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Integrated Health Maintenance Reminders for Improved HPV Vaccine Administration: Towards Improvements in Completion Disparities

Jess D. Rames, MD, MEng^{*,1,2,3}, Nicholas A. Frisco, MD^{*,1}, Rong Jiang, PhD⁴, Kevin P. Shah, MD, MBA⁵, Russel R. Kahmke, MD, MMCI^{1,7}, Liana Puscas, MD, MHS, MA¹, Nosayaba Osazuwa-Peters, BDS, PhD, MPH^{1,6,7}, Daniel J. Roche, MD, JD^{1,7}

¹Duke University, Department of Head and Neck Surgery & Communication Sciences, Durham, North Carolina, USA.

²Duke University Pratt School of Engineering, Durham, North Carolina, USA.

³Mayo Clinic, Department of Plastic and Reconstructive Surgery, Rochester, Minnesota, USA.

⁴Department of Psychiatry and Behavioral Sciences, School of Medicine, Duke University, Durham, North Carolina, USA.

⁵Department of Medicine, Duke Primary Care, Durham, North Carolina, USA.

⁶Duke University School of Medicine, Durham, North Carolina, Department of Population Health Sciences, Durham, North Carolina, USA

⁷Duke Cancer Institute, Durham, North Carolina, USA

Abstract

Objectives—To evaluate the effect of a health maintenance reminder (HMR) on Human Papillomavirus (HPV) vaccine administration and completion across different age, insurance, and race cohorts.

Study Design—Retrospective pre-post analysis

Setting—Academic primary care

Corresponding Author: Daniel J. Roche, MD, JD, Department of Head and Neck Surgery and Communication Sciences, School of Medicine, Duke University, 40 Duke Medicine Cir, Durham, NC 27710-4000, USA. daniel.roche@duke.edu. Phone: 919-684-2426.

*Authors contributed equally to the generation of this manuscript

Authors Contributions:

Jess D. Rames, conception and design of work, acquisition, analysis and interpretation of data, drafting, final approval, agreement to be accountable. **Nicholas A. Frisco**, conception and design of work, acquisition, analysis and interpretation of data, drafting, final approval, agreement to be accountable. **Rong Jiang**, analysis and interpretation of data, drafting, final approval, agreement to be accountable. **Kevin P. Shah**, interpretation of data, drafting, final approval, agreement to be accountable. **Russel R. Kahmke**, interpretation of data, revision drafting, final approval, agreement to be accountable. **Liana Puscas**, interpretation of data, revision drafting, final approval, agreement to be accountable. **Nosayaba Osazuwa-Peters**, conception and design of work, analysis and interpretation of data, revision drafting, final approval, agreement to be accountable. **Daniel J. Roche**, conception and design of work, acquisition, interpretation of data, revision drafting, final approval, agreement to be accountable.

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Methods—Patients aged 9-26 who had initiated the HPV vaccine series from 2016 to 2021 were analyzed, based on current age-based standards. Cohort was divided based on vaccine uptake before and after implementation of HMR program in February 2020. Multivariate analysis estimated odds of vaccine completion based on sociodemographic factors, and variable interactions were investigated to determine independent associations between sociodemographic factors and HMR implementation.

Results—There were 7,654 individual patients (mean age was 15.8 years; 46.7 were males; and 50.7% were White). HPV vaccine completion rates increased post-HMR implementation by 59.2% (37% pre-, and 58.9% post-HMR; $p<0.001$) in the entire cohort. Overall, Black patients (aOR = 0.68; 95% CI 0.60, 0.70) and patients 18 years (aOR = 0.13; 95% CI 0.11, 0.15) were significantly less likely to complete their vaccine series; however, this improved significantly following HMR in these groups ($p<0.001$). Post-HMR, race and insurance status were not independently associated with disparate vaccine completion rates, however, age was, and patients 14 or younger had higher odds of vaccine completion (aOR = 3.54; 95% CI 2.91, 4.32).

Conclusion—The implementation of an HMR was associated with increased HPV vaccine uptake across age and race groups in this single institution study. Future research should explore barriers to implementing HMRs in different healthcare settings.

