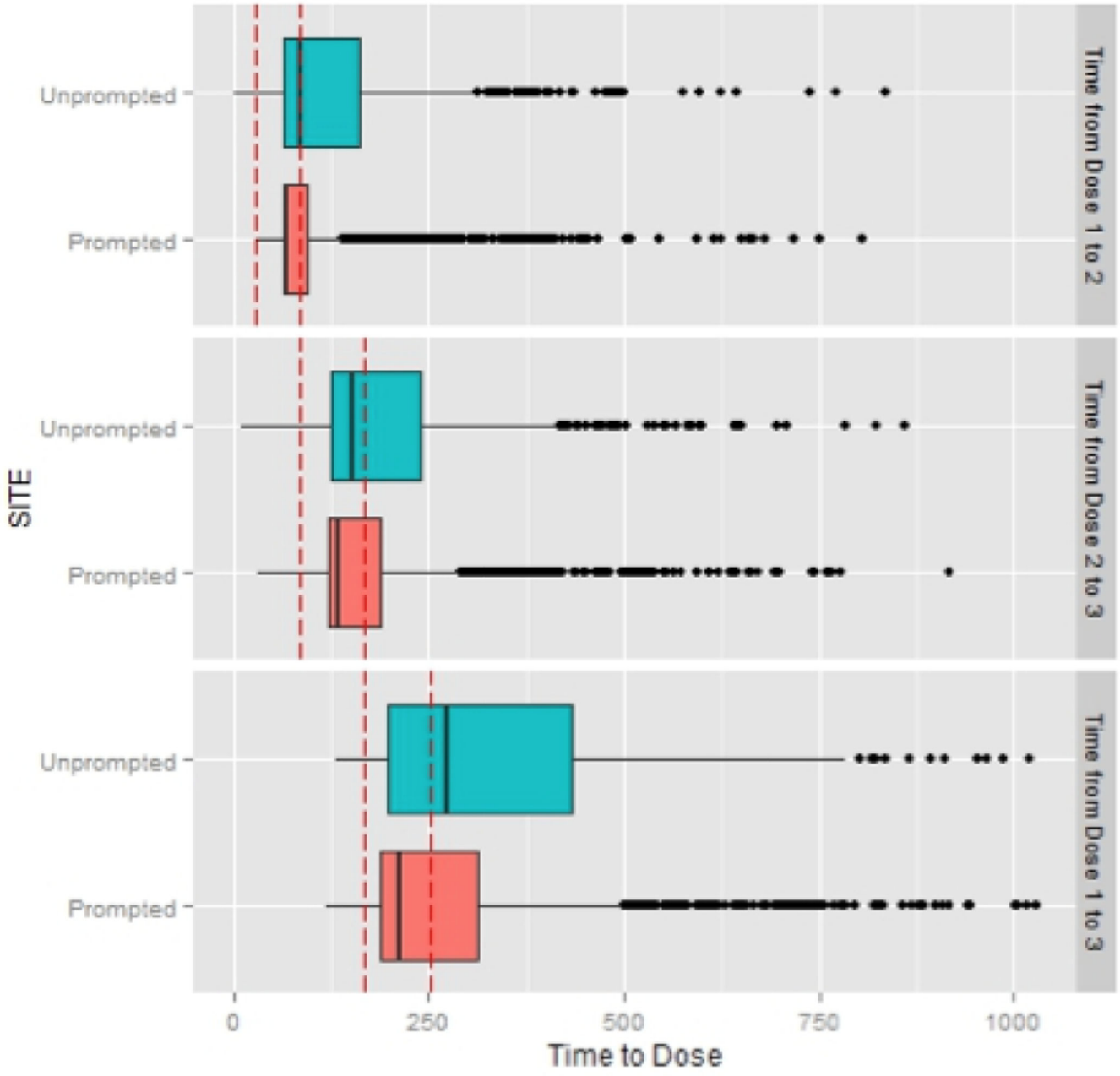


**Figure 3.**

Time to each vaccine dose

Shaded box represents interquartile range (25th to 75th percentile), solid vertical line within shaded box represents median, dots are outliers beyond 1.5 times the interquartile range from 75th percentile. Red dashed lines in each panel represent the ‘on time’ time range for each interval.

