American Journal of Epidemiology

Vol. 171, No. 3
DOI: 10.1093/aje/kwp365
Advance Access publication: January 4, 2010

Original Contribution

Correlates for Human Papillomavirus Vaccination of Adolescent Girls and Young Women in a Managed Care Organization

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Initially submitted March 31, 2009; accepted for publication October 8, 2009.

The authors studied the characteristics of those who initiated the human papillomavirus (HPV) vaccine versus those who did not. Female members of Kaiser Permanente Southern California aged 9–26 years were identified and assessed for HPV vaccination between October 2006 and March 2008. Multivariable log-binomial regression was used to examine the association of the following factors with vaccine initiation: 1) demographics, 2) provider characteristics, 3) health care utilization, 4) women's health-related conditions, and 5) selected immune-related conditions. The study included 285,265 females. All analyses were stratified by 2 age groups: 9–17 years and 18–26 years. Black race (relative risk $(RR)_{9–17\ years} = 0.93$, $RR_{18–26\ years} = 0.82$), having a male primary care provider ($RR_{9–17\ years} = 0.93$, $RR_{18–26\ years} = 0.84$), and history of hospitalizations were associated with a lower likelihood of vaccine initiation. Higher neighborhood income level, physician office visits, and history of influenza vaccination ($RR_{9–17\ years} = 1.20$, $RR_{18–26\ years} = 1.34$) were associated with higher HPV vaccine uptake. Those with a history of sexually transmitted diseases were more likely and those with immune-related conditions were not less likely to initiate the HPV vaccine. These findings are helpful for interpreting the results of observational safety studies and providing insights for developing targeted HPV vaccination programs.

female; human papillomavirus 6; human papillomavirus 11; human papillomavirus 16; human papillomavirus 18; managed care programs; papillomavirus vaccines; vaccination

Abbreviations: CI, confidence interval; HPV, human papillomavirus; Pap, Papanicolaou; RR, relative risk; STD, sexually transmitted disease.

The human papillomavirus (HPV) vaccine HPV4 presents an opportunity to reduce the burden of cervical cancer and other conditions caused by HPV types 6, 11, 16, and 18 (1, 2). HPV4 is indicated for adolescent girls and young women aged 9–26 years and is given in 3 injections (3). The Advisory Committee on Immunization Practices recommends routine HPV immunization of girls aged 11–12 years (3). Although this committee recommends the vaccine, it is in general not required by US state law. As a result, not all eligible females will receive the vaccine.

Understanding the characteristics of those who obtain the vaccine versus those who do not could have important implications for future policy making. For example, socioeconomically disadvantaged women in the United States are at increased risk of cervical cancer (4, 5). If these women are unlikely to receive the vaccine, the vaccine's full potential to reduce the burden of cervical cancer will not be realized. Moreover, if current vaccine recipients differ systematically from nonrecipients regarding risk of outcomes that may be associated with HPV vaccination, results from previous and ongoing safety studies may not apply to broader target populations. Therefore, knowledge of the correlates of HPV vaccine uptake may provide important insights for future vaccine-targeting efforts and for the generalizability of ongoing safety surveillance studies.

MATERIALS AND METHODS

Study population

Kaiser Permanente Southern California is the largest managed care organization in southern California. The organization serves more than 3 million members who are broadly representative of the diverse racial/ethnic and socioeconomic background of the source population in this geographic location. Because of the nature of the Kaiser Permanente Southern California prepaid managed care system, members have relatively equal health care coverage. In particular, the HPV4 vaccines are offered to eligible female members without additional out-of-pocket cost (variations in office-visit copayments exist but are small). Female members aged 9–26 years on October 1, 2006, who maintained Kaiser Permanente Southern California membership between October 2006 and March 2008 were included in this study. The study protocol was approved by the Kaiser Permanente Southern California institutional review board.

HPV4 initiation

Information on HPV4 vaccination was obtained by using the Kaiser Immunization Tracking System, the Kaiser Permanente Southern California legal record for immunization. HPV4 vaccination records in this tracking system were linked to the female members through their unique medical record number. Date and dose of vaccination were available from the Kaiser Immunization Tracking System.