Keywords

Human Papillomavirus; Oropharyngeal Cancer; HPV Vaccine; Preventative Health; Health Maintenance; Quality Improvement

Introduction:

Human papillomavirus (HPV) remains one of the most common sexually transmitted infections,¹ with many high-risk variants classically associated with the development of diseases such as oropharyngeal and anogenital cancers.² For these indications, the implementation of the HPV vaccine in adolescents has proven effective for the prevention of long-term infectious and oncologic sequelae.^{3,4} More recently, the growing prevalence of HPV-associated oropharyngeal cancer (OPC) has prompted the expansion of indications to include the prevention of OPC and recommendation of catch-up vaccines in adults aged up to 26¹ and previously unvaccinated adults aged up to 45.⁵ Given that over 40,000 incident cases of HPV-associated cancers occur yearly,⁶ all qualified individuals should be encouraged to complete the HPV vaccine series, including individuals beyond the age of primary vaccination.

Despite the expansion of clinical indications, current vaccine completion rates remain relatively low. Recent National Immunization Survey-Teen data demonstrate that only 61.4% and 56.0% of adolescent females and males, respectively, were up to date on HPV vaccination in 2020.⁷ Furthermore, national claims data suggest that timely receipt of subsequent doses of the vaccine is low for both females and males.⁸ Pertinent barriers to vaccine completion include patient concerns over vaccine safety and efficacy, cost constraints, disparities in healthcare access, and other social factors.^{5,9} Specifically, race has been linked as an important negative predictor of HPV vaccine completion, with Black and

Hispanic patients having reduced completion rates compared to their White counterparts.¹⁰ Additionally, the ongoing COVID-19 pandemic has been associated with a reduction in the utilization of preventative health services,¹¹ and a decline in median doses administered of the HPV vaccine has been observed during the Spring of 2020 compared to previous years.¹²

Provider recommendation remains an integral factor in addressing existing barriers to HPV vaccination initiation and completion.¹³ Given the longitudinal nature of such care, the implementation of electronic health record (EHR) health maintenance reminder (HMR) systems has demonstrated improved vaccine uptake in different adolescent cohorts.^{14,15} Despite this, the effect of HMR on young adult cohorts encompassed by the expanded vaccination guidelines has not been well characterized, particularly in males up to 26 years old. Furthermore, few studies have assessed the impact of a standardized intervention like an HMR on existing racial disparities in vaccine completion.

Thus, the primary goal of this study was to assess the effect of an institution-wide HMR reminder on HPV vaccination completion rates, especially as it relates to newly covered age cohorts and historically marginalized racial groups. Ultimately, although otolaryngologists primarily manage HPV-associated OPC, by remaining removed from vaccination discussions, we are missing opportunities to prevent these conditions from occurring in the first place. This study explores the impact of a collaborative effort to improve HPV vaccination among otolaryngologists and primary care physicians at one institution.

Materials and Methods:

Study Participants and HPV Health Maintenance Reminder

Following approval from the Duke University Institutional Review Board, a retrospective analysis was conducted using patient data extracted from April 2016 to August 2021. A total of 7,654 individual patients aged 9 to 26 from 40 Duke Primary Care outpatient centers were included, all utilizing a common EHR. Pre- and post-intervention cohorts were defined with relation to the implementation of the EHR HPV HMR system in February 2020. The HMR was designed after prior alerts on health maintenance topics that had been implemented previously at our institution and was added to an existing interface containing other HMRs (for example, Diabetes screenings and childhood vaccines) by EHR superusers, who are employees that provide EHR operational support. After implementation, the reminder was pushed out to all physician, mid-level, and nursing staff of clinics using the EHR. When an eligible patient's chart was accessed, the provider would be automatically prompted to make a decision on outstanding HPV vaccination tasks, based on the patient's age, vaccine type, and vaccine dose in series. Providers were required to mark the task as "complete" or "incomplete" and provide a reason for the latter. If not completed, the alert would again populate on the next encounter with the patient.

Data Extraction

Data were extracted from all eligible patients using EHR SlicerDicer[®] (Epic)¹⁶ functionality. Relevant patient demographic features, including age, sex, race, and insurance

status were collected. Additional treatment data, including date of HPV vaccination, dose in series, vaccine type, and location of administration were extracted, along with data on total Duke Primary Care visits before and during the pandemic.

Cohort Division and Series Completion Definition

Patients included in the study must have had all doses of their vaccine administered within the Duke Health network to be included. Any patient starting the first dose of the HPV vaccine series within a year of the study's conclusion period was excluded from the study as it was not possible for these patients to receive the full complement of vaccines.

