Title
Two Shots to Cancer Prevention: Improving Uptake of the Human Papillomavirus (HPV) Vaccine among Preadolescent Patients of a Primary Care Network

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Two Shots to Cancer Prevention: Improving Uptake of the Human Papillomavirus (HPV) Vaccine among Preadolescent Patients of a Primary Care Network

By

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A dissertation submitted in partial satisfaction of the

requirements for the degree of

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Abstract

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The current HPV vaccine uptake rate is not on track to achieve the Healthy People 2020 goal of 80%, nor attain the desired reduction in HPV-related cancer burden that could be achieved through optimal uptake. Increasing the HPV vaccination rates to 80% could prevent an additional 53,000 future cervical cancer cases in the U.S among girls who are 12 years or younger over the course of their lifetime as well as many additional cases of other cancers, precancers, and genital warts in both sexes. Understanding the current HPV vaccination trends, determining predictors of vaccination, and identifying the characteristics of primary care visits that are missed opportunities for HPV vaccination allows for the development of more effective strategies that can accelerate HPV vaccine uptake.

My dissertation, comprised of three papers, examines the multiple levels of influence associated with uptake of the HPV vaccine among preadolescents ages 11-12 at the provider, patient/parent, and visit levels. The findings will help elucidate salient factors that influence the provider's decision to recommend the HPV vaccine to their patients, the parent's decision to accept and follow through with that recommendation, the processes of care that are required to ensure that recommendation is carried out, and the relationships among these various factors. The first and second paper utilizes electronic medical records and administrative data to identify: 1) patient and provider factors associated with HPV vaccine uptake and 2) patient, provider and visit factors associated with missed clinical opportunities to recommend and administer the HPV vaccine. The third paper explores the clinic, primary care team and parent level factors that affect uptake of the HPV vaccine through semi-structured key-informant interviews.

The primary conclusions from this research highlight the importance of developing and implementing multi-level interventions that engage parents, all clinic staff (e.g. providers and support staff) and health care systems. Education, training and communication for HPV vaccines should focus on emphasizing the importance of timely vaccinations, bundling the HPV vaccines with other vaccines due at the same time, and ensuring that all clinic staff provide a strong and consistent HPV vaccination recommendation.

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Paper 1

Patient and Provider Factors Associated with Uptake of the Human Papillomavirus Vaccine among Preadolescent Patients in a Primary Care Network

Abstract

Purpose: Despite the availability of the human papillomavirus (HPV) vaccine, rates of vaccination remain low. The purpose of this study is to examine patient and provider factors associated with HPV vaccine uptake defined as HPV vaccination coverage with: a) ≥ 1 dose; b) ≥ 2 doses; and c) ≥ 3 doses among patients ages 11-12 in a large primary care network.

Methods: Electronic medical record data and administrative data from October 2014 – March 2016 were analyzed for patients ages 11-12 (n=4,666) of a primary care network. Mixed effects logistic regression models were used to examine patient and provider characteristics associated with uptake of the HPV vaccination among these patients.

Results: Among the 4,666 patients in the sample, 16.5% completed the 3-dose HPV vaccine series. In adjusted analyses, the odds of initiating the vaccine series were higher for girls than boys (OR 1.6; 95% CI 1.3 -1.9), greater for patients with more medical visits, greater for patients who received the meningococcal conjugate (OR 11.4; 95% CI 8.7 – 15.0), tetanus-diphtheria-pertussis (OR = 1.8; 95% CI: 1.4 – 2.4) and influenza (OR 2.1; 95% CI:1.8 – 2.5) vaccines compared to those who did not receive these vaccines and lower for patients whose primary care provider have been in practice longer (OR = 0.97, 95% CI: 0.95 – 0.99). There were no racial/ethnic differences in odds of HPV vaccination.

Conclusion: Administering the HPV vaccine in conjunction with other vaccines recommended for preadolescents could increase HPV vaccination. Future interventions should focus on how to recommend the HPV vaccination with other preadolescent vaccines, particularly the meningococcal vaccine.

Introduction

During 2008-2012, an average of 38,793 cases of cancer was diagnosed annually in parts of the body where the human papillomavirus (HPV) is commonly found. The Centers for Disease Control (CDC) estimates that among these cases, 28,500 (73%) can be attributed to HPV types that are preventable with the 9-valent HPV vaccine (Viens et al., 2016). However, despite the compelling evidence for cancer prevention (Zur Hausen, 2002), a 10-year record of safety, efficacy (Ferris et al., 2017), support from cancer prevention and adolescent health leaders from across the nation (Brady et al., 2012), and recommendations from the Advisory Committee on Immunization Practices (ACIP) (Petroksky et al., 2015), the uptake rate for the human papillomavirus (HPV) vaccine remains well below the Healthy People 2020 target of 80%.

In 2016, among U.S. adolescents aged 13-17, HPV vaccination coverage with ≥1 dose was 56.1% (49.8% for boys and 62.8% for girls), with ≥2 doses was 45.4% (39.0% for boys and 52.2% for girls), and with ≥3 doses was 34.9% (28.1% for boys and 41.9% for girls) (Reagan et al., 2015). Increasing the HPV vaccination rates from current levels to 80% could prevent an additional 53,000 future cervical cancer cases in the U.S among girls who are 12 years or younger over the course of their lifetime as well as many additional cases of other cancers, pre-cancers, and genital warts in both sexes (Centers for Disease Control and Prevention, 2013; Rimer, Harper, & Witte, 2014).

Screening for the HPV infection has made great strides on decreasing the overall cervical cancer incidence and mortality rates, however, significant disparities exist among U.S racial/ethnic groups (Downs et al, 2008; McCracken et al., 2007). In 2017, it is estimated that approximately 12,820 new cases of invasive cervical cancer will be diagnosed in the U.S and that an estimated 4,210 women will die from the disease; the majority will be women of color (Siegel, Miller, & Jemal, 2017). Cervical cancer rates per 100,000 are higher among Black (9.2) and Hispanic (9.7) women compared to White (7.1) women (Viens et al., 2016). While the incidence rate (per 100,00) among Asian Americans/Pacific Islanders (6.1) when reported in the aggregate is lower than for White (7.0) women (Siegel, Miller, & Jemal, 2017), when disaggregated, Cambodian (12.7) and Vietnamese (9.5) women have some of the highest incidence rates of cervical cancer among all ethnicities (Torre et al., 2016). Asian American women also have the lowest cervical cancer screening among all racial/ethnic groups with 70.1% reporting a Papanicolaou (Pap) test in 2013 compared to 80.2% for White women (Sabatino et al., 2013). The HPV vaccine, almost 100% effective in preventing precancerous cervical cells fcaused by HPV strains 16 and 18, has the potential to prevent a majority of cases of invasive cervical cancer (Chatterjee, 2014) and therefore can mitigate cervical cancer disparities before they can even occur.

HPV vaccination efforts face several unique barriers because: 1) the HPV vaccine is not required for school entry in all states (Centers for Disease Control and Prevention, 2017); 2) the nature and consequences of the HPV infection are poorly understood by the public (Dell et al., 2000); and 3) the HPV vaccine is a series that requires multiple shots and visits (American Academy of Pediatrics Committee on Infectious Diseases, 2006).

Although, children can begin the series as early as age nine and females and males aged 13 to 26 can receive a “catch up vaccine,” if they have not initiated or completed the series, the recommended age group for the vaccine is boys and girls ages

11-12 years old (Centers for Disease Control and Prevention, 2017). However, despite being the targeted group for the vaccine, few studies have examined the rates and factors associated with HPV vaccine coverage for specifically 11-12 year olds (Bractic, Seyferth, & Bocchini, 2016; Kessels et al., 2012). Examining HPV vaccine uptake among this age group is important because: 1) it is the recommended age group for routine HPV vaccination; 2): the HPV vaccine is most effective if given prior to HPV exposure through sexual contact (Centers for Disease Control and Prevention, 2017); and 3) widespread HPV vaccination is expected to reduce the overall burden of HPV-associated cancers for all racial/ethnic groups and will help narrow the disparity gap (Burger et al., 2016).

The goal of the current study is to identify patient and provider characteristics associated with HPV vaccine uptake in a sample of patients ages 11-12. I have the unique opportunity to examine patient and provider sociodemographic and patient healthcare utilization factors associated with each dose in the vaccine series using electronic medical record and administrative data. I hypothesized that boys, patients with public medical insurance and racial/ethnic minorities would have lower HPV vaccination uptake than girls, patients with private medical insurance, and White patients.

Methods

Study setting and study population

Electronic medical records (EMR) from a Primary Care Network (PCN) were queried to capture all outpatient visits for girls and boys ages 11-12 years old that occurred within the following PCN departments: family practice, general practice, internal medicine, obstetrics/gynecology, pediatrics, and urgent care between October 1, 2014 and -March 31, 2016. These outpatient encounters occurred at 15 outpatient clinics of University of California, Davis Health (UCDH) PCN. Although academically affiliated with UC Davis, this PCN functions as a Medical Group with each clinic designated as a Patient Centered Medical Home. These clinics are located in Sacramento, CA and nine surrounding communities. During the study period these clinics saw 5,109 unique patients ages 11-12.

Visits were identified using the International Classification of Diseases, 9th Revision (ICD-9) codes. The following ICD-9 codes were excluded from the analysis: current pregnancy (V22 and V23); acute appendicitis (5400 and 5409); acute leukemia (20802); acute osteomyelitis (73006, 73008); acute pancreatitis (5770); acute parametritis and pelvic cellulitis (6143); acute pharyngitis (462); acute pyelonephritis without lesion of renal medullary necrosis (59010); acute respiratory failure (51881); acute tonsillitis (463); diabetes with ketoacidosis, type I, uncontrolled (25013); fever (78060); influenza (4878 and 4871); malaria (0846); malignant hyperthermia (99586); meningitis (3207 and 3229); pneumococcal pneumonia (481); pneumonia (4830, 4838, and 486); Q fever (Q830); relapsing fever (0879); scarlet fever (0341); and varicella without mention of complication (0529). These ICD-9 codes represent conditions in which patients are advised not to get the HPV vaccine or should wait (i.e., people who are moderately or severely ill and women who are pregnant). All other ICD-9 codes were included in the analysis. Additionally, I only included providers who specialized in the following: pediatrics, family, and internal medicine. I excluded 439 patients based on ICD-9 codes and 13 patients due to provider

specialization for a final sample of 4,666 patients (91.3%). The University of California, Davis Institutional Review Board (IRB), approved the study protocol.

Subject Characteristics

All patient-level data were obtained from the UCDH EMR and all provider level data were obtained from the EMR and through queries of the UCDH provider biography webpages (webpages are updated annually based on new information and were reviewed in October 2016). Patient variables selected included: gender (boy or girl); race (White, Black, Asian, American Indian/Alaskan Native, Native Hawaiian/Pacific Islander, or unknown/other); ethnicity (non-Hispanic, Hispanic, or unknown/other); language preference (English or non-English); insurance type (private, public, or other); number of medical visits during the study period (1, 2, 3, 4, or 5 or more); and whether or not the patient received the meningococcal (MenACWY), tetanus-diphtheria-pertussis (Tdap) vaccine, and/or the influenza vaccine during the study period. MenACWY, Tdap and the influenza vaccines represent the Advisory Committee on Immunization Practices (ACIP) vaccine recommendation for adolescents ages 11-12 (Centers for Disease Control and Prevention, 2016). Provider variables selected included: gender (male/female); specialty (pediatrics, family, or internal medicine.); and years in practice.