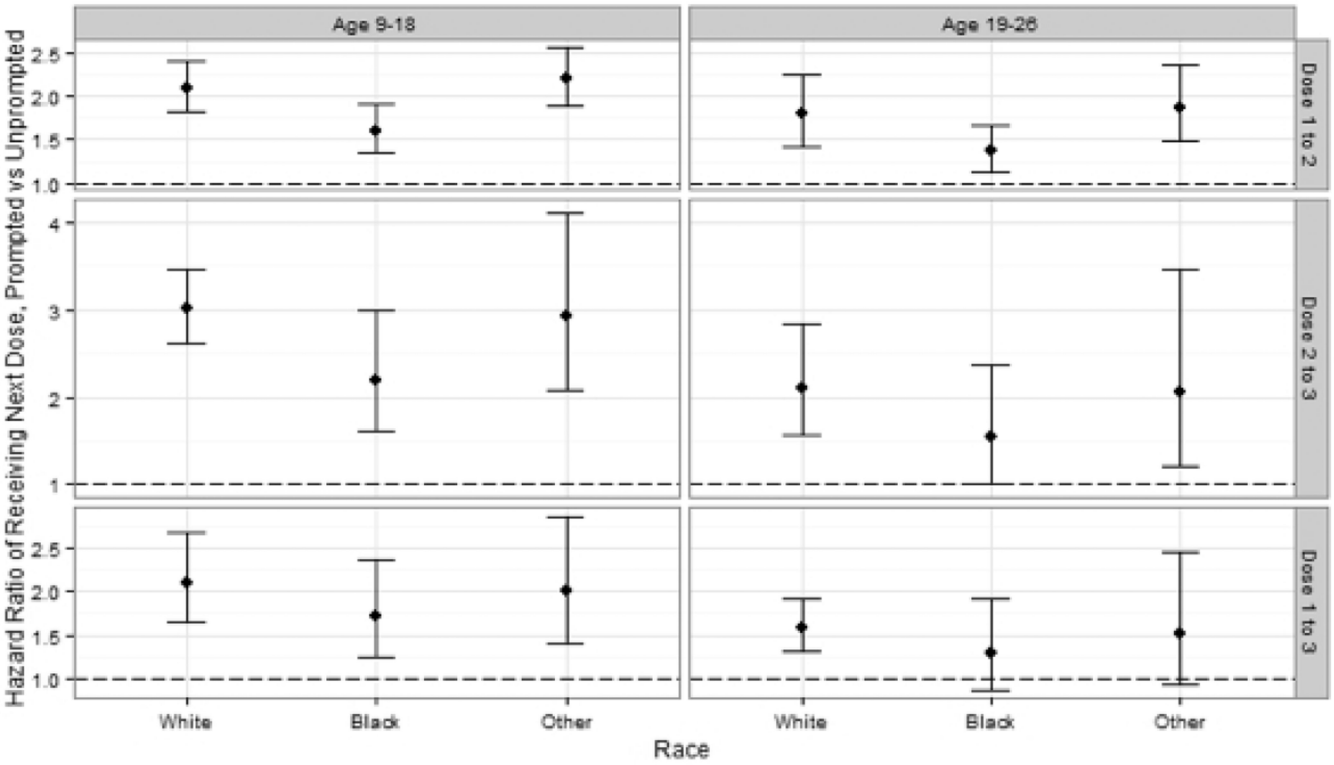


**Figure 4.**

Time between Dose 1 to 2, 2 to 3, and 1 to 3 by Age and Race for each Cohort

Hazard Ratios estimated using Cox Proportional Hazard models, with clustered standard errors, including age, race, study site, age*site and race*site. Analysis for dose 1 to dose 2 and dose 1 to dose 3 performed on the 4,019 patients who initiated the series. Analysis for dose 2 to dose 3 performed on the 2,731 patients who received a second dose during the study period. Dotted line represents a hazard ratio of 1, which would indicate no significant site effect.

**Table 1**

Characteristics of clinics by cohort

| | Prompted Cohort | | | | | Unprompted Cohort | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Clinic 1** | **Clinic 2** | **Clinic 3** | **Clinic 4** | **Clinic 5** | **Clinic 6** | **Clinic 7** | **Clinic 8** | **Clinic 9** |
| **Full Time Equivalent Faculty Physicians** | 9 | 8.7 | 4.7 | 8.1 | 4.7 | 10 | 11 | 6 | 10 |
| **Middle Level Clinicians** | Yes | Yes | Yes | Yes | Yes | No | Yes | No | No |
| **Medical Students** | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| **Residents** | No | Yes | No | No | Yes | Yes | Yes | Yes | Yes |
| **Patients Visits 2007** | 31,611 | 30,321 | 16,213 | 18,389 | 22,022 | 26,215 | 30,367 | 21,540 | 29,595 |
| **Patient Visits Per Full Time Equivalent Faculty Physician** | 3,512.3 | 3,485.2 | 3,449.6 | 2,270.2 | 4,685.5 | 2,621.5 | 2,760.6 | 3,590.0 | 2,959.5 |