For our analysis, patients were subdivided along race-based, insurance-based, and age-based categories. Completion was defined based on the total number of vaccine doses received and the recorded age at first dose administration. In accordance with the age-based recommendations set by the Center for Disease Control's Advisory Committee on Immunization Practices, patients 14 or younger at their first dose required two doses to be considered complete. Comparatively, patients 15 or older needed three doses. Patients were considered complete upon receipt of all required doses within 12 months. Additionally, individuals were subcategorized based on when they received their last recorded HPV vaccine dose; patients were placed into "Before" and "After" categories with relation to the HMR implementation in February 2020.

Statistical Analysis

Relevant demographic characteristics were summarized with respect to HMR. Differences in proportions in the "Before" and "After" categories were interrogated using Fisher's Exact and Pearson's Chi Square test as appropriate based on contingency table parameters. Student's two-tailed t-tests were performed to determine the difference between continuous variables as needed. A multivariate logistic regression model was created to investigate the effect of race, insurance, gender, vaccine type, HMR implementation, and age on vaccination completion. Additionally, pairwise interaction covariance was included in subsequent multivariate modeling to determine the independent effect of HMR implementation on vaccination completion. A post-hoc contrast analysis was computed for the effect modifiers age, race, and insurance. Data analysis was performed in SAS (v. 9.4, SAS Analytics Software and Solutions, Cary, NC) while figure preparation was performed in R (v. 4.0.3, The R Foundation for Statistical Computing, Vienna, Austria).

Results:

Patient Population

During the study, relevant demographic data were collected from 7654 patients before and after the implementation of the HPV vaccine HMR. There were significant differences according to race ($p=0.006$), insurance status ($p<0.0001$), vaccine type ($p<0.0001$), and age (15.85 [4.16] years vs. 15.59 [4.52] years, $p=0.032$) before and after HMR. Overall, there was a slightly higher racial representation of White (51.7% vs 50.4%), Asian (8.7% vs 7.1%), and Other (12.2% vs 11.0) after the HMR. Additionally, there were more patients with private (73.7% vs 66.5%) or other (1.5% vs 1.1%) forms of insurance, and less

patients that were self-paid (4.7% vs 8.2%) after the change. After the HMR, only HPV 9-valent vaccines were administered (100% vs 97.8%). The gender distributions were not significantly different before and after the HMR ($p=0.819$). A full demographic breakdown can be appreciated in Table 1. Notably, outpatient visits decreased by 18% in 2020 during the pandemic compared to the prior 3 years. Total number of HPV vaccine doses administered concomitantly fell with outpatient visits during the pandemic (Figure 1).

Identifying Categorical Vaccine Completion Disparities

Multivariate analysis of completion identified reduced completion rates in Black (aOR = 0.68; 95% CI 0.60, 0.77), Other [Race] (aOR = 0.76; 95% CI 0.64, 0.90), patients 18 and older (aOR = 0.13; 95% CI 0.11, 0.15), and patients receiving the quadrivalent vaccine series (aOR = 0.17; 95% CI 0.10, 0.29). Patients with private insurance compared to Medicaid (aOR = 1.70; 95% CI 1.49, 1.93), those receiving vaccines after the HMR (aOR = 2.51; 95% CI 2.21, 1.85), and female patients (aOR = 1.12; 95% CI 1.01, 1.25) were more likely to complete their vaccine series. (see Table 2).

The Effect of HMR on Completion by Age, Race, and Insurance Status

Vaccine series completion was increased in all age cohorts after the implementation of the HPV vaccine HMR (37.0% vs 58.9%, $p<0.0001$). Statistically significant changes in completion were appreciated for patients 14 and under (55.8% vs 82.7%, $p<0.0001$), 15 to 17 (22.4% vs 41.2%, $p<0.0001$), and those 18 and over (18.8% vs 27.8%, $p<0.0001$). A breakdown of the complete vs. non-complete age counts and proportions is available in Figure 2. The proportion of complete vaccine series increased after HMR for White (40.5% vs 60.3%, $p<0.0001$), Asian (37.5% vs 65.7% $p<0.0001$), Black (31.6% vs 54.7%, $p<0.0001$), and Other (35.7% vs 57.8%, $p<0.0001$) patients. A breakdown of the complete vs. non-complete counts and proportions for race is seen in Figure 3. Patients who were self-paid (27.5% vs 49.3%, $p<0.0001$), had Medicaid (34.8% vs 62.0%, $p<0.0001$), or private insurance (39.0% vs 58.9%, $p<0.0001$) all had improved completion rates after HMR. Patients with other insurance had a less significant rise in completion (30.0% vs 47.8%, $p=0.13$).