Statistical Analyses

The distribution of patient demographics and patient personal health practices were compared across four HPV vaccination coverage groups: 1) 0 dose; 2) ≥ 1 doses; 3) ≥ 2 doses; and 4) 3 doses. I compared patients who did not receive any doses of the HPV vaccine to those who had at least one dose of vaccine using Chi square tests. Patient demographics and patient personal health practices were also compared by gender using Chi square tests. Provider demographics were summarized by clinic site using frequencies and percentages.

Multivariable logistic regression analysis was performed to examine the extent to which patient and provider factors were associated with the uptake of the HPV vaccine among early adolescents. Mixed effects logistic regression models were used because of the hierarchical structure of the data using random provider and clinic effects to account for the clustering of patients within providers clustered within clinics. Separate analysis were performed to identify correlates of: 1) initiation of the HPV vaccination series (≥1 dose vs. 0 dose); 2) initiation but not completing the HPV vaccine series (≥2 doses vs. 0-1 dose); and 3) completion of all three shots in the HPV vaccine series (3 doses vs. 0-2 doses). The fully adjusted models included the following variables: patient characteristics (gender, race/ethnicity, English language preference, and insurance type); patient health care utilization (number of medical visits and vaccinations received at ages 11-12); and provider characteristics (specialty, gender, and years in practice). Results are expressed in terms of odds ratios (ORs) and 95% confidence intervals (CIs). Statistical significance was assessed at the 0.05 level (2-sided). All analyses were performed using STATA version 14.

Results

A total of 4,666 patients (n=2,386 boys and n=2,280 girls) aged 11-12 had at least one visit between October 2014 and March 2016. Table 1 displays the characteristics of the study population by HPV vaccination coverage. The majority of patients were boys (51.1%); non-Hispanic White (52.6%); English-speaking (96.3%); had private insurance (82.9%); and received the Tdap (74.6%), MenACWY (66.0%), and Influenza (61.2%) vaccines. In terms of HPV vaccination coverage, 16.5% completed the series (3 doses), 25.8% had at least two shots (≥ 2 doses), 35.2% had at least one shot (≥ 1 doses) and 64.8% did not start the series. In terms of HPV vaccination coverage by race/ethnicity, non-Hispanic whites had the greatest proportion of those who did not receive any doses of the HPV vaccine (55.4%), Blacks had the greatest proportion of those who had at least one dose (45.7%), and Asian Americans had the greatest proportion of those who completed the series (21.9%). HPV vaccine uptake with at least one dose was significantly associated with patient gender, race/ethnicity, insurance status, number of medical visits and with other vaccinations received at ages 11-12.

Table 2 shows the characteristics of the study population, stratified by gender. HPV vaccination coverage with at least one dose (31.8% versus 38.8%), at least two doses (23.1% versus 28.6%), and with three doses (14.5% versus 18.6%) was considerably higher for girls than boys. Additionally, a greater proportion of girls received the Tdap vaccine (76.6% versus 72.7%) than boys. Patient gender was significantly associated with receiving the Tdap vaccine and with HPV vaccination coverage.

Table 3 summarizes provider characteristics by clinic site. A total of 364 providers had at least one visit with patients aged 11-12 between October 2014 and March 2016. The majority of the providers specialized in pediatrics (54.1%) and were women (51.6%). The average number of patients aged 11-12 seen per clinic was 311 with a range of 46 to 889 patients.

At least one dose of the HPV vaccine (≥ 1 doses)

The odds of receiving at least one dose of the HPV vaccine series was higher for girls than boys (OR = 1.6, 95% CI: 1.3 - 1.9); patients with 3 or more medical visits were more likely to receive at least one dose of the series than patients with only 1 visit (3 visits OR = 1.5, 95% CI: 1.2 - 1.9; 4 visits OR = 1.5, 95% CI: 1.1-2.0; 5 or more visits OR = 1.4, 95% CI: 1.1 - 1.8); patients who received the TDap (OR = 1.8, 95% CI: 1.4 - 2.4), MenACWY (OR = 11.4, 95% CI: 8.7 – 15.0) and Influenza vaccines (OR = 2.1, 95% CI: 1.8 – 2.5) at age 11-12 were more likely receive at least one dose of the series than those who did not receive these vaccines at these ages; and patients whose provider has been in practice longer were less likely to receive at least one dose of the series (OR = .97 per year, 95% CI: 0.95-0.99). No racial/ethnic differences in HPV vaccination rates were found (Table 4).

Two or more doses (≥ 2 doses)

Patients with 3 or more medical visits were more likely to receive at least two doses of the series than patients with only 1 visit (3 visits OR = 1.9, 95% CI: 1.3 - 2.7; 4 visits

OR = 2.6, 95% CI: 1.6 - 4.1; 5 or more visits OR = 3.3, 95% CI: 2.1 - 5.2); and patients who received the MenACWY (OR = 2.8, 95% CI: 1.8 – 4.4) and Influenza vaccines (OR = 1.5, 95% CI: 1.1 – 2.0) at age 11-12 were more likely to receive at least two doses of the series than those who did not receive these vaccines at these ages (Table 4).

Three doses

Patients with public health insurance were less likely to complete the series compared to patients with private insurance (OR = 0.5, 95% CI: 0.3 – 0.8) and patients who received the MenACWY (OR = 2.1, 95% CI: 1.2-3.7) at age 11-12 were more likely to complete the series than those who did not receive these vaccines at these ages. No racial/ethnic differences in HPV vaccination rates were found (Table 4).

Discussion

In a primary care network of a predominantly insured and racially and ethnically diverse population of 11-12 year old girls and boys I found low HPV vaccine uptake rates (≥1 = 35.2%; ≥ 2 doses = 25.8%; and ≥ 3 doses = 16.5%). Being a boy, having public insurance (Medi-Cal) and having a provider who has been in practice longer was associated with lower HPV vaccination uptake while having more frequent health care visits and receiving other recommended adolescent vaccines was associated with higher HPV vaccination uptake. This is consistent with the literature that has identified similar patient and provider factors associated with HPV vaccine uptake for adolescents ages 9-17 [Kessels et al., 2012; Tiro et al., 2012; Dempsey et al., 2012; Holman et al., 2014). I found that most patient and provider variables associated with HPV vaccine uptake were the same for receiving at least two doses of the HPV vaccine as for receiving three doses of the HPV vaccine. My findings may inform the development of interventions that are applicable to the new ACIP guidelines that simplify the schedule from a 3-dose to a 2-dose series for routine immunization (Meites, Kempe, & Markowitz, 2016).

While gender differences were large in magnitude in my multivariable model, racial/ethnic differences were not found, which is contrary to other studies which have reported lower completion rates for minority adolescents in other settings (Dorell et al., 2011; Kester et al., 2013; Perkins et al., 2012). The demographic composition of my sample population as well as their access to clinical care may account for this difference. A majority of the patients spoke English (96.3%) and had health insurance (92.5%). Additionally, patients with Medi-Cal insurance coverage had lower odds of completing the series. However, this decrease is very likely to be a result of this PCN ending their Medi-Cal managed care contracts. During this time frame about 3,700 of the PCN's Medi-Cal patients (including children) had to find new providers. Despite having to find new providers outside of the network, Medi-Cal patients in my sample continued to have medical visits including visits to receive the second dose of the HPV vaccine. Thus, given equivalent financial access (i.e., no lack of commercial insurance), racial/ethnic characteristics did not factor into the receipt of HPV vaccinations in this PCN.

The strongest predictor of receiving the HPV vaccine was receiving a MenACWY vaccine. Among those who received the MenACWY vaccine, the odds of initiating the HPV vaccine series was 11.4 times higher compared to those who did not receive the

MenACWY vaccine. HPV vaccines can be safely co-administered with other routine recommended vaccines and the ACIP recommends administrative of all age-appropriate vaccines during a single visit (Centers for Disease Control and Prevention, 2017).

Limitations

Several study limitations should be considered when interpreting the findings. First, there is potential for misclassified data in the EMR. HPV vaccinations may be administered outside of the PCN such as in school or pharmacies and potentially not entered into the PCN EMR. Misclassification can occur if this information is not reported by the patient/parent. However, since the vaccine is covered by health plans accepted by the PCN, the impact of misclassification is likely low. In terms of missing data, I did not have demographic data (gender, specialty, and years in practice) for all providers because some patients do not have a designated primary care provider (1.5%). Consequently, I excluded 70 patients for which provider data was missing from the multivariable analyses and the findings on provider gender, specialty and years in practice only apply to those whose information was available.

Additionally, the study examined data from October 2014-March 2016, when the ACIP HPV vaccine recommendation for children ages 11-12 was three doses spread over a six-month period. In December 2016, the ACIP revised their recommendation. As the vaccine still requires more than one dose spread over a six-month period, the current study's findings are still relevant to understanding factors associated with multiple doses.

Strengths

In spite of limitations, my study has unique strengths. The design allowed for minimal participation bias and the use of electronic medical records to verify receipt of the HPV vaccine which avoids self-report/recall bias. The EMR allowed me to compare vaccination uptake by dose for HPV and to compare them with Tdap and MenACWY for the same cohort of patients for the same period of time. Furthermore, my sample size of 4,666 from a single PCN represents one of the largest analyses of HPV vaccination uptake for patients, ages 11-12, with both genders using a review of electronic medical records. Additionally, I was also able to associate HPV vaccination uptake by provider characteristics (e.g. gender and specialization, and HPV vaccination by medical specialty). While I did not find any difference in HPV vaccination uptake by provider gender and specialization, I did find a negative association between receiving at least one and at least two doses of the HPV vaccine series and the number of years a provider has been in practice.

Conclusion

Over an 18-month period, only 16.5% of patients ages 11-12 of a primary care network completed the three-dose HPV vaccination series. Most patients, however, received the three other recommended vaccines for this age group, Tdap (74.6%), MenACW (66%), and the Influenza (61.2%) vaccines. In this predominantly insured and English speaking sample, no racial/ethnic differences in HPV vaccine uptake were found.

Thus, I posit that financial access to care (i.e., provision of health insurance to cover HPV vaccinations) could be an equalizer for all racial/ethnic patients.

Clinic-based strategies to promote bundling vaccinations among adolescents may improve HPV vaccine uptake and reduce HPV-associated cancer. Strategies include: 1) co-administering of the HPV vaccination with other adolescent vaccines recommended for this age group, particularly with the MenACWY and 2) reducing the number of missed opportunities to administer the vaccine by recommending the HPV vaccine at every medical visit in which a patient is eligible for the vaccine.