Subject characteristics

Demographics and socioeconomic status. Age, race/ethnicity, and length of health plan membership were available from the Kaiser Permanente Southern California membership files. Health plan members' addresses were mapped to US Census tract data (6), which provided information on neighborhood education and income status. Medi-Cal status, California's Medicaid health care program that covers children and adults with limited income and resources, was used as an indicator for individual-level socioeconomic status.

Because race/ethnicity information was missing from the membership file for approximately half of the subjects, we performed race/ethnicity imputation using a previously validated algorithm. In brief, race/ethnicity was assigned for individuals by using hospital-based service utilization, geocoding methods, spoken language, and surname criteria (for Hispanics and Asians). Validation studies using self-reported race/ethnicity data for women of childbearing age showed high accuracy for the race/ethnicity assignment made by this algorithm, with positive predictive values of 0.84~0.94 and negative predictive values of greater than 0.90 across all race/ethnicity groups (Dr. Stephen Derose, Kaiser Permanente Southern California, personal communication, 2009). A secondary approach, Rubin's multiple imputation (7,) was also used to address this issue of missing race/ethnicity information. The results from both approaches were compared.

Primary care provider characteristics. The characteristics of the girls'/women's primary care provider, including medical specialty, age, gender, and affiliated medical center, were obtained from the Kaiser Permanente Southern California provider files.

Historical health care utilization. Historical health care utilization in a 2-year interval prior to study baseline (October 2006) was characterized by 1) number of all outpatient visits, 2) number of primary care visits, 3) number of inpatient hospitalizations (excluding pregnancy-related hospitalizations), 4) number of emergency room visits, 5) number of out-of-plan visits, and 6) use of influenza vaccine (yes/no).

Women's health-related medical history. Obstetric history, history of sexually transmitted diseases (STDs; including genital/anal warts, chlamydia, gonorrhea, genital herpes, trichomoniasis, and syphilis), Papanicolaou (Pap) screening, abnormal Pap results, and use of oral contraceptive pills/birth control patches were assessed. Specific medical histories were ascertained by computer search of corresponding *International Classification of Diseases*, Ninth Revision codes; laboratory procedures; and medication dispensed. Clinical guidelines require that women receive at least one Pap screening every 3 years (8). Therefore, Pap screening within the 3-year interval prior to study baseline was assessed.

Selected immune-related conditions. We evaluated immune-related medical conditions because they were of interest for postmarket safety surveillance for the vaccine. Several prespecified conditions were assessed in the 2 years prior to baseline: 1) rheumatoid conditions; 2) asthma; 3) general allergy (including hay fever, eczema, contact dermatitis, urticaria, food allergies, and unspecified allergy); 4) drug allergy; 5) number of infections (including urinary tract, respiratory tract, intestinal, and skin); and 6) antibiotic use for bacterial infections. Notations of at least 2 *International Classification of Diseases*, Ninth Revision codes specific to rheumatoid conditions, asthma, and general allergy were required to define a history of that condition (to reduce false positives and to capture the more severe cases). Drug allergy was assessed by either *International Classification of Diseases*, Ninth Revision codes or through documentation in electronic health records of drug allergic/adverse reactions. Antibiotic use included only oral use and excluded prescriptions of 21 days or longer for tetracycline, minocycline, doxycycline, erythromycin, and clindamycin to reduce the impact of antibiotic used for acne treatment.

Statistical analysis

The proportion of vaccination in the 18-month assessment period was calculated by yearly age. The distribution of subject characteristics was compared between HPV4 vaccine recipients and nonrecipients, stratified by 2 age groups: 9–17 years (adolescent girls) and 18–26 years (young women). The age stratification was made because 1) the rate of HPV vaccination initiation was substantially different in these 2 age groups; and 2) factors associated with vaccine uptake may be different for adolescent girls and young women (e.g., parental consent is usually required for those younger than age 18 years). Because HPV vaccine is best given before sexual debut, we also conducted subanalyses among girls aged 9–12 years to further understand correlates