Assessment of Inter-variable Interactions on Vaccine Completion

Post-hoc sub-analyses contrasting the effect of HMR controlling for age group revealed a disproportionate increase in vaccination completion rates among younger patients. Patients aged 14 or younger had the highest relative increase in odds of vaccine completion (aOR 3.54, 95% CI 2.91– 4.32) compared to those aged 15 to 17 (aOR 2.35, 95% CI 1.76– 3.13) or 18 or older (aOR 1.60, 95% CI 1.27– 2.20). Conversely, there was an appreciable age-dependent effect when comparing vaccine completion between different age categories when controlling for HMR. Patients aged 15 to 17 (aOR 0.66, 95% CI 0.47-0.94) and 18 or older (aOR 0.45, 95% CI 0.33-0.61) had relative reduced aORs when compared to those aged 14 or younger. Additionally, separate multivariate models were constructed to account for potential covariate relationships between HMR implementation and age, race, and insurance status, respectively, affecting vaccination rates. Only age was determined to be statistically significantly linked ($p<0.0001$) to differential HMR effects on vaccine completion. A summary of both sub-analyses can be seen in Table 3.

Discussion:

In this large, single healthcare system analysis of patients who initiated the HPV vaccine, sociodemographic factors, specifically Black race and age 15 years or older, were associated with reduced series completion rates. Implementation of an EHR-based HMR for the HPV vaccine helped bolster immunization completion rates in both males and females across all age-groups, insurance status, and self-identified race groups. When accounting for interaction, the before and after effect of the HMR on vaccine completion was significantly modified by patient age, with the greatest effect at younger ages. However, the effect of the HMR was not impacted by insurance status or race, with consistently improved completion rates for all groups in the main effects model. Overall, in contrast to prior studies, our study uniquely assesses the efficacy of HMRs on HPV vaccine completion in both males and females across a broad age-range of eligibility in relation to sociodemographic influences.

While improving primary vaccine series initiation remains the gold standard for the prevention of HPV-associated malignancy, vaccine series completion is necessary to ensure adequate immunologic response.¹⁷ Although some reports have shown modest improvement in completion rates of a 3-dose HPV vaccine series in women over time,¹⁴ a significant deficit in series completion among vaccine initiators remains.¹⁸ Several barriers to HPV vaccine completion have been identified previously.¹⁹⁻²¹ In our study, patients over the age of 15 years were less likely to complete their vaccine series when compared to those initiating their primary vaccine series, especially those over 18. This corroborates national reports that have shown only 16% completion rates in men and women ages 18-26 years, which is far less than that of adolescents.²² Those over age 18 represent a unique patient population that is newly autonomous in making healthcare decisions. Amplified by the propensity for insurance coverage to change during young adulthood,²³ this transition point represents an opportunity for patients to place a diminished priority on preventive care services. Providers play an important role in guiding these patients as they learn to navigate the healthcare system, especially as these patients may not be aware of HPV-associated cancers and the benefits of a vaccine for which they remain eligible.

When compared to White patients, Black patients who initiated the HPV vaccine series in our study were also less likely to complete the series. Black patients have been shown to have reduced initiation, completion, and catch-up vaccination rates for the HPV vaccine.^{24,25} This is particularly worrisome given the higher prevalence of high-risk HPV subtypes and disproportionate morbidity and mortality of HPV-associated cervical cancer in Black women compared to White women.^{21,26} Since non-Hispanic Blacks are less likely to be aware of the HPV vaccine overall,²⁶ provider recommendation aimed at promoting knowledge in a patient-specific manner and ensuring prompt follow-up will be crucial to reducing these inequities.