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**Table 2**

Characteristics of study patients

| | Prompted N=5,994 | Unprompted N=9,027 | p-value |
|---|---|---|---|
| **Characteristic** | **n (%)** | **n (%)** | |
| **Age** | | | <0.001 |
| 9–18 | 3304 (55.1) | 4585 (50.8) | |
| 19–26 | 2690 (44.9) | 4442 (49.2) | |
| Mean (SD) | 17.8 (4.3) | 18.5 (4.8) | <0.001 |
| **Race** | | | <0.001 |
| White | 4026 (67.2) | 1437 (15.9) | |
| African American | 1101 (18.4) | 2957 (32.8) | |
| Other | 769 (12.9) | 1643 (18.2) | |
| Missing | 98 (1.6) | 2990 (33.1) | |
| **HPV Vaccine** | | | <0.001 |
| 0 | 3899 (65.0) | 7103 (78.7) | |
| 1 | 456 (7.6) | 832 (9.2) | |
| 2 | 431 (7.2) | 588 (6.5) | |
| 3 | 1199 (20.0) | 492 (5.5) | |
| >3 | 9 (0.2) | 12 (0.1) | |

**Table 3**

HPV Vaccine given by clinic site within each cohort

| | Prompted Sites | | | | | Unprompted Sites | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Clinic 1** | **Clinic 2** | **Clinic 3** | **Clinic 4** | **Clinic 5** | **Clinic 6** | **Clinic 7** | **Clinic 8** | **Clinic 9** |
| **Age of Patients Eligible for HPV Vaccine during the Study Period*** | | | | | | | | | |
| 9–18 | 911 (52.2) | 738 (62.9) | 475 (53.8) | 591 (66.1) | 589 (45.4) | 1134 (52.2) | 879 (50.7) | 1066 (40.1) | 1506 (61.2) |
| 19–26 | 835 (47.8) | 436 (37.1) | 408 (46.2) | 303 (33.9) | 708 (54.6) | 1039 (47.8) | 855 (49.3) | 1593 (59.9) | 955 (38.8) |
| Mean (SD) | 18.0 (4.4) | 17.3 (4.2) | 17.8 (4.6) | 16.8 (4.3) | 18.8 (4.1) | 18.4 (4.9) | 18.5 (4.8) | 19.7 (4.4) | 17.3 (4.6) |
| **Race of HPV Eligible Patient Seen During Study Period*** | | | | | | | | | |
| White | 1175 (67.3) | 1116 (95.1) | 512 (58.0) | 778 (87.0) | 445 (34.3) | 210 (9.7) | 354 (20.4) | 611 (23.0) | 262 (10.6) |
| African American | 331 (19.0) | 9 (0.8) | 90 (10.2) | 10 (1.1) | 661 (51.0) | 450 (20.7) | 208 (12.0) | 1184 (44.5) | 1115 (45.3) |
| Other | 233 (13.3) | 37 (3.2) | 250 (28.3) | 69 (7.7) | 180 (13.9) | 548 (25.2) | 619 (35.7) | 301 (11.3) | 175 (7.1) |
| Missing | 7 (0.4) | 12 (1.0) | 31 (3.5) | 37 (4.1) | 11 (0.8) | 965 (44.4) | 553 (31.9) | 563 (21.2) | 909 (36.9) |
| **HPV Vaccine Given During Study Period*** | | | | | | | | | |
| 0 | 1169 (67.0) | 729 (62.1) | 652 (73.8) | 594 (66.4) | 755 (58.2) | 1602 (73.7) | 1160 (66.9) | 2114 (79.5) | 2227 (90.5) |
| 1 | 102 (5.8) | 87 (7.4) | 40 (4.5) | 58 (6.5) | 169 (13.0) | 255 (11.7) | 238 (13.7) | 218 (8.2) | 121 (4.9) |
| 2 | 114 (6.5) | 66 (5.6) | 52 5.9) | 42 (4.7) | 157 (12.1) | 182 (8.4) | 187 (10.8) | 154 (5.8) | 65 (2.6) |
| 3 | 360 (20.6) | 292 (24.9) | 136 (15.4) | 199 (22.3) | 212 (16.3) | 129 (5.9) | 147 (8.5) | 168 (6.3) | 48 (2.0) |
| >3 | 1 (0.1) | 0 (0.0) | 3 (0.3) | 1 (0.1) | 4 (0.3) | 5 (0.2) | 2 (0.1) | 5 (0.2) | 0 (0.0) |

*Significant differences found between clinics, within cohort, on all three variables (ANOVA and Chi-square p-values<0.001).