Table 1. Demographics and Health Care Utilization Among Patients Ages 11-12 by HPV Vaccine Coverage, UCD Health Primary Care Network, October 1, 2014 – March 31, 2016[a]						
	0 (n = 3024)	**≥ 1 doses (n = 1642)**	**≥ 2 doses (n = 1205)**	**3 doses (n = 772)**	**All (n = 4666)**	**P-Value[b]**
Patient Demographics						
Boy	1,628 (53.8%)	758 (46.0%)	552 (45.6%)	347 (44.9%)	2,386 (51.1%)	**<.0001**
Race/Ethnicity						
White	1,674 (55.4%)	780 (47.5%)	589 (48.9%)	393 (50.9%)	2,454 (52.6%)	**<.0001**
Hispanic	489 (16.2%)	296 (18.0%)	216 (17.9%)	123 (15.9%)	785 (16.8%)	
AANHPI	365 (12.1%)	275 (16.8%)	207 (17.2%)	140 (18.1%)	640 (13.7%)	
Black	199 (6.6%)	168 (10.3%)	107 (8.9%)	63 (8.2%)	367 (7.9%)	
AI/AN	22 (0.7%)	15 (1.0%)	10 (0.8%)	7 (0.9%)	37 (0.8%)	
Unknown	156 (5.2%)	49 (3.0%)	31 (2.6%)	18 (2.3%)	205 (4.4%)	
Declined	119 (3.9%)	59 (3.6%)	45 (3.7%)	28 (3.6%)	178 (3.8%)	
English	2,898 (95.8%)	1,594 (97.1%)	1169 (97.0%)	749 (97.0%)	4,492 (96.3%)	0.2
Insurance						
Private	2,472 (81.8%)	1,398 (85.1%)	1,044 (86.6%)	694 (89.9%)	3,870 (82.9%)	**<.0001**
Public	320 (10.6%)	128 (7.8%)	80 (6.6%)	34 (4.4%)	448 (9.6%)	
Other	232 (7.7%)	116 (7.1%)	81 (6.7%)	44 (5.7%)	348 (7.5%)	
Patient Health Care Utilization						
Medical Visits						
1	1,490 (49.3%)	578 (35.2%)	374 (31.0%)	228 (29.4%)	2,068 (44.3%)	**<.0001**
2	712 (23.5%)	388 (23.6%)	276 (22.9%)	174 (22.5%)	1,100 (23.6%)	
3	361 (11.9%)	294 (17.9%)	231 (19.2%)	154 (19.9%)	655 (14.0%)	
4	198 (6.6%)	165 (10.1%)	136 (11.3%)	90 (11.6%)	363 (7.8%)	
≥ 5	263 (8.7%)	217 (13.2%)	188 (15.6%)	129 (16.7%)	480 (10.3%)	
Vaccines[e]						
Tdap	1,974 (65.3%)	1,507 (91.8%)	1,101 (91.4%)	695 (90.0%)	3,481 (74.6%)	**<.0001**
MenACWY	1,574 (52.1%)	1,506 (91.7%)	1,129 (93.7%)	733 (95.0%)	3,080 (66.0%)	**<.0001**
Influenza	1,580 (52.2%)	1,277 (77.8%)	974 (80.8%)	625 (90.0%)	2,857 (61.2%)	**<.0001**

[a] Percentages may not total 100% because of rounding. Percentages are percentages of the row total.
[b] 0 shots versus at least 1 dose comparison using Chi-square tests
[c] Vaccinations received at age 11-12
*Abbreviations: AANHPI = Asian American, Native Hawaiian, and Pacific Islanders; AI/AN = American Indian/Alaskan Native; Tdap = Tetanus, diphtheria, & pertussis; MenACWY = Meningococcal group A, C, W-135, & Y

Table 2. Demographics and Health Care Utilization Among Patients Ages 11-12 by Gender, UCD Health Primary Care Network, October 1, 2014 – March 31, 2016[a]

	Boys (n = 2386)	Girls (n = 2280)	All (n = 4666)	P-Value[c]
Patient Demographics				
Race/Ethnicity				
White	1,263 (52.9%)	1,191 (52.2%)	2,454 (52.6%)	0.3
Hispanic	393 (16.5%)	392 (17.2%)	785 (16.8%)	
AANHPI	331 (13.9%)	309 (13.6%)	640 (13.7%)	
Black	191 (8.0%)	176 (7.7%)	367 (7.9%)	
AI/AN	16 (0.7%)	21 (0.9%)	37 (0.8%)	
Unknown/Other	114 (4.8%)	91 (4.0%)	205 (4.4%)	
Declined to State	78 (3.3%)	100 (4.4%)	178 (3.8%)	
English Language Preference	2,298 (96.3%)	2,194 (96.2%)	4,492 (96.3%)	0.9
Insurance Status				
Private	1,974 (82.7%)	1,896 (83.2%)	3,870 (82.9%)	0.8
Public	228 (9.6%)	220 (9.7%)	448 (9.6%)	
Other	184 (7.7%)	164 (7.2%)	348 (7.5%)	
Patient Health Care Utilization				
Medical Visits				
1	1,042 (43.7%)	1,026 (45.0%)	2,068 (44.3%)	0.2
2	541 (22.7%)	559 (24.5%)	1,100 (23.6%)	
3	357 (15.0%)	298 (13.1%)	655 (14.0%)	
4	195 (8.2%)	168 (7.4%)	363 (7.8%)	
≥ 5	251 (10.5%)	229 (10.0%)	480 (10.3%)	
Vaccines[b]				
Tdap	1,734 (72.7%)	1,747 (76.6%)	3,481 (74.6%)	**0.002**
MenACWY	1,553 (65.1%)	1,527 (67.0%)	3,080 (66.0%)	0.2
Flu	1,452 (60.9%)	1,405 (61.6%)	2,857 (61.2%)	0.6
HPV				
0	1,628 (68.3%)	1,396 (61.2%)	3,024 (64.8%)	**<.0001**
≥ 1	758 (31.8%)	884 (38.8%)	1,642 (35.2%)	**<.0001**
≥ 2	552 (23.1%)	653 (28.6%)	1,205 (25.8%)	**<.0001**
≥ 3	347 (14.5%)	425 (18.6%)	772 (16.5%)	**<.0001**

[a] Percentages may not total 100% because of rounding. Percentages are percentages of the row total.
[b] Vaccinations received at age 11-12
[c] Girls versus boys comparison using Chi-square tests
*Abbreviations: AANHPI = Asian American, Native Hawaiian, and Pacific Islanders; AI/AN = American Indian/Alaskan Native; Tdap = Tetanus, diphtheria, & pertussis; MenACWY = Meningococcal group A, C, W-135, & Y

Table 3. Provider Characteristics Among Patients Ages 11-12 by Clinic Site, UCD Health Primary Care Network, October 1, 2014 – March 31, 2016[a] (N = 364)					
	Gender	Provider Specialty			No. of patients seen[b] (n = 4,666)
Clinic Site	Male (n = 176)	Pediatrics (n = 197)	Family/General (n = 159)	Internal Medicine (n = 8)	
1	8 (50.0%)	5 (31.3%)	10 (62.5%)	1 (6.3%)	889 (19.1%)
2	5 (62.5%)	2 (25.0%)	6 (75.0%)	0	258 (5.5%)
3	1 (25.0%)	1 (25.0%)	3 (75.0%)	0	52 (1.1%)
4	1 (25.0%)	0	4 (100.0%)	0	46 (1.0%)
5	2 (50.0%)	1 (25.0%)	3 (75.0%)	0	271 (5.8%)
6	4 (25.0%)	4 (25.0%)	11 (68.8%)	1 (6.3%)	429 (9.2%)
7	31 (43.7%)	17 (23.9%)	54 (76.1%)	0	164 (3.5%)
8	6 (46.2%)	3 (23.1%0	10 (76.9%)	0	392 (8.4%)
9	95 (50.0%)	149 (78.4%)	37 (19.5%)	4 (2.1%)	660 (14.1%)
10	2 (100%)	0	2 (100%)	0	46 (1.0%)
11	3 (37.5%)	8 (100%)	0	0	93 (2.0%)
12	2 (66.7%)	1 (33.3%)	2 (66.7%)	0	117 (2.5%)
13	7 (58.3%)	7 (58.3%)	4 (33.3%)	1 (8.3%)	480 (10.3%)
14	5 (55.6%)	7 (77.8%)	1 (11.1%)	1 (11.1%)	676 (14.5%)
15	4 (100%)	0	4 (100%)	0	93 (2.0%)

[a] Percentages may not total 100% because of rounding.
[b] Patients ages 11-12.

Table 4. Patient and Provider Characteristics Associated with Uptake of the HPV Vaccine, by HPV Vaccination Coverage, UCD Health Primary Care Network, October 1, 2014 – March 31, 2016						
	≥ 1 dose (n=4617)[a]		≥ 2 doses (n=1639)[b]		3 doses (n = 1203)[c]	
	Odds Ratio (95% CI)	**P-Value**	**Odds Ratio (95% CI)**	**P-Value**	**Odds Ratio (95% CI)**	**P-Value**
Patient Demographics						
Gender						
Boy	Ref.		Ref.		Ref.	
Girl	**1.6 (1.3 - 1.9)**	**<.0001**	1.1 (0.9 – 1.5)	0.4	1.1 (0.9 – 1.5)	0.3
Race/Ethnicity						
White	Ref.		Ref.		Ref.	
Hispanic	1.1 (0.9 - 1.4)	0.4	1.0 (0.7 – 1.4)	0.9	0.8 (0.5 – 1.1)	0.1
AANHPI	1.1 (0.9 - 1.4)	0.4	1.0 (0.7 – 1.4)	1.0	1.1 (0.8 – 1.6)	0.5
Black	1.3 (1.0 - 1.8)	0.1	0.7 (0.5 – 1.0)	0.1	0.9 (0.6 – 1.5)	0.7
AI/AN	1.3 (0.6 - 3.1)	0.5	0.6 (0.1 – 1.7)	0.4	1.2 (0.3 – 5.4)	0.6
Unknown/Other	0.9 (0.6 - 1.3)	0.5	0.7 (0.3 – 1.3)	0.2	0.7 (0.3 – 1.6)	0.5
Declined to State	0.9 (0.6 - 1.5)	0.7	1.0 (0.5 – 2.0)	1.0	0.9 (0.4 – 1.8)	0.7
Language						
English	Ref.		Ref.		Ref.	
Non-English	0.7 (0.4-1.0)	0.1	1.0 (0.5 – 2.2)	0.9	1.3 (0.6 – 2.8)	0.6
Insurance						
Private	Ref.		Ref.		Ref.	
Public	1.0 (0.7-1.4)	0.9	0.9 (0.6 – 1.5)	0.7	0.5 (0.3 – 0.8)	**0.01**
Other	1.1 (0.8-1.5)	0.6	0.9 (0.6 – 1.5)	0.8	0.6 (0.4 – 1.0)	0.06
Patient Health Care Utilization						
Medical Visits						
1	Ref.		Ref.		Ref.	
2	1.1 (0.9-1.4)	0.2	1.2 (0.9 – 1.7)	0.2	1.1 (0.8 – 1.5)	0.7
3	**1.5 (1.2-1.9)**	**.001**	1.9 (1.3 – 2.7)	**<.0001**	1.3 (0.9 – 1.8)	0.2
4	**1.5 (1.1-2.0)**	**.005**	2.6 (1.6 – 4.1)	**<.0001**	1.3 (0.8 – 1.9)	0.3
≥ 5	**1.4 (1.1-1.8)**	**.011**	3.3 (2.1 – 5.2)	**<.0001**	1.4 (1.0 – 2.1)	0.1
Vaccines for ages 11-12						
Tdap	**1.8 (1.4-2.4)**	**<.0001**	0.6 (0.4 – 1.0)	0.07	0.8 (0.7 – 1.0)	0.1
MenACWY	**11.4 (8.7-15.0)**	**<.0001**	2.8 (1.8 – 4.4)	**<.0001**	2.1 (1.2 – 3.7)	**0.005**
Influenza	**2.1 (1.8-2.5)**	**<.0001**	1.5 (1.1 – 2.0)	**0.002**	1.0 (0.7 – 1.4)	1.0
Primary Care Provider						
Specialty						
Pediatrics	Ref.		Ref.		Ref.	
Family	1.0 (0.6-1.6)	1.0	**1.1 (0.8 – 1.7)**	0.5	1.3 (0.9 – 2.0)	0.2
Internal Medicine	1.3 (0.4-4.7)	0.7	**0.4 (0.1 – 1.3)**	0.1	2.1 (0.3 – 13.7)	0.4
Gender						
Male	Ref.		**Ref.**		Ref.	
Female	0.7 (0.5-1.1)	0.1	**1.0 (0.7 – 1.5)**	0.8	1.2 (0.8 – 1.7)	0.5
Years in practice	**0.97 (0.95-0.99)**	**<.0001**	**1.0 (1.0 – 1.3)**	0.2	1.0 (1.0 – 1.02)	0.2