There were less pronounced differences in completion according to sex, which may reflect improved awareness of HPV-associated disease in males and more intentional efforts to vaccinate this group. Payer status, however, was significantly associated with completion of a 2 or 3-dose series. In particular, patients with private insurance were significantly more likely to complete their series within 12 months across the study period. These results are

in line with Mansfield and colleagues,²⁷ who conducted a mixed methods study assessing HPV vaccine completion in the same geographic location as the current study. However, this association has been bi-directional in the broader literature.^{28,29}

Although multi-level strategies have attempted to reduce barriers to accessing preventative health services,^{30,31} EHR-based clinician prompts are minimally labor-intensive interventions that have shown promise in improving reliable vaccine delivery.³² Particularly in the setting of the HPV vaccine, EHR reminder systems have been utilized to improve both vaccine initiation and completion rates in females across the age spectrum of vaccine eligibility¹⁴, as well as bolster initiation rates in young males.³³ In our study, HPV vaccine completion rates significantly improved in females and males across all ages, but when accounting for the differential association of HMR and vaccine completion by patient age groups, those less than 15 years old were most likely to complete the series with HMR prompting. This is unsurprising as adolescents experience increasing disconnects from healthcare as they transition into young adulthood,³⁴ and patients with a routine place of healthcare have significantly greater odds of being adherent to HPV vaccine recommendations.³⁵ The effect of regular visits would compound an intervention whose impact is dependent on provider-patient interfaces, such as an EHR HMR. This contrast may be further explained by provider perceptions, as efforts to improve vaccination rates have historically been aimed at those receiving the primary vaccine series. However, the overall positive impact of HMR on those receiving catch-up vaccinations is promising and is in line with prior research.¹⁴

In addition, HMR implementation was associated with consistently increased vaccine completion rates across all race groups. This is important because known racial disparities had no impact on the effect of the HMR. For example, despite having lower completion rates overall, Black patients had a comparable increase in vaccine completion to White patients after HMR implementation. In agreement with Ruffin and colleagues,¹⁴ who found that EHR reminder systems improved HPV vaccine initiation rates in Black females, our findings suggest that standardized alert systems may provide an unbiased method to ensure the timely delivery of follow up vaccine doses. Given that non-Hispanic Black males with HPV-associated OPC have been found to have higher cancer-specific mortality compared to other races, regardless of stage at presentation or treatment modality,³⁶ any effort to improve preventative measures such as HPV vaccination in this population is critical.

Key limitations to this study include that this was an analysis of a single-healthcare system, which was associated with a large academic center. Thus, our findings are unique to this high-resource practice setting with a centralized EHR. Other limitations include the effect of unmeasured confounders on vaccine completion rates. In particular, the beginning of the COVID-19 pandemic was near-concurrent with the implementation of the EHR HMR. Although we demonstrate that overall clinic visits were decreased during the period, it is difficult to determine the exact impact of the pandemic on provider practices and patient preferences during this time. Additionally, variables such as socioeconomic status, healthcare utilization metrics and clinical variables were not captured in our dataset, which may have informed more complete conclusions. Finally, this was a retrospective, pre-post study design without randomization, thus limiting our conclusions on causality.

Despite these limitations, this study has key strengths, including the large sample size and granularity with respect to vaccine administration data, rather than relying on self-reported data. As a result, this is the first study to examine HPV vaccine completion barriers and the effect of an EHR reminder system on improving series completion despite these barriers in males and females across expanded ages of vaccine eligibility. Therefore, EHR HMR represents a scalable, provider-level intervention that improves provider awareness of eligible populations and mitigates barriers to HPV vaccine uptake.

Overall, provider recommendation remains at the heart of HPV vaccination efforts. The incidence of tobacco-associated head and neck cancers has declined by over 50%³⁷, owing to public health campaigns and patient education efforts that otolaryngologists have actively participated in. As experts on the diagnosis and treatment of HPV-positive OPC, otolaryngologists are well-poised to deliver strong vaccine recommendations. Although over 90% of head and neck surgeons discuss HPV as a risk factor for OPC, less than half actually discuss the HPV vaccine with patients, according to national survey data.^{38,39} While otolaryngologists may feel removed from preventative health interventions, we stand to make a significant impact by actively participating in vaccination discussions and recognizing eligible patients. Even via actions as simple as mentioning the vaccine during routine pediatric otolaryngology visits, we may reduce the suffering and debility of conditions like OPC. Through collaboration between the otolaryngology and primary care communities, as demonstrated in the current study, evidence-based and sustainable interventions can be developed to increase HPV vaccine coverage.