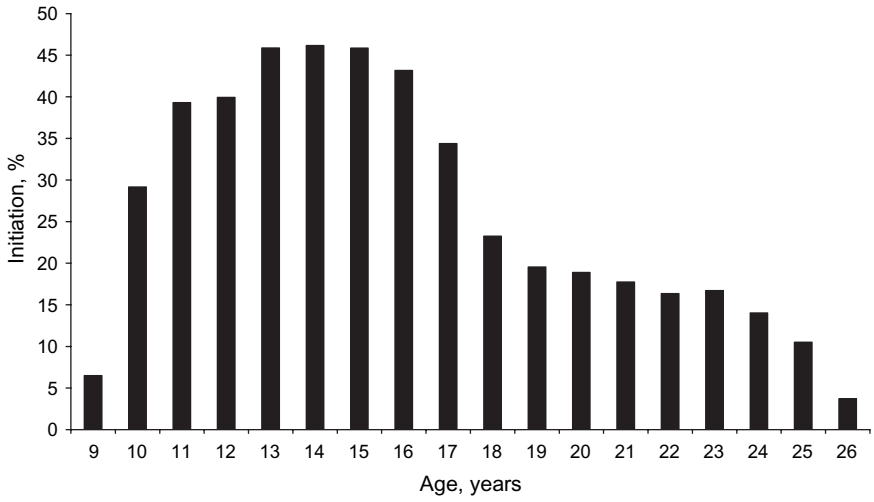

Figure 1. Percentage of adolescent girls and young women who initiated the human papillomavirus vaccine during an 18-month period between October 2006 and March 2008, by age, Kaiser Permanente Southern California.

for these younger girls who most likely have not been sexually active.

Crude and adjusted associations with HPV4 initiation were estimated as relative risks by using log-binomial models, stratified by age group. When the log-binomial model failed to converge properly, a Poisson model with robust error variance was used as an approximation (9). To construct the multivariable models, Pearson's correlation coefficients were first calculated to identify measures that appeared to assess similar constructs (potential collinearity). Then, based on the relative risk estimate and the associated *P* value for each variable mutually adjusted for other measures in the same category, a subset (2 or 3) of measures from each category was selected for the multivariable analysis. The selection criteria were based on significant associations both in terms of *P* value (<0.05) and magnitude of the point estimate of the odds ratio (e.g., >1.20). Furthermore, subjective knowledge was used to select measures likely to represent different underlying constructs. All demographic and socioeconomic status variables, length of membership, and provider affiliated medical center were always included in the multivariable analysis. Women's health-related medical history was considered for only young women (aged 18–26 years) because these conditions were either rare or very infrequently identified in adolescent girls when diagnosis codes were used.

Using the method described above, we selected the following measures from each subject characteristic category to build the final multivariable model: all demographic variables, provider specialty and gender, primary care provider visits, hospitalizations, emergency room visits, history of influenza vaccination, history of asthma/allergy (combined), and drug allergy. In addition, for young women, obstetric history, history of STDs, and Pap smear screening were included.

Because there is no regular or prespecified health care encounter for females in these age groups, initiation of HPV4 may be highly related to visiting a physician for other health reasons. To further understand the potential mechanisms affecting vaccine initiation beyond having a vaccination opportunity, we conducted a secondary analysis restricted to those who visited a primary care physician/obstetrician/gynecologist during the assessment period. Factors associated with visiting a primary care provider/obstetrician/gynecologist during the assessment period were examined before building these multivariable models. All analyses were conducted by using SAS statistical software, version 9 (SAS Institute, Inc., Cary, North Carolina).

RESULTS

A total of 285,265 females aged 9–26 years were enrolled in the health plan from October 2006 to March 2008 (179,580 adolescent girls and 105,685 young women). During this assessment period, 37% of the adolescent girls and 16% of the young women initiated the course of HPV vaccine. The percentages that initiated the HPV vaccine, by yearly age, are shown in Figure 1. The distribution of demographics and other characteristics, by HPV4 initiation status, as well as the crude associations with HPV4 initiation stratified by age, are shown in Table 1. In the crude analyses, most immune-related conditions (except rheumatoid conditions) and women's health-related conditions (except obstetric history) were positively associated with HPV4 initiation.