[a] Random effects estimates for ≥ 1 dose
Clinic = .1; S.E. = .11
Provider = .91; S.E. = .19

[b] Random effects estimates for ≥ 2 doses
Clinic = .06; S.E. = .06
Provider = .10; S.E. = .08

[c] Random effects estimates for 3 doses
Clinic = .03; S.E. = .06
Provider = .62; S.E. = .17

* Odds ratios are adjusted for all tabulated variables using logistic regression mixed effects models.

**Abbreviations: AANHPI = Asian American, Native Hawaiian, and Pacific Islanders; AI/AN = American Indian/Alaskan Native; Tdap = Tetanus, diphtheria, & pertussis; MenACWY = Meningococcal group A, C, W-135, & Y

Paper 2
Missed Clinical Opportunities for Human Papillomavirus (HPV) Vaccination among Preadolescents in a Primary Care Network

Abstract

Objective: To identify factors associated with missed clinical opportunities (having an in-person encounter, but remaining unvaccinated) for human papillomavirus (HPV) vaccination among preadolescents patients ages 11-12 in a large primary care network.
Methods: Electronic health records and administrative data for patients ages 11-12 (October 1, 2014 – March 31, 2016), which included patient demographics, visit type, provider demographics and vaccination information, were analyzed. The primary outcome was missed clinic opportunities for HPV vaccination, defined as the proportion of visits where an eligible patient remained unvaccinated for HPV after the visit. Mixed effects logistic regression models estimated the patient, provider and visit characteristics associated with not missing clinic opportunities for HPV vaccinations among vaccine eligible preadolescent patients.
Results Four thousand seven hundred twenty-one patients had 11, 051 visits during the study period. The percentage of missed opportunities for receiving the first dose of the HPV vaccine was 70.1% and 29.6% for any follow up HPV vaccine doses. In adjusted analyses, the odds of having a missed clinic opportunity for receiving the first dose of the HPV (HPV1) vaccine were higher for boys than girls (OR = 0.6, 95% CI: 0.6 – 0.7), patients with public insurance compared to patients with private insurance (OR = 0.7, 95% CI: 0.5 – 1.0), patients whose language preference was not English (OR = 0.5, 95% CI: 0.4 – 0.7), patients whose primary care provider have been in practice longer (OR = 0.96, 95% CI: 0.9 – 1.0), and problem focused visits compared to routine visits (OR = 0.6, 95% CI: 0.5 – 0.7). Missed clinic opportunities were less likely among patients who received a Tdap (OR = 2.1, 95% CI: 2.1 – 1.7), MenACWY (OR = 8.9, 95% CI: 7.2 – 11.0) and the influenza (OR = 2.4, 95% CI: 2.1 – 2.7) vaccination.
Conclusion: Missed clinic opportunities for HPV vaccination are common, particularly during problem-focused visits. Clinic and provider interventions focused on taking advantage of opportunities for HPV vaccination during problem-focused visits may accelerate timely uptake of the HPV vaccine.

Introduction

The Center for Disease Control and Prevention's (CDC), Advisory Committee on Immunization Practice (ACIP) has recommended routine vaccination against human papillomavirus (HPV) at age 11 or 12 years for females since 2006 and for males since 2011. While "catch-up" vaccinations for those who have not been previously vaccinated is also recommended for males ages 13-21 and for females ages 13-26 (Meites, Kempe, Markowitz, 2016) timely completion of the HPV vaccine at the appropriate age is important because the vaccine produces a stronger immune response among preadolescents compared to older adolescents and young adults (Frazer, 2007; Dobson et al., 2013; Walker et al., 2016).

Research suggests that reducing missed clinical opportunities for administering and recommending the HPV vaccine is one of the most essential strategies for accelerating HPV vaccine uptake because most HPV vaccines are delivered in the context of primary care (Rimer, Harper, Witte, 2014). Missed clinical opportunities for vaccination occurs when a vaccine-eligible patient has a healthcare encounter and does not receive the vaccine (Wong et al., 2013). Studies suggest that missed clinical opportunities for HPV vaccination happen because providers do not make a strong enough recommendation for vaccination (Gilkey et al., 2016); parents refuse and/or want to delay vaccination until the child is older (Dorell et al., 2010); and because adolescents lack regular routine check-ups and usually see a provider only when they are sick (Nordin, Solberg, & Parker, 2010). The Centers for Disease Control and Prevention (CDC) reported that if all missed clinical opportunities for vaccination were eliminated, more than 90% of girls would have received at least one dose of the HPV vaccine (Stokley et al., 2014). Reducing missed clinical opportunities to recommend and administer HPV vaccines is the first goal in the President's Cancer Panel Report on HPV vaccination (Rimer, Harper, & Witte, 2014).

To develop interventions that will reduce missed clinical opportunities for HPV vaccination we must first assess the prevalence of missed clinical opportunities in a variety of health care settings that provide primary care to adolescents and determine factors associated with these healthcare encounters. More research is needed to quantify these missed clinical opportunities for preadolescents to ensure timely administration of the HPV vaccine for all eligible patients at every clinic visit. Timely administration of the HPV vaccine is important because older adolescents have less preventative care visits compared to younger adolescents (Rimer, Harper, & Witte, 2014), unvaccinated individuals are vulnerable to HPV infections, and because the vaccine is most effective prior to sexual debut (Frazer, 2007; Dobson et al., 2013; Block et al., 2006).

This study is among the first to determine the rate of and the multi-level (patient, provider and visit level) factors associated with missed clinical opportunities for HPV vaccination among 11 to 12 year old preadolescent patients seen at outpatient clinics of a Primary Care Network (PCN). I hypothesize 1) high rates of missed clinical opportunities for receiving the initial dose of the HPV vaccine and 2) the majority of missed clinical opportunities would occur during problem-focused visits.

Methods

Study population

The study population included boys and girls ages 11-12 seen at the University of California, Davis (UCD) Primary Care Network (PCN), an academically affiliated Medical Group which operates 15 clinics in Sacramento, CA and the nine surrounding communities. During the study period, from October 1, 2014 through March 31, 2016, the UCD PCN saw 5,109 unique patients ages 11-12 with 11,686 visits.

Study inclusion criteria were clinic encounters made during the study period by boys and girls 11-12 years of age at the time of the visit. Visits were identified using the International Classification of Diseases, 9th Revision (ICD-9) codes. The following ICD-9 codes were excluded from the analysis because these ICD-9 code represent medical contraindications in which patients are advised not to get the HPV vaccine and are advised to wait: current pregnancy (V22 and V23); acute appendicitis (5400 and 5409); acute leukemia (20802); acute osteomyelitis (73006, 73008); acute pancreatitis (5770); acute parametritis and pelvic cellulitis (6143); acute pharyngitis (462); acute pyelonephritis without lesion of renal medullary necrosis (59010); acute respiratory failure (51881); acute tonsillitis (463); diabetes with ketoacidosis, type I, uncontrolled (25013); fever (78060); influenza (4878 and 4871); malaria (0846); malignant hyperthermia (99586); meningitis (3207 and 3229); pneumococcal pneumonia (481); pneumonia (4830, 4838, and 486); Q fever (Q830); relapsing fever (0879); scarlet fever (0341); and varicella without mention of complication (0529). All other ICD-9 codes were included in the analysis. I excluded 635 visits based on the ICD-9 codes for a final sample size of 4,722 patients (92.4%) and 11,051 visits (94.6%).

Study design

All patient and visit level data were obtained from the UCD EMR system. Provider level data were obtained from the UCD EMR system, queries of the UCDH provider biography webpages (webpages are updated annually based on new information and were reviewed in October 2016) and through conducting a google search for providers who were no longer with the network. Patient variables included gender, race/ethnicity (I combined the race and ethnicity categories), language preference (English or other), age at each visit and insurance coverage (private, public, or other). Provider information included gender, specialty (pediatrics, family practice, other/unknown) and years in practice. Vaccination variables included date of vaccination and age at vaccination for meningococcal (MenACWY), tetanus-diphtheria-pertussis (Tdap) vaccine, human papillomavirus (HPV) vaccine and/or the influenza vaccine during the study period. MenACWY, Tdap, HPV and the influenza vaccines represent the Advisory Committee on Immunization Practices (ACIP) vaccine recommendation for adolescents ages 11-12 (Robinson et al., 2018). All vaccination variables were coded at the visit level

Visit information included visit date and visit type (prevention or problem-focused). Visits were classified as prevention visits if the only reason for the visit were for the following ICD-9 codes: V20.2 (routine infant or child health check), V70.0 (routine general medical examination at a health care facility), V07.9 (unspecified prophylactic or

treatment measure), V70.3 (other general medical examination for administrative purposes), V70.5 (health examination of defined subpopulations), V03.1 (need for prophylactic vaccination and inoculation against typhoid-paratyphoid alone), V03.89 (other specified vaccination), V04.0 (need for prophylactic vaccination and inoculation against poliomyelitis), V04.81 (need for prophylactic vaccination and inoculation against influenza), V04.89 (need for prophylactic vaccination and inoculation against other viral diseases), V05.3 (need for prophylactic vaccination and inoculation against viral hepatitis), V05.4 (need for prophylactic vaccination and inoculation against varicella), V05.9 (need for prophylactic vaccination and inoculation against unspecified single disease), V06.1 (need for prophylactic vaccination and inoculation against diphtheria-tetanus-pertussis, combined), V06.8 (need for prophylactic vaccination and inoculation against other combinations of diseases. All other outpatient visits were classified as problem-focused visits.