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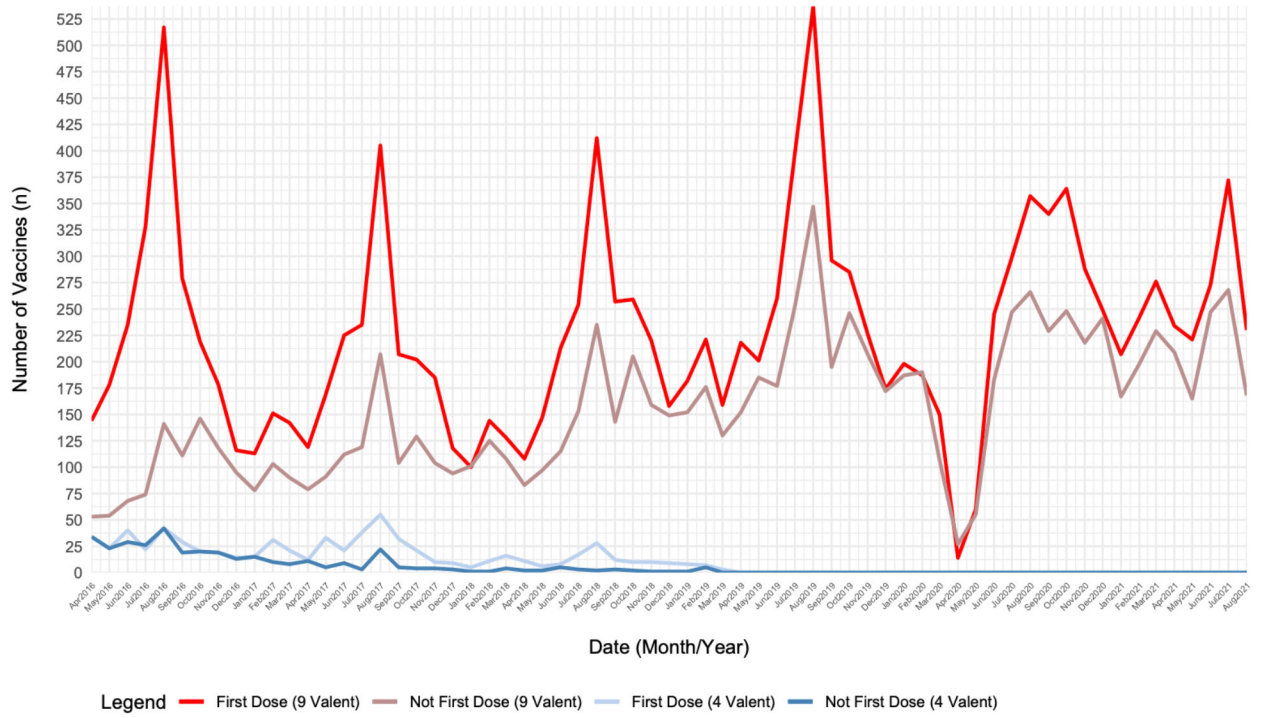


Figure 1. Total number of HPV vaccine doses administered at study locations by month and dose in series.