Multivariable results

Adolescent girls (aged 9–17 years). In the multivariable model for adolescent girls, older age, Hispanic ethnicity, having a pediatrician as a primary care provider, primary care provider office visit, emergency room visit, and history of drug allergy were positively correlated with vaccine initiation (Table 2). Medi-Cal status and history of influenza

Table 1. Distribution of Demographics, Provider Characteristics, Health Care Utilization, and Medical History Among Female HPV4 Vaccine Recipients and Nonrecipients, Kaiser Permanente Southern California, October 2006[a]

	Age 9–17 Years							Age 18–26 Years						
	Vaccine Recipients (n = 67,297)[b,c]		Vaccine Nonrecipients (n = 112,283)[b,c]		RR	95% CI	P Value[d]	Vaccine Recipients (n = 16,607)[b,c]		Vaccine Nonrecipients (n = 89,078)[b,c]		RR	95% CI	P Value[d]
	No.	%	No.	%				No.	%	No.	%			
Demographics														
Age, years[e]														
9–10/18	6,432	9.6	29,325	26.1	0.45	0.44, 0.47	<0.01	3,124	18.8	10,305	11.6	Referent		
11–12/19–20	15,365	22.8	23,392	20.8	Referent			4,869	29.3	20,432	22.9	0.83	0.80, 0.86	<0.01
13–14/21–22	19,215	28.6	22,520	20.1	1.16	1.14, 1.18	<0.01	3,703	22.3	17,946	20.1	0.74	0.70, 0.77	<0.01
15–16/23–24	19,808	29.4	24,693	22	1.12	1.10, 1.14	<0.01	3,216	19.4	17,716	19.9	0.66	0.63, 0.69	<0.01
17/25–26	6,477	9.6	12,353	11	0.87	0.85, 0.89	<0.01	1,695	10.2	22,679	25.5	0.30	0.28, 0.32	<0.01
Race/ethnicity														
White	12,758	19	19,310	17.2	Referent			4,296	25.9	17,925	20.1	Referent		
Black	5,366	8	9,299	8.3	0.92	0.90, 0.94	<0.01	1,115	6.7	6,930	7.8	0.72	0.67, 0.76	<0.01
Hispanic	33,394	49.6	49,647	44.2	1.01	0.99, 1.03	0.18	5,585	33.6	36,013	40.4	0.69	0.67, 0.72	<0.01
Asian	3,765	5.6	6,518	5.8	0.92	0.89, 0.95	<0.01	1,178	7.1	6,215	7	0.82	0.78, 0.87	<0.01
Other/unknown	12,014	17.9	27,509	24.5	0.76	0.75, 0.78	<0.01	4,433	26.7	21,995	24.7	0.87	0.84, 0.90	<0.01
Length of health plan membership, years (mean (SD))	4.7 (4.42)		4.3 (4.10)		1.01	1.01, 1.01	<0.01	4.7 (5.63)		3.6 (4.78)		1.03	1.03, 1.03	<0.01
US Census tract educational level (mean (SD))[f]	70.8 (20.42)		71.9 (19.75)		0.99	0.99, 1.00	<0.01	76.9 (18.86)		72.4 (19.89)		1.08	1.07, 1.09	<0.01
US Census tract household income, $ (mean (SD))[g]	58,224.3 (26,894.18)		57,584.7 (25,828.16)		1.01	1.01, 1.01	<0.01	63,835.9 (29,216.39)		56,788.6 (25,784.33)		1.04	1.04, 1.05	<0.01
Medi-Cal[h] enrollee	7,703	11.4	9,178	8.2	1.26	1.24, 1.28	<0.01	369	2.2	2,585	2.9	0.91	0.82, 1.00	0.05
Primary care provider characteristics														
Specialty														
Family medicine	8,161	12.5	16,879	16.4	0.73	0.71, 0.74	<0.01	11,438	70.7	56,437	69.6	1.16	1.11, 1.22	<0.01
Internal medicine	498	0.8	812	0.8	0.73	0.68, 0.78	<0.01	2,849	17.6	17,232	21.2	1.03	0.97, 1.09	0.35
Other	1,599	2.4	2,526	2.5	0.97	0.93, 1.01	0.13	237	1.5	1,349	1.7	0.96	0.85, 1.09	0.51
Pediatrics	55,260	84.3	82,680	80.4	Referent			1,654	10.2	6,106	7.5	Referent		
Age, years (mean (SD))	45.1 (9.4)		45.1 (9.5)		1.00	1.00, 1.00	0.01	40.9 (8.5)		41.0 (8.6)		0.99	0.99, 1.00	<0.01
Gender: male	22,328	33.7	40,119	39.9	0.89	0.87, 0.90	<0.01	5,638	35.1	32,540	41.8	0.83	0.80, 0.85	<0.01