My primary study outcome was missed clinical opportunities for initial HPV (HPV1) and HPV follow-up (HPV2 and/or HPV3) vaccinations. A missed clinical opportunity for HPV vaccination was defined as any healthcare encounter where a patient was due for either the first, second or third dose of the vaccine and did not receive it. Visits occurring four or more weeks after HPV1 were considered eligible for HPV2 and visits occurring twelve or more weeks after HPV2 were considered eligible for HPV3. I chose to combine HPV2 and HPV3 into one variable (HPV follow-up) because of the revised 2016 ACIP guidelines recommending two instead of three HPV vaccine doses for preadolescents ages 11-12. Secondary outcomes included identifying patient, provider and visit factors associated with missed clinical opportunities for HPV vaccination.

The University of California, Davis Institutional Review Board (IRB), approved the study protocol.

Data Analysis

Missed clinical opportunity for HPV vaccination was calculated as the total number of visits at which a patient was eligible for the vaccine and did not receive it divided by the total number of visits at which a patient was eligible for the vaccine (regardless of whether they received the vaccine). Patients who received any HPV vaccine doses prior to the study period were excluded from the analysis.

Multivariable logistic regression was performed to assess variables associated with unmissed clinical opportunities for vaccination (HPV1 and HPV follow-up doses). Mixed effects logistic regression models were used because of the hierarchical structure of the data. The dependent variable was receipt of a dose of the vaccine before the next visit. I included a random intercept for patients to account for within-patient correlation between visits and provider and clinic random effects to account for the clustering of patients within providers clustered within clinics. The fully adjusted models included the following variables: patient characteristics (gender, race/ethnicity, English language preference, insurance type, vaccines received up to visit date), provider characteristics (specialty, gender, and years in practice), and visit type. Results are expressed in terms of odds ratios (ORs) and 95% confidence intervals (CIs). Statistical significance was assessed at the 0.05 level (2-sided). All analyses were performed using STATA version 14.

Results

4,721 patients (n=2,409 boys and n=2,312 girls) aged 11-12 had 11,051 visits between October 2014 and March 2016. Table 1 displays the characteristics of the study population. Approximately half of the patients were boys (51.0%) andnon-Hispanic White (52.4%); the majority were English-speaking (96.2%); had private insurance (82.8%); and received the Tdap (76.6%), MenACWY (64.6%), and Influenza (73.5%) vaccines. In terms of HPV vaccination coverage during the study, 15.7% completed the series (3 doses), 8.8% had just two doses, 9.7% had only 1 dose.

I examined the potential for missed clinical opportunities for HPV vaccination by visit type (prevention or problem-focused). I found that of the 9,799 visits in which patients were eligible for HPV1, only 30.3% of those visits resulted in the patient receiving the vaccine (Table 2). Adolescents were more likely to have missed clinical opportunities for HPV1 at problem-focused visits (73.5%) compared to prevention visits (59.3%). I found less missed clinical opportunities for HPV follow-up doses (29.6%) with most missed clinical opportunities occurring during problem-focused visits (34.5%) compared to prevention visits (19.2%).

Missed clinical opportunities for initial HPV vaccine dose (HPV1)

The odds of having a missed clinical opportunity for HPV1 were higher for boys than girls (OR = 0.6, 95% CI: 0.6 – 0.7); higher for patients with public insurance compared to patients with private insurance (OR = 0.7, 95% CI: 0.5 – 1.0); higher for patients whose language preference was not English (OR = 0.5, 95% CI: 0.4 – 0.7); higher for patients whose primary care provider have been in practice longer (OR = 0.96, 95% CI: 0.9 – 1.0); and higher for problem focused visits (OR = 0.6, 95% CI: 0.5 – 0.7). Patients who received a Tdap (OR = 2.1, 95% CI: 2.1 – 1.7), MenACWY (OR = 8.9, 95% CI: 7.2 – 11.0) and the influenza (OR = 2.4, 95% CI: 2.1 – 2.7) vaccine were less likely to have missed clinical opportunities for HPV1 (Table 3).

Missed clinical opportunities for follow-up HPV vaccine dose

The odds of having a missed clinical opportunity for HPV vaccine follow up doses were higher for Hispanic patients compared to white patients (OR = 0.7, 95% CI: 0.5 – 0.8); higher for patients with public insurance compared to patients with private insurance (OR = 0.5, 95% CI: 0.3 – 0.8); and higher for problem focused visits (OR = 0.5, 95% CI: 0.4 – 0.6). Patients who received MenACWY (OR = 4.6, 95% CI: 3.0 – 7.0) and the influenza (OR = 1.6, 95% CI: 1.2 - 2.3) vaccine were less likely to have missed clinical opportunities for follow-up HPV vaccine doses. Patients were less likely to have missed opportunities for the second HPV vaccine dose compared to the third HPV vaccine dose (OR = 2.9, 95% CI: 2.5 – 3.5) (Table 3).

Discussion

Despite the vast literature on factors associated with uptake of the HPV vaccine (Kessels et al., 2012; Holman et al. ,2014) and the implementation of interventions (Fu et al., 2014; Niccolai & Hansen, 2015; Smulian, Mitchell, & Stokley, 2016) to increase uptake

of the vaccine, HPV vaccination rates remain low. To prevent cervical cancer and other HPV-caused cancers, alternative approaches to understanding and addressing barriers to HPV vaccination is necessary. A growing body of research suggest that missed clinical opportunities for HPV vaccination is the reason the U.S has not achieved high rates of HPV vaccine uptake (Stokley et al., 2014). I found high rates of missed clinical opportunities for HPV1 (70.1%) and lower rates for missed clinical opportunities for HPV follow up doses (29.6%). The only other study I found that reported missed clinical opportunities for HPV vaccination for 11-12 year old boys and girls found rates of 32.9% for girls and 38.7% for boys (Oltearn, et al., 2016). However, that study defined missed clinical opportunities as the number of visits at which doses of other adolescent vaccines were administered without administration of the first dose of the HPV vaccine and utilized a state-wide immunization tracking system. My study includes additional comparisons by quantifying all visits in which the HPV vaccine could have been given but was not, by including provider level predictors, and through use of electronic medical records to mitigate underestimation of missed clinical opportunities.

Other studies have found missed clinical opportunity rates of 89% (Dempsey et al., 2010), 82.1% (Wong et al., 2013) and 47.2% (Kepka et al., 2016); however, these rates were only determined for adolescent girls (ages 11-17). I expand on this research to assess missed clinical opportunities for HPV vaccination for both boys and girls ages 11-12 and include patient, provider, and visit level factors related to these visits. My focus on characterizing missed clinical opportunities is based on systematic reviews suggesting that educational interventions (Fu et al., 2014) and single-level interventions (Smulian, Mitchell, & Stokley, 2016) are not enough to increase uptake of the HPV vaccine. These reviews concluded that interventions that include intervening at the clinic level (Smulian, Mitchell, & Stokley, 2016) may be more successful in increasing HPV vaccine uptake. Additionally, while I found more opportunities for missed clinical opportunities for HPV3 compared to HPV2, the new ACIP guidelines switching from a three dose to a two-dose series for 11-12 year olds may mitigate that finding in the future (Meites, Kempe, & Markowitz, 2016.

My study supports findings that affirm that missed clinical opportunities for HPV vaccination are common, particularly among problem focused visits (Dempsey et al., 2010; Wong et al., 2013). This pattern of not vaccinating during problem visits suggest that these types of visits are not being considered by providers as opportunities to recommend the HPV vaccine. Providers may be hesitant to recommend the HPV vaccine during problem-focused visits because of limited time they have with patients and the need to address the main reason for the visit. In a national survey of physicians, less than half reported checking vaccination of adolescents at problem-focused visits (Schaffer et al., 2001). These findings stress the importance of utilizing all medical visits as opportunities to vaccinate and the need to review vaccination status at all visits. Vaccination rates increase when providers utilize other opportunities to vaccinate (Stinchfield, 2008) and is a best practice recommended by the Advisory Committee on Immunization Practice (ACIP) (Kroger, Duchin, & Vazquez, 2017). Reminder/recall systems, provider electronic prompts and ensuring that all medical staff review patient records prior to the visit are all strategies that may ensure that the HPV is recommended and administered across all visit types. Future research is needed to evaluate the extent to which these interventions reduce missed clinical opportunities for HPV vaccination.

Gender and racial/ethnic disparities in missed clinical opportunities for HPV vaccination exist. The gender disparity observed in my study is consistent with previous research reporting that providers are less likely to offer the HPV vaccine to boys compared to adolescent girls (Lindley et al., 2016; Perkins & Clark, 2012) and CDC data revealing that 37.5% of adolescent males completed the HPV vaccination series compared to 49.5% of adolescent females (Walker et al., 2016). Further evidence of this is that boys have significantly more missed clinical opportunities than girls. Adolescent males have less preventative care visits compared to adolescent females (Marcell et al., 2002), highlighting the importance of using every clinic visit as an opportunity to vaccinate and emphasizing the benefits and importance of vaccinating males.

Significant racial/ethnic differences were found in missed clinical opportunities for follow-up HPV doses among Hispanic preadolescents compared to White preadolescents, despite other findings that report lower percentage of missed opportunity visits for adolescent Hispanics girls (Kepka, 2016). This finding suggests that when Hispanic preadolescents come in for additional medical visits they may not be getting reminders for HPV follow-up doses and may not be aware of the importance of completing the series. One study, of why adolescents do not complete the HPV vaccine series reported that parents and providers are not intentionally stopping the series, but rather providers and parents are relying on each other to ensure that the series is completed (Perkins et al., 2016). Another study indicated that providers are not discussing series completion with their patients when recommending vaccination (Alexander et al., 2012; Alexander et al., 2015). Not completing the series leaves these adolescents vulnerable to future HPV infections and may give adolescents a false sense of protection. This is particularly unfortunate because Hispanics have high acceptance for HPV vaccination (Perkins et al., 2010). Culturally tailored and linguistically appropriate interventions (Fu et al., 2014; Kepa et al., 2011) for Hispanics are needed to eliminate racial/ethnic disparities in HPV-associated cancers (Burger et al., 2016) in the U.S.

This study found that patients with public insurance were more likely to have missed clinical opportunities for HPV1 and follow-up HPV doses compared to patients with private insurance, this is presumably a result of UCD no longer accepting public insurance plans three months into the study period. UCD's last Medi-Cal (California's Medicaid health care program) contract ended in January 2015 and patients seeking primary care services had to pay out pocket for these services. Other studies did not find an association between insurance coverage and missed clinical opportunities for the HPV vaccine (Wong et al., 2013; Kepka et al., 2016), as most private health insurance and public insurance programs cover the vaccine.