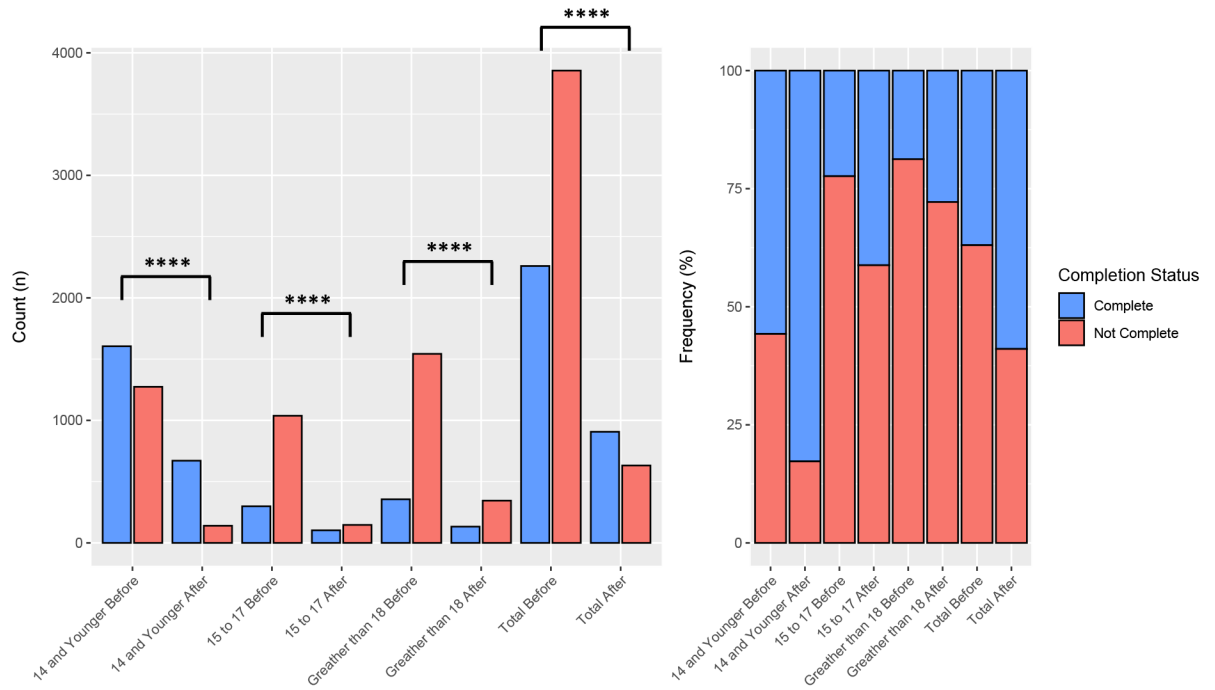


Figure 2. Proportions of Vaccine Completion Before and After HMR Implementation by Age Group.

The left side of the graph represents the raw counts per group while the right represents the relative scaled proportions. **** indicates statistically significant differences where $p < 0.0001$.

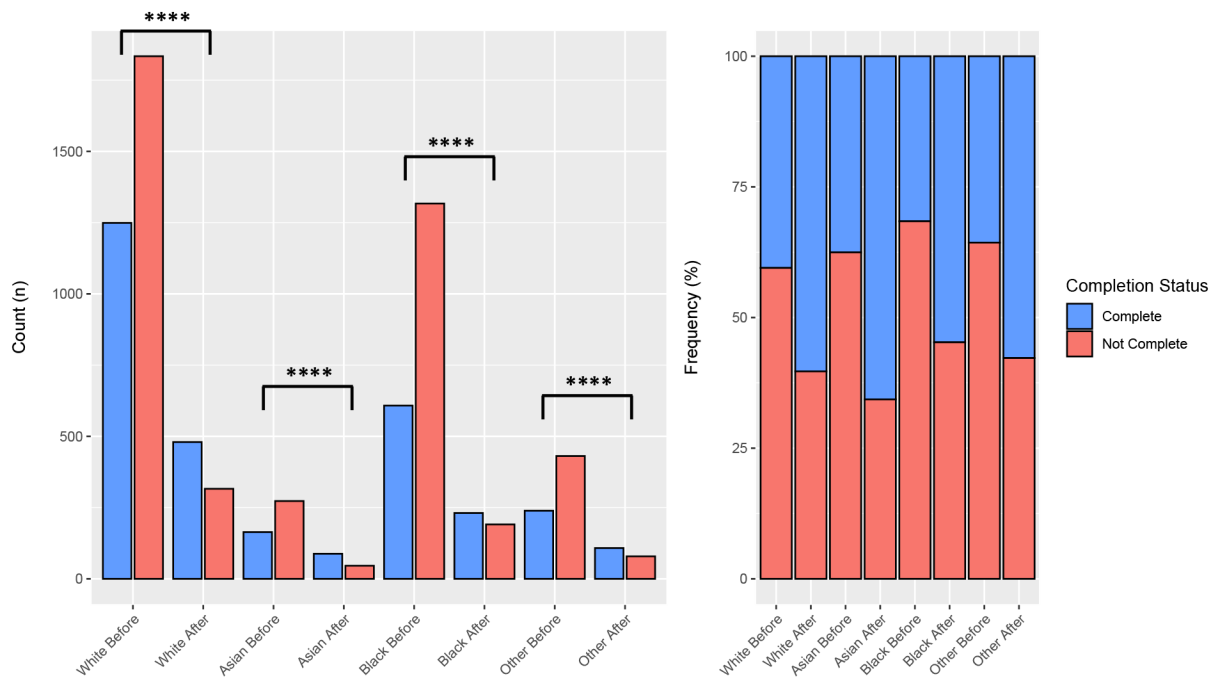


Figure 3. Proportions of Vaccine Completion Before and After HMR Implementation by Race. The left side of the graph represents the raw counts per group while the right represents the relative scaled proportions. **** indicates statistically significant differences where $p < 0.0001$.