Health care utilization in 2 years (mean (SD))														
No. of outpatient visits	6.7 (7.97)		4.8 (6.68)		1.01	1.01, 1.01	<0.01	9.9 (11.45)		8.7 (10.91)		1.01	1.01, 1.01	<0.01
No. of primary care provider visits	4.2 (4.09)		3.1 (3.64)		1.02	1.02, 1.02	<0.01	6.1 (6.30)		5.7 (6.71)		1.01	1.01, 1.01	<0.01
No. of hospitalizations	0.0 (0.32)		0.0 (0.31)		0.97	0.95, 0.99	<0.01	0.1 (0.39)		0.2 (0.56)		0.79	0.75, 0.82	<0.01
No. of emergency room visits	0.2 (0.67)		0.2 (0.57)		1.04	1.04, 1.05	<0.01	0.4 (1.02)		0.4 (1.16)		1.00	0.99, 1.01	0.92
No. of out-of-plan visits	0.2 (1.20)		0.2 (1.26)		1.00	0.99, 1.00	0.56	0.3 (1.54)		0.3 (1.64)		1.00	0.99, 1.01	0.60
Influenza vaccination	10,439	15.5	10,885	9.7	1.36	1.34, 1.38	<0.01	2,122	12.8	7,242	8.1	1.49	1.43, 1.55	<0.01
Women's health-related medical history														
Obstetric history								1,869	11.3	20,100	22.6	0.59	0.56, 0.62	<0.01
Sexually transmitted diseases								428	2.6	2,041	2.3	1.24	1.14, 1.35	<0.01
Pap screening								9,115	54.9	46,729	52.5	1.38	1.34, 1.42	<0.01
Abnormal Pap results								1,536	9.2	7,868	8.8	1.21	1.16, 1.27	<0.01
Use of oral contraceptive pills/patches								8,191	49.3	37,005	41.5	1.50	1.46, 1.54	<0.01
Immune-related medical conditions														
Rheumatologic conditions	32	0.05	37	0.03	1.18	0.92, 1.50	0.20	11	0.1	93	0.1	0.73	0.42, 1.26	0.26
Asthma	3,914	5.8	4,786	4.3	1.22	1.19, 1.25	<0.01	732	4.4	2,862	3.2	1.22	1.14, 1.30	<0.01
Allergies	3,298	4.9	3,866	3.4	1.24	1.21, 1.27	<0.01	905	5.4	3,239	3.6	1.37	1.29, 1.45	<0.01
Drug allergies/ adverse reaction	7,344	10.9	9,260	8.2	1.16	1.14, 1.19	<0.01	3,204	19.3	13,943	15.7	1.22	1.18, 1.27	<0.01
Infections	1,388	2.1	2,109	1.9	1.08	1.04, 1.13	<0.01	1,404	8.5	6,390	7.2	1.22	1.16, 1.28	<0.01
No. of antibiotic prescriptions (mean (SD))	0.8 (1.4)		0.6 (1.2)		1.03	1.02, 1.03	<0.01	1.5 (2.1)		1.1 (1.8)		1.06	1.06, 1.07	<0.01

Abbreviations: CI, confidence interval; HPV, human papillomavirus; Pap, Papanicolaou; RR, relative risk; SD, standard deviation.

[a] For all demographic characteristics and length of health plan membership, crude relative risks are given; for primary care provider characteristics, health care utilization, health-related medical history, and other medical history, relative risks were adjusted for age, race/ethnicity, and length of health plan membership.

[b] Data columns represent number and percent except where otherwise indicated.