Presenting the HPV vaccine, as a standard bundle of adolescent immunizations due for all preadolescents at ages 11-12, has been widely cited as an effective strategy to increase uptake of the HPV vaccine (Farmar et al., 2016). While these findings suggest that preadolescents who received the Tdap, MenACWY and influenza vaccine were less likely to have missed clinical opportunities for HPV vaccination, the overall uptake rate of the HPV vaccine remained low (34.1% for HPV1, 24.4% for HPV2 and 15.7% for HPV3) compared to the other recommended vaccines (76.6% for Tdap, 64.6% for MenACWY and 73.5% for influenza). This suggest there is still a disconnect among the HPV vaccine and other adolescent vaccines and that efforts to bundle the HPV vaccine with others have not been optimally integrated. The HPV vaccine, unlike Tdap and MenACWY are

not required for school entry in most states and studies have cited that communication regarding the HPV vaccine has been treated differently than for the other two vaccines (Gilkey et al., 2015). Additionally, while the HPV vaccine can be safely co-administered with other vaccines, parents may be hesitant to do multiple same day dosing. Future studies should investigate the extent to which providers were able to successfully bundle the HPV vaccine and the communication strategies associated with willingness to vaccinate.

While studies have reported lower rates of missed clinical opportunities for HPV among pediatricians (Irving et al., 2018); however, no differences in missed clinical opportunities were found among provider specialties. A positive association between having a missed clinical opportunity for HPV1 and the number of years a provider has been in practice was found. This could be a result of greater emphasis on the importance of HPV vaccination in current medical school education. More research is needed to understand why providers who have been in practice longer may have more missed clinical opportunities.

Strengths and Limitations

This study has considerable strengths. This study is one of the first attempts to characterize missed clinical opportunities for timely uptake of the HPV vaccine and may represent one of the largest analysis of preadolescents. Additionally, this study examined variables not previously included in other studies of missed clinical opportunities for HPV vaccination. To the best of my knowledge, this study is one of the first to document gender and racial disparities in missed clinical opportunities for HPV vaccination. Further disparities associated with providers who have been in practice longer among preadolescents has been understudied. The inclusion of patient, provider and visit level factors is important for informing multilevel interventions.

This study has some limitations that should be considered when interpreting the results. The Primary Care Network (PCN) studied was a single health care system study and the clinics provide care to a predominately privately insured, white population. The findings may not be generalizable to patients of safety net system settings or other networks. Future research is needed in different health care settings to improve the generalizability and validity of the results related to the factors associated with missed clinic opportunities. Additionally race/ethnicity data for approximately 8% of patients was incomplete, limiting my interpretation of the “unknown” race/ethnicity category on missed opportunities for HPV vaccination. These data primarily came from electronic medical records and may not capture vaccinations administered outside of the PCN. As a result, these may be a potential overestimation of missed opportunities; however, the majority of patients had multiple visits during the study period indicating that the preadolescents utilize the clinics as their source of primary care.

Conclusions

This study found that a majority of preadolescent patients had at least one missed clinic opportunity for HPV vaccination and that the majority of missed opportunities for HPV vaccination occurred during problem-focused visits. The results highlight the

significant potential to increase uptake of the HPV vaccine by treating every clinic encounter as an opportunity to vaccinate regardless of reason for a visit. Interventions aimed at eliminating these missed opportunities will accelerate timely uptake of the HPV vaccine. Further research is needed to explore communication and educational strategies that focus on presenting the HPV vaccine to families as a bundled package with other adolescent vaccines, ensuring that providers recommend the vaccines to both boys and girls at every visit, and tailoring HPV vaccination campaigns to address the needs of diverse communities.

Table 1. Characteristics of Study Patient Sample, UCD Health Primary Care Network, October 1, 2014 – March 31, 2016	
	N (%)
Patient Characteristics (n = 4,721)	
Gender	
Girl	2,312 (49.0)
Race/Ethnicity	
White	2476 (52.4)
Black	795 (16.8)
Hispanic	649 (13.7)
AANHPI	369 (7.8)
AIAN	38 (0.8)
Unknown	394 (8.3)
Language	
English	4,541 (96.2)
Non-English	180 (3.8)
Insurance	
Private	3,907 (82.8)
Public	468 (9.9)
Self-Pay/Other	346 (7.3)
Number of visits per patient, average (SD)	
Vaccination coverage during study	2.3 (2.0)
Tdap	3,614 (76.6)
MenACWY	3,051 (64.6)
Influenza	3,469 (73.5)
HPV1	1,609 (34.1)
HPV2	1,153 (24.4)
HPV3	739 (15.7)
Primary Care Provider Characteristics (n = 397)	
Specialty	
Pediatrics	205 (51.8)
Family	167 (42.2)
Other/Unknown	25 (6.3)
Gender	
Female	204 (51.5)
Years in practice, average (SD)	23.1 (11.5)
*Abbreviations: AANHPI = Asian American, Native Hawaiian, and Pacific Islanders; AI/AN = American Indian/Alaskan Native; Tdap = Tetanus, diphtheria, & pertussis; MenACWY = Meningococcal group A, C, W-135, & Y; HPV1 = human papillomavirus first dose; HPV2 = human papillomavirus second dose; HPV3 = human papillomavirus third dose	

Table 2. Missed clinical opportunities for HPV vaccination by visit type, UCD Health Primary Care Network, October 1, 2014 – March 31, 2016[a]		
	Eligible for HPV vaccine at time of visit, n[b]	Missed clinical opportunities, n (%)
HPV1		
Prevention	2,311	1,370 (59.3)
Problem-focused	7,488	5,502 (73.5)
Total Visits	9,799	6,872 (70.1)
HPV Follow-up		
Prevention	1,278	246 (19.2)
Problem-focused	2,701	932 (34.5)
Total Visits	3,979	1,178 (29.6)

[a] All characteristics are presented at the visit level because the visit was the unit of analysis

[b] Visits for patients who received the HPV prior to the study were excluded from the analysis

*Abbreviations: HPV1 = human papillomavirus first dose; HPV Follow-up = human papillomavirus second and/or third dose

Table 3. Multivariate analysis of patient, primary care provider and visit characteristics associated with unmissed clinical opportunities for HPV vaccination, UCD Health Primary Care Network, October 1, 2014 – March 31, 2016[a]

	HPV1 (n= 9,577)[b]		HPV Follow-Up (3,950)[c]	
	Odds Ratio (95% CI)	**P-Value**	**Odds Ratio (95% CI)**	**P-Value**
Patient Characteristics				
Gender				
Girl	**Ref.**		**Ref.**	
Boy	0.6 (0.6 – 0.7)	**< .0001**	0.9 (0.7-1.0)	0.1
Race/Ethnicity				
White	**Ref.**		**Ref.**	
Black	1.2 (1.0 – 1.5)	0.1	1.4 (1.0 – 2.0)	0.1
Hispanic	0.9 (0.8 – 1.1)	0.4	0.7 (0.5 – 0.8)	**0.001**
AANHPI	1.0 (0.8 – 1.2)	0.9	0.8 (0.6 – 1.1)	0.2
AIAN	1.5 (0.8 – 2.7)	0.2	0.6 (0.3 – 1.2)	0.2
Unknown	1.2 (0.9 -1.5)	0.2	0.6 (0.4 – 0.9)	**0.005**
Language				
English	**Ref.**		**Ref.**	
Non-English	0.5 (0.4 – 0.7)	**< .0001**	1.1 (0.6 – 1.8)	0.8
Insurance				
Private	**Ref.**		**Ref.**	
Public	0.7 (0.5 – 1.0)	**0.030**	0.5 (0.3 – 0.8)	**0.003**
Self-Pay/Other	0.8 (0.6 – 1.1)	0.1	0.9 (0.6 – 1.4)	0.6
Vaccines received **up** to time of visit				
Tdap	2.1 (1.7 – 2.7)	**< .0001**	0.7 (0.3 – 1.9)	0.5
MenACWY	8.9 (7.2 – 11.0)	**< .0001**	4.6 (3.0 – 7.0)	**< .0001**
Influenza	2.4 (2.1 – 2.7)	**< .0001**	1.6 (1.2 – 2.3)	**0.005**
Primary Care Provider Characteristics				
Specialty				
Pediatrics	**Ref.**		**Ref.**	
Family	0.9 (0.5 – 1.7)	0.8	2.8 (0.6 – 12.6)	0.2
Other/Unknown	0.8 (0.1 – 6.0)	0.9	0.3 (0.0 – 11.2)	0.5
Gender				
Male	**Ref.**		**Ref.**	
Female	1.2 (0.6 – 2.2)	0.6	2.5 (0.7 – 8.5)	0.2
Years in practice	0.96 (0.9 – 1.0)	**0.001**	1.0 (0.9 – 1.0)	0.5
Visit Characteristics				
Type of visit				
Prevention	**Ref.**		**Ref.**	
Problem-focused	0.6 (0.5 – 0.7)	**< .0001**	0.5 (0.4 – 0.6)	**< .0001**
Due for Follow-up dose				
3rd Dose	N/A		**Ref.**	
2nd Dose	N/A		2.9 (2.5 – 3.5)	**< .0001**

[a] All characteristics are presented at the visit level because the visit was the unit of analysis

[b] Random effects estimates for HPV1
- Clinic = 0.00; S.E. = 0.00
- Provider = 3.0; S.E. = 0.6
- Patient = 0.00; S.E = 0.00

[c] Random effects estimates for HPV Follow-Up
- Clinic = 0.8; S.E. = 0.8
- Provider = 5.9; S.E. = 1.6
- Patient =0.00; S.E = 0.00

* Odds ratios are adjusted for all tabulated variables using logistic regression mixed effects models.

**Abbreviations: AANHPI = Asian American, Native Hawaiian, and Pacific Islanders; AI/AN = American Indian/Alaskan Native; Tdap = Tetanus, diphtheria, & pertussis; MenACWY = Meningococcal group A, C, W-135, & Y; HPV1 = human papillomavirus first dose; HPV Follow-up = human papillomavirus second and/or third dose

Paper 3
"There's Always Next Year": Provider, Clinic Support Staff and Parent Perspectives on the Human Papillomavirus Vaccine

Abstract

Objective: Studies have reported high levels of human papillomavirus (HPV) vaccine acceptance among parents and providers; however, the uptake of the HPV vaccine remains low. Little is known about organizational factors that may influence uptake of the HPV vaccine. Interviews with providers, clinic support staff and parents of adolescent patients were conducted to better understand the team and patient care processes that impede HPV vaccine uptake.

Methods: Between July 2016 and February 2017, I conducted semi-structured interviews with 40 participants (18 providers, 12 clinic support staff and 10 parents of adolescent patients) in a primary care network.

Results: Clinic support staff and organizational factors, such as electronic provider reminders, availability of vaccine only appointments, and knowledgeable staff contributed to HPV vaccine uptake. While all participants were in support of HPV vaccination, parents justified non-vaccination as a decision to delay rather than refuse the HPV vaccine. Physicians and clinic support staff often suggested revisiting HPV vaccination in the future, giving patients the impression that receiving the vaccine was not time-sensitive.

Conclusion: Strategies to accelerate HPV vaccine uptake should address individual and organizational level factors to ensure that HPV vaccination is prioritized. Multi-level interventions that engage parents, providers, and the entire medical team may be needed because improving HPV vaccine uptake appears to be facilitated through the alignment of priorities.