Table 1:

Characteristics of HPV Cohort Before and After HPV Vaccination HMR; N=7654

Characteristic:	Number of Patients, n (%)			p-value
	Total	Before	After	
Race				
White	3879 (50.7)	3038 (50.4)	796 (51.7)	
Asian	571 (7.5)	437 (7.1)	134 (8.7)	
Black	2347 (30.7)	1925 (31.5)	422 (27.4)	
Other	857 (11.2)	670 (11.0)	187 (12.2)	0.006
Insurance Status				
Medicaid	1788 (23.4)	1480 (24.2)	308 (20.0)	
Private	5199 (67.9)	4064 (66.5)	1135 (73.7)	
Self-Paid	574 (7.5)	501 (8.2)	73 (4.7)	
Other	93 (1.2)	70 (1.1)	23 (1.5)	<0.0001
Vaccine Type				
HPV 4-Valent	132 (1.7)	132 (2.2)	0 (0)	
HPV 9-Valent	7522 (98.3)	5983 (97.8)	1539 (100)	<0.0001
Gender				
Male	3568 (46.7)	2855 (46.7)	713 (46.3)	
Female	4086 (53.3)	3260 (53.3)	826 (53.7)	0.819
Age				
	Mean (SD)			
	15.80 (4.2)	15.85 (4.2)	15.59 (4.5)	0.032
	Number of Patients, n (%)			
14 or Younger	3690 (31.1)	2879 (47.1)	811 (52.7)	
15 to 17	1587 (20.7)	1337 (21.9)	250 (16.2)	
18 or Older	2377 (31.1)	1899 (31.1)	478 (31.1)	<0.0001
Vaccine Completion				
Yes	3167 (41.4)	2260 (37.0)	907 (58.9)	
No	4487 (58.6)	3855 (63.0)	632 (41.1)	<0.0001

Abbreviations: HPV= Human Papillomavirus; HMR = Health Maintenance Reminder.

Data presented as N (%) unless otherwise specified. Percentages may not add up to 100 due to rounding or missing values.

Table 2:

Multivariate Analysis of HPV Vaccine Series Completion, Main Effect Model

Characteristic:	Vaccine Series Completion	
	Odds Ratio (95% CI)	p-value
Race		
White	REF	
Asian	1.03 (0.84-1.26)	0.77
Black	0.68 (0.60-0.77)	<0.0001
Other	0.76 (0.64-0.90)	0.001
Insurance Status		
Medicaid	REF	
Private	1.70 (1.49-1.93)	<0.0001
Self-Paid	1.10 (0.87-1.38)	0.43
Other	1.03 (0.63-1.69)	0.91
Gender		
Male	REF	
Female	1.12 (1.01-1.25)	0.027
Vaccine Type		
Nine-Valent	REF	
Quadrivalent	0.17 (0.10-0.29)	<0.0001
HMR Notification		
Before	REF	
After	2.51 (2.21-2.85)	<0.0001
Age		
14 or Younger	REF	
15 to 17	0.19 (0.17-0.22)	<0.0001
18 or Older	0.13 (0.11-0.15)	<0.0001

Abbreviations: HPV= Human Papillomavirus; HMR= Health Maintenance Reminder

Table 3:

Contrast Analysis of the Effects of HMR Implementation by Age and Multivariate Interaction Modeling

Groups:			Vaccine Series Completion		
HMR		Age	Odds Ratio (95% CI)	p-value	
After	Before	14 and Younger	3.54 (2.91-4.32)	< 0.0001	
After	Before	15 to 17	2.35 (1.76-3.13)	< 0.0001	
After	Before	18 or Older	1.60 (1.27-2.02)	< 0.0001	
	Age	HMR			
15 to 17	14 or Younger	HMR Effect	0.66 (0.47-0.94)	< 0.0207	
18 or Older	15 to 17	HMR Effect	0.67 (0.56-0.80)	< 0.0001	
18 or Older	14 or Younger	HMR Effect	0.45 (0.33-0.61)	< 0.0001	
Interaction Terms:			F Statistic	p-value	
Age		HMR	13.10	< 0.0001	
Race		HMR	2.35	0.07	
Insurance		HMR	1.95	0.12	

Abbreviations: HMR= Health Maintenance Reminder

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