[c] Percentages may not add to 100% because of missing values.

[d] *P* value from chi-square test or *t* test.

[e] The first value(s) applies to the age category 9–17 years; the second applies to the category 18–26 years.

[f] Percentage of adults with a high school diploma in the census tract where the subject resided; relative risks for neighborhood educational level are for a 10% increase in the percentage of adults with a high school diploma in the census tract.

[g] Median household income in the census tract where the subject resided; relative risks for neighborhood income level are for a $10,000 increase in median census tract household income.

[h] Medi-Cal refers to California's Medicaid health care program.

Table 2. Relative Risks[a] for Vaccination From Multivariable Log-Normal Regression, by Age Group, Kaiser Permanente Southern California, October 2006–March 2008

	Adolescent Girls Aged 9–17 Years			Young Women Aged 18–26 Years			Subanalysis of Younger Girls Aged 9–12 Years		
	RR[b]	95% CI	*P* Value	RR[b]	95% CI	*P* Value	RR[b]	95% CI	*P* Value
Demographics									
Age, years[c]									
9–10/18	0.45	0.44, 0.46	<0.01	Referent			0.45	0.43, 0.46	<0.01
11–12/19–20	1			0.81	0.78, 0.84	<0.01	Referent		
13–14/21–22	1.17	1.15, 1.18	<0.01	0.72	0.69, 0.76	<0.01			
15–16/23–24	1.14	1.12, 1.16	<0.01	0.67	0.64, 0.71	<0.01			
17/25–26	0.94	0.91, 0.96	<0.01	0.31	0.29, 0.33	<0.01			
Race/ethnicity									
White	Referent			Referent			Referent		
Black	0.93	0.90, 0.95	<0.01	0.82	0.77, 0.88	<0.01	0.99	0.94, 1.04	0.66
Hispanic	1.04	1.03, 1.06	<0.01	0.95	0.91, 0.99	0.01	1.11	1.07, 1.14	<0.01
Asian	0.93	0.91, 0.96	<0.01	0.95	0.90, 1.01	0.12	0.97	0.92, 1.02	0.24
Other/unknown	0.87	0.85, 0.89	<0.01	0.95	0.92, 0.99	<0.01	0.90	0.86, 0.94	<0.01
US Census tract educational level[d]	0.99	0.98, 0.99	<0.01	1.03	1.02, 1.04	<0.01	0.97	0.96, 0.98	<0.01
US Census tract household income[e]	1.02	1.01, 1.02	<0.01	1.03	1.02, 1.03	<0.01	1.01	1.01, 1.02	<0.01
Medi-Cal enrollee[f]	1.19	1.17, 1.21	<0.01	1.02	0.92, 1.12	0.74	1.20	1.16, 1.24	<0.01
Primary care provider characteristics									
Specialty									
Pediatrics	Referent			Referent			Referent		
Family medicine	0.81	0.79, 0.83	<0.01	1.06	1.01, 1.11	0.01	0.82	0.78, 0.86	<0.01
Internal medicine	0.93	0.87, 1.00	0.04	0.91	0.86, 0.97	<0.01	0.64	0.33, 1.25	0.19
Other	1.10	1.04, 1.15	<0.01	0.91	0.81, 1.03	0.14	1.10	0.99, 1.21	0.07
Gender									
Female	Referent			Referent			Referent		
Male	0.92	0.91, 0.93	<0.01	0.84	0.81, 0.86	<0.01	0.96	0.94, 0.98	<0.01
Health care utilization									
Primary care provider visit (per visit)	1.03	1.03, 1.03	<0.01	1.02	1.02, 1.02	<0.01	1.03	1.02, 1.03	<0.01
Hospitalization (per visit)	0.86	0.83, 0.89	<0.01	0.83	0.79, 0.88	<0.01	0.88	0.83, 0.93	<0.01
Emergency department visit (per visit)	1.01	1.00, 1.02	<0.01	0.97	0.96, 0.99	<0.01	1.01	0.99, 1.02	0.57
Influenza vaccination	1.20	1.18, 1.22	<0.01	1.34	1.28, 1.39	<0.01	1.22	1.19, 1.26	<0.01
Women's health-related medical history									
Sexually transmitted diseases				1.13	1.04, 1.24	<0.01			
Pap test				1.25	1.21, 1.30	<0.01			
Obstetric history				0.53	0.50, 0.56	<0.01			
Immune-related medical conditions									
Asthma or allergy	1.01	0.99, 1.03	0.55	1.05	1.01, 1.10	0.01	1.00	0.97, 1.04	0.91
Drug allergy	1.05	1.03, 1.07	<0.01	1.07	1.04, 1.10	<0.01	1.04	1.00, 1.08	0.03