Introduction

The human papillomavirus (HPV) is the most common sexually transmitted disease in the United States. Approximately, 79 million Americans are currently infected and roughly 14 million Americans will acquire a new infection each year (Satterwhite et al., 2013). Spread through skin-to-skin contact and most commonly contracted through sexual contact, HPV impacts everyone, regardless of gender and sexual orientation. The Advisory Committee on Immunization Practices (ACIP) recommends routine vaccination of the 2-dose series at ages 11-12 years with catch up 3-dose vaccination (for those who were not previously vaccinated) through age 26 years for females and through age 21 years for males for the prevention of several HPV-associated diseases (Meites, Kempe & Markowtiz, 2017). HPV vaccination is the optimal primary prevention strategy against HPV related diseases. Vaccination against human papillomavirus can prevent about 28,500 new cancer cases in the United States annually and almost all cases of genital warts (Viens, 2016).

Despite these recommendations and the public health implications of full vaccination coverage, the completion rate for the HPV vaccine remains low. In 2016, only 34.9% of U.S. adolescents aged 13-17 were fully vaccinated (Reagan-Steiner et al., 2016). Although this is an overall increase in uptake from previous years, it is still substantially lower than the coverage for the other two recommended vaccines at these ages, the tetanus, diphtheria and acellular pertussis (Tdap) at 87.1% and the meningococcal vaccine (MenACWY) at 81.3% (Reagan-Steiner et al., 2016).

While there has been a wave of studies and systematic reviews that have examined the barriers and facilitators to HPV vaccination uptake (Bratic, Seyferth, & Bocchini 2016; Holman et al, 2014; Kessels et al., 2012) many of the findings from these studies have been inconsistent. These studies report high levels of vaccine acceptability among parents and providers; however, nationally, HPV vaccine uptake remains low. The majority of studies have focused on one or two levels of influences (e.g. parents and/or providers), however, parents and providers have reported that their views on the HPV vaccine are influenced by each other as well as by factors related to the health care system (Bratic, Seyferth, & Bocchini 2016).

The purpose of this study was to conduct qualitative interviews with providers, clinic support staff and parents of adolescents of a primary care network to better understand HPV vaccine delivery at the point of care. I sought to move beyond parent and physician factors to include the perspective of other health care team members (e.g., nurses, medical assistants, clinic managers, etc.) and factors related to the practice setting (e.g., decision support, infrastructure, electronic health system, etc.). A better understanding of how these multiple levels of influences can contribute to the decision and follow through of HPV vaccination is needed because completing the HPV vaccine series is a result of multiple levels of influences. First providers have to recommend the vaccine to the patient, secondly the patient/parent has to accept that recommendation, and lastly the clinic has to carry out the recommendation. At each level, multiple converging and integrative processes determine whether vaccination occurs.

Methods

Setting

This qualitative study was conducted within the University of California, Davis Health System (UCDHS) Primary Care Network (PCN). The PCN consists of 15 outpatient clinics located in Sacramento, CA and the 9 surrounding communities. The majority of patients are privately insured. Interviews occurred between July 2016 through February 2017 at 9 participating clinics. The study protocol was approved by the University of California, Davis Institutional Review Board.

Participants

To be eligible for the study, participants had to be either a parent/guardian (hereby referred to as 'parents') of a UCDHS patient ages11-17; a UCDHS physician that provided primary care to patients ages of 11-17; or a UCDHS staff who worked at a PCN clinic that provided primary care to patients ages 11-17. Recruitment flyers were displayed at the PCN clinics for parents and individual emails were sent to all PCN providers and staff. Interested individuals called the number on the flyer and/or emailed the study coordinator directly to determine eligibility. Convenience (those who responded to the email or flyer) and snowball (referral from participants) sampling was used to recruit the participants. All interviews were conducted in English. Parents and clinic staff received a $20 gift card as compensation for their participation and providers received a $40 gift card.

Interview and Data Analysis

Three separate interview guides, one for each category of informant (provider, staff and parent) were developed with probes for clarification to facilitate responses to the semi-structured and open-ended interview questions. Parent interviews explored barriers and facilitators to accepting a recommendation from a provider to get their child vaccinated; provider interviews explored the barriers and facilitators to making a successful HPV vaccine recommendation for their patient; and staff interviews explored barriers and facilitators to carrying out that recommendation once a provider has made it and a parent has accepted it. All three interview categories included individual, provider and clinic/visit level questions and probes. Interview guides were also reviewed by clinical operations management and a parent whose adolescent was not receiving care through this PCN for appropriateness and comprehensiveness. Interviews were no longer than thirty minutes and began with a short survey to capture socio-demographics and clinic setting data. Open ended questions focused on HPV vaccine knowledge, attitudes and beliefs; barriers and facilitators to HPV vaccination; and the required resources to increase HPV vaccine uptake (desired support).

Provider and staff interviews were conducted face to face while half of the parent interviews were conducted over the phone and the other half were conducted face to face. All interviews were digitally recorded, transcribed verbatim and uploaded into Dedoose, a software package for managing and analyzing qualitative research data. Answers to open-ended questions were coded according to predefined categories based on the interview guide: 1) barriers; and 2) facilitators; 3) attitudes, knowledge and beliefs

about HPV vaccination and HPV-related disease. I started with these categories to identify key points within the data (themes), created additional themes and subthemes as they emerged, and then I reconciled, summarized and categorized the findings. Three researchers independently coded the transcripts and then met to review codes and their meanings. Codes and themes were discussed to resolve initial differences and modifications of codes were made until agreement among all codes was achieved. Code reports were analyzed for patterns and were used to identify emergent themes. Data collection continued until saturation was reached, with no new themes emerging.

Results

Description of participants

A total of 40 individuals participated in the interviews (10 parents/guardians, 12 clinic support staff and 18 providers). The majority of participants were female; White; between the ages of 30 and 39; and born in the US. All the parents interviewed were female and the majority were between the ages of 40 and 49. Providers included 10 pediatricians, an internal medicine specialist, 6 family practice physicians and a physician assistant. The majority of providers were: female; between the ages of 30 to 39; and were born in the U.S. Clinic support staff included 8 medical assistants (MAs), 1 licensed vocational nurse (LVN), and 3 clinic managers. The majority of clinic support staff were female and between the ages of 30 to 39 (Table 1 here). Major themes and the barriers, facilitators, and desired support at each level (practice, provider/staff, and parent) are summarized in Table 2.

Qualitative results by theme

Practice Level

HPV vaccination at point of care. When asked how HPV vaccines are administered, clinic support staff and providers explained that once a family consented to vaccination, the provider placed a HPV vaccine order in the patient's electronic medical record and after the provider completed the visit, a clinic staff (e.g. MA, LVN, etc.) would come into the exam room to administer the shot. Prior to administering the vaccine, the clinic staff asked the family if they had any questions and if they did, they are given the HPV Vaccine Information Sheet (VIS). Many of the MA's and LVN's who administered the vaccine stated that parents usually had additional questions regarding the vaccine, even after agreeing to vaccination. When families have additional questions the MA/LVN would "*refer them back to their provider*" and at that point the staff would *"go back to the doctor and tell them they changed their minds."* As explained by the LVN, "*when they (parents) get the handout (VIS) and they look at it and the first thing that they see is sexually. So I think the way it is presented to them kind of pushes them off…and then they change their minds, they are like, I don't want to get this."*

Infrastructure. All participants agreed that having a strong organizational infrastructure that was conducive to HPV vaccination aided in the administration of the vaccine. When

asked what has helped with recommending the vaccine, one provider stated, *"I get a little warning in their medical records saying they're due for it, so it makes it easy for me to remember to ask them.*" Another provider mentioned, "*I have a great shot clinic that people can just walk in and go to and I think the availability of that is pretty open*." Parents also agreed that it was "*super easy to schedule an appointment"* and as one parent exclaimed, *"you don't necessarily have to see the doctors, you just show up to the immunization nurses and they handle it really quickly. I just go in, there is no co-pay for the immunization."*

Parent Primer (desired support). All participants felt that the health system could support HPV vaccination efforts by providing HPV vaccine education to parents prior to their child's medical visit. As one provider described, *"we are a big health system, at some point we should have a health campaign or something that you know talks about getting the vaccine for your kid."* Another provider suggested having the health system send out educational mailers to parents of 9 and 10 year olds "*so we can refer back to that, rather than hitting the parents with the information during visit*." Another provider remarked, "*It would be nice if people heard about the vaccine from places other than their doctor's office, because then when they come in here, I just need to reinforce something that they already heard about. It's always hard when they hear something completely new and then they are all nervous about it, and then they say well, I haven't heard much about the vaccine, I wish I had more information*." Parents agreed that, *"some parents want to be informed before the appointment, then they can send a brochure out through the mail and say hey this is coming up, just kind of a FYI."*

Provider and Staff Level

Dealing with HPV vaccine hesitant parents. When parents expressed a desire to delay getting the vaccine, staff and provider did not push for same day vaccination. Providers described the vaccine as "*optional*", "*not required for school*," and "*not urgent*". For example, when asked how he dealt with parents who wanted to wait, one provider stated he would tell families, "*we have until you turn 26 to do this. It's not an urgent vaccine and the next time you come in we can discuss it again*." Another provider stated that he, "*prints out the HPV vaccination sheet information, hand it to them (the family) and tell them whenever they are ready, I say call me and I can get it done*." One MA added, "*maybe we will revisit it the next time they come in because there is a wide range of ages…they might refuse and say well can we do it next year or the year after*." Another MA responded, *"I tell them they don't have to do it today, the order is valid for two years depending on how the doctor ordered it and that they can come back once they do the research for it*."

Effective Strategies. Providers and staff agreed that emphasizing the message of cancer prevention and normalizing the vaccine were the two most effective strategies they have utilized. When asked why she chose to vaccinate her daughter, one mother exclaimed, "*I don't want my daughter or kids to have cervical cancer or anything. I would want my daughter to be prevented from any form of disease that will keep her from living her life.*" Agreeing, the LVN stated, *"they have to know the purpose of the vaccination is that it prevents diseases such as cervical cancer."* When describing his strategy, one

provider explained, "*I usually start off talking that it's to help prevent cancer. I talk about the importance of cancer prevention.*"

Providers would also present the vaccine as they would any other vaccine by "*listing it (*the HPV vaccine*) as a package expected at this age,*" and stating that "*the American Academy of Pediatrics recommends the following shots: HPV, TDAP, meningococcal vaccine*. As described by one provider, "*Once I defined my approach of just packaging the HPV as part of a normal package deal for an 11-year-old, things started to become easier.*" To normalize the vaccine, one provider stated that she also makes the following analogy to parents, "*I just kind of reassure them that when they* (their child) *was first born, we gave them the Hepatitis B vaccine and that is also a sexually transmitted disease, and you* (the parent) *were okay with giving them that right at birth."*

Provider and staff education (desired support). Providers and clinic support staff agreed that everyone (e.g. providers, administrative staff, medical assistants, nurses, etc.) at the clinic would benefit from "*more HPV education*" and that "*the more people who mention it throughout the clinic visit, then the more receptive the parents are to have it done*." As one MA explained, "*It doesn't make any senses for you* (staff) *to go in a room and give somebody injections that you are not educated on. Oh, you* (the parent) *have a question, give me one moment to go back and ask the doctor, that is not efficient work at all."* Additionally, staff reported being asked by parents about their opinion on the HPV vaccine. For example, one medical assistant said, *"I would just discuss with them where I come from, I would let them know a little bit of my religious background, how my parents wouldn't vaccinate me and how I felt as an adult now as vulnerable as a child."* Another medical assistant added that when parents asked her about the vaccine she would respond with, *"I have 2 kids, and when they are old enough, they will be vaccinated as well."*

When asked what would make the greatest impact on increasing the HPV vaccine uptake rate, a provider stated, *"If we were to focus on what would make the biggest difference, it would be having a continuity of people bringing it up so when the MA's in the room with the patients them saying, hey has anyone asked you about the HPV vaccine or it looks like your're due for your HPV vaccine, let's talk about it…on the clinic side its getting hit at least once or preferably more than once so people realize this seems to be important because they keep bringing it up."* Agreeing, a one mother shared her HPV vaccine experience, "*He (the doctor) put in the order, and then his LVN came in. She is very good, she explained what she was going to do and it was very quick*."

Parent Level

Sexual Debut. All participants cited that a major challenge to vaccination is the fact that because the virus is sexually transmitted, parents are worried that receiving the HPV vaccine would encourage their children to become sexually active. While the parents I interviewed did not cite sexual activity as a barrier to vaccinating their own children, they stated that it is a barrier for many parents including for their friends and family members with children. As one parent explained, "…*like I said a lot of parents think that if you get the vaccine it's because you're going to have sex*." A MA added, "*You get it through being sexually active… They* (parents) *are going to say, not my child, they don't need to be*

vaccinated because my child wouldn't do that, and my child is not sexually active." Providers agreed that there is "*this misconception that somehow giving the vaccine is condoning sexual activities, sort of as if we are putting their kids on birth control or something…that we are expecting them to become sexually active.*"

Delaying HPV vaccination. When asked if her daughter's provider had discussed the vaccine during the visit, a mother said, "*In all truthfulness, the doctor went over this with me, and as she was explaining, I was up to do it, but just not yet*." Providers and clinic support staff agreed that parents "*usually don't outright refuse, they will say we will not at this time,*" and would request to "*wait until their child is older*." As described by one provider, "*Parents feel that (the HPV vaccine) it isn't necessary. They don't feel like their kids need to have it... they think it's too early, and they want to do it later*."

Misinformation. When asked about challenges to vaccination, all participants commented that media coverage of the HPV vaccine has led many parents to have inaccurate or incomplete information regarding the vaccine. As explained by one parent, "*I think that there was so much damage that has been done in the past with the study that correlated autism with immunization. I have to say that out of the people I have spoken with* (that have children)*, that is the reason; because they strongly believe that there is a correlation between the two*." Another mother echoed the same sentiment, "*There were a couple of articles that I read and a couple of them seem to be like severe cases…you know those things are out there so just making sure that those are being address so people who aren't misinformed about it*." One provider remarked that "*when they (parents) go on the Internet, they get the wrong information. They might hear about, you know, adverse thing that may have happened, and they are scared about it*…"

Discussion

Interventions to improve HPV vaccine uptake usually focus on patients/parents or healthcare providers, without addressing the role of other healthcare team members and the practice setting (Smulian, Mitchell, & Stokley, 2016). I conducted this study with providers, clinic support staff and parents to better understand how HPV vaccination occurs at point of care. By examining multiple perspectives, I identified several themes that can explain the low HPV vaccination rates and identified several strategies that can inform future interventions. My findings show that clinic support staff and organizational support for HPV vaccination were important factors related to vaccine uptake. Future studies to accelerate uptake of the HPV vaccine should include both individual and organizational strategies to address these multiple levels of influences.

I found that despite the overall acceptance and support for the HPV vaccine, participants reported delayed vaccination. Similar to Hughes et al., my study revealed that parents were not refusing vaccination, but rather wanted to delay vaccination until their child was older, and when parents voiced this desire to wait, providers and clinic staff did not push for same day vaccination (Hughes et al., 2016). The main reason cited for delaying vaccination was that parents did not feel that their child needed to be protected against a sexually transmitted disease at their current age because they believed their child is not sexually active nor will they be sexually active soon. However,

according to the 2015 Youth Risk Behavior Surveillance Survey, 41.2% of high school students reported ever having sexual intercourse and 30.1% reported currently being sexually active, thus parents may be underestimating their teen's sexual activity (Kann et al. 2016). This lack of urgency to vaccinate on the same day as the medical visit is concerning because older adolescents have less preventative care visits compared to younger adolescents (Rand et al., 2007), unvaccinated individuals are vulnerable to HPV infections, and because the vaccine is most effective prior to sexual debut.

I also found a disconnect between provider recommendation of the HPV vaccine and clinic follow through of vaccine delivery. Providers reported recommending the vaccine to their patients and parents expressed high acceptance of the vaccine; however, when staff came to administer the vaccine, in some cases the vaccine was not given. I found several explanations for this pattern. While clinic staff supported HPV vaccination, they expressed varying knowledge of HPV vaccination. When encountering families that had follow up HPV questions, staff would refer families back to their provider and suggest vaccination at a future appointment. Staff also reported being asked about their personal opinion on the vaccine. This is consistent with findings from Chuang et al., which also found health care team and clinic level factors that affect HPV vaccine uptake (2016). Prior studies have focused on the importance of a provider's strong HPV vaccination (Gilkey 2016), however, clinic support staff are usually the first point of contact for families during a patient visit and they are also usually the ones who administer the HPV vaccine and as such their recommendation can reinforce that of the providers. Similar to Hudson et al (2016), my findings also provide evidence that having a pro HPV vaccine clinic culture, where all clinic staff and providers are on the same page, could accelerate the HPV uptake rate. Future interventions should include training clinic support staff on how to offer a strong HPV vaccine recommendation.

In addition to the widely cited strategies of emphasizing the message that HPV is cancer prevention (Malo et al., 2016) and normalizing the vaccine (Farmar, 2016), providers also attributed having a strong organizational vaccine infrastructure (e.g. provider alert, flexible clinic hours, tracking systems, etc.) as a factor that contributed to vaccination. This finding is consistent with the literature that indicates that vaccine protocols and procedures (Szilagyi et al., 2008) and practice attitudes towards vaccination (Tiro et al., 2012; Conroy et al., 2009) are practice level factors that influence HPV vaccine uptake.

Lastly, my study findings indicate that while most parents have heard of the HPV vaccine, parents were not sufficiently primed for vaccination prior to office visit. Time constraints has been cited as a major barrier to vaccination by providers (Holman, Benard, & Roland, 2014) and a desired support to abate time constraints suggested by providers and clinic staff was to provide education to the parents before the office visit. Providers can then focus their time on answering any lingering questions parents may have.

Limitations

Participants were recruited from the UCDHS, thus generalization from this population is limited both by the demographic composition of the sample population as well as their access to clinical care (a majority of the sample had health insurance). For example, all

the parent participants were mothers and the majority of providers and staff were females. Responses to the questions might have reflected their personal bias associated with vaccinations, their socioeconomic status, and/or their experiences with health care and illness. However, my objective was not to generate results generalizable to a population, but rather to develop a deeper understanding of the mechanisms involved in a provider's HPV vaccine recommendation, parental acceptance of that recommendation and clinic follow up to ensure that the vaccination occurs.

Conclusion

By examining parent, provider and clinic staff perceptions of the HPV vaccine, several salient factors that can help explain low HPV vaccination rates and strategies to accelerate HPV vaccine uptake were identified. These factors include: the role of clinic support staff in hindering or enhancing a provider's HPV vaccination recommendation, increasing organizational support for HPV vaccination and the overall low urgency for HPV vaccination among providers, clinic staff and parents. The results underscore that interventions to accelerate HPV vaccine uptake should be multi-component and include methods and strategies at the parent, provider, clinic support staff and practice setting levels. The effectiveness of HPV interventions that include clinic-wide HPV vaccination trainings should be examined in future research. Training may help align interests so that clinic support staff and providers are giving the same consistent timely message around HPV vaccination to all families.

Table 1. Characteristics of Interview Participants			
	Parents (n = 10)	Providers (n = 18)	Staff (n = 12)
Gender			
Male	0	7 (39%)	1 (8%)
Female	10 (100%)	11 (61%)	11 (92%)
Race/Ethnicity			
White	7 (70%)	6 (33%)	4 (33%)
Black	0	3 (17%)	5 (42%)
Asian	2 (20%)	7 (39%)	2 (17%)
Hispanic	1 (10%)	2 (11%)	1 (8%)
Age			
20-29	0	0	0
30-39	4 (40%)	9 (50%)	6 (50%)
40-49	6 (60%)	5 (28%)	1 (8%)
50-59	0	2 (11%)	4 (33%)
60+	0	2 (11%)	1 (8%)
Fluent in a second language			
Yes	2 (20%)	7 (39%)	5 (42%)
No	8 (80%)	11 (61%)	7 (58%)
USA Born			
Yes	9 (90%)	13 (72%)	11 (92%)
No	1 (10%)	5 (28%)	1 (8%)

Table 2. Summary of key findings of practice, provider, staff and parent factors associated with HPV vaccine uptake and the desired support/resources to accelerate HPV vaccine uptake.

Levels	Barriers	Facilitators	Desired Support
Practice	• Providers and staff cited that HPV vaccination may not be a clinic priority.	• Providers and parents stated that clinic infrastructure makes ordering the vaccine simple and easy (e.g. automated alerts, provider prompts, electronic medical records, & vaccine tracking system) • Providers and parents stated that flexible clinic hours & walk in clinics made administering the vaccine easier. • Parents liked having the option of vaccine only appointments	• Providers wanted health system/clinic wide HPV awareness campaign.
Provider/ Staff	• When faced with vaccine hesitant parents, providers and staff did not push for same day vaccination. • Reasons providers, staff and parents cited for delaying vaccinations included: the wide age range for vaccination and the vaccine not being required for school entry. • Provider and staff gave varying HPV vaccination recommendations.	• All participants stated that emphasizing cancer prevention is the most important HPV educational message. • Providers and staff stated effective strategies included: normalizing the vaccine (e.g. bundle with other vaccines due at the same time), citing the recommending guidelines, and using Hepatitis B as an analogy.	• Providers and staff wanted clinic-wide HPV vaccination trainings to ensure everyone is on the same page regarding vaccinations.
Parent	• Providers, staff and parents cited that parents are worried that getting the vaccine will encourage their children to become sexually active. • Provider and staff cited that parents delayed rather than refused vaccination. • Providers, staff and parents cited media and public misinformation regarding the vaccine as a major barrier to vaccination.	• Parents stated that believing that the HPV vaccine is important • Parents and staff stated that a provider's recommendation is influential in the decision to vaccinate.	• Providers, parents and staff suggested developing community campaign to address media and public misinformation regarding the vaccine. • Providers and parents thought parents should receive HPV vaccine education prior to the medical visit.

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