Abbreviations: CI, confidence interval; Pap, Papanicolaou; RR, relative risk.
[a] The multivariable model was also adjusted for provider medical center and girls'/women's length of health plan membership (relative risks not shown).
[b] A relative risk of >1 suggests a greater chance of vaccination compared with the reference group.
[c] The first value(s) applies to the age category 9–17 years; the second applies to the category 18–26 years.
[d] Relative risks for neighborhood educational level are for a 10% increase in the percentage of adults with a high school diploma in the census tract where the subject resided.
[e] Relative risks for neighborhood income level are for a $10,000 increase in median census tract household income in the census tract where the subject resided.
[f] Medi-Cal refers to California's Medicaid health care program.

vaccination were strongly associated with higher likelihood of HPV4 initiation (relative risk (RR) = 1.19, 95% confidence interval (CI): 1.17, 1.21 and RR = 1.20, 95% CI: 1.18, 1.22, respectively). Neighborhood income and educational level were also associated with vaccine initiation, although the magnitude of associations for both variables was small (RR = 1.02 per $10,000 increase in median household income and 0.99 per 10% increase in adults with a high school diploma). On the other hand, black race and Asian race (RR = 0.93, 95% CI: 0.90, 0.95 and RR = 0.93, 95% CI: 0.91, 0.96, respectively), having a male primary care provider (RR = 0.92, 95% CI: 0.91, 0.93), and number of hospitalizations (RR = 0.86, 95% CI: 0.83, 0.89 per hospitalization) were inversely associated with HPV4 initiation. However, Asian race was not associated with HPV4 initiation when multiple imputation for race/ethnicity was used. With multiple imputation, the relative risk estimates for black, Hispanic, Asian, and other race were 0.94 (95% CI: 0.91, 0.97), 1.08 (95% CI: 1.06, 1.11), 0.98 (95% CI: 0.95, 1.02), and 1.02 (95% CI: 0.96, 1.08), respectively.

Younger girls (aged 9–12 years). Results for younger girls aged 9–12 years were mostly similar to those for adolescent girls. Hispanic ethnicity was slightly more strongly associated with higher HPV4 uptake in this age group (RR = 1.11, 95% CI: 1.07, 1.14; Table 2, right).

Young women (aged 18–26 years). In the multivariable model for young women, younger age, high neighborhood income and educational level, primary care provider office visit, history of STDs, Pap screening, and history of asthma/allergy and drug allergy were positive correlates of HPV4 initiation (Table 2, middle). History of influenza vaccination was strongly associated with HPV4 initiation (RR = 1.34, 95% CI: 1.28, 1.39). Medi-Cal status was not associated with vaccination. On the other hand, those of black race and those with histories of hospitalizations and emergency room visits were less likely to initiate the vaccine. The multiple imputation method provided consistent findings on race/ethnicity (RR = 0.84, 95% CI: 0.79, 0.89 for blacks; RR = 0.94, 95% CI: 0.91, 0.99 for Hispanics; RR = 0.96, 95% CI: 0.90, 1.02 for Asians; and RR = 0.99, 95% CI: 0.89, 1.10 for other races).

Correlates for HPV4 uptake among those who had an opportunity for vaccination. Racial/ethnic minority status (i.e., black, Hispanic, and Asian) and neighborhood indicators for lower income, but not Medi-Cal status, were inversely associated with visiting a primary care provider/obstetrician/gynecologist. Older age, all types of health care utilization, and all medical histories of interest (i.e., women's health-related and immune-related conditions) were positively associated with visiting a primary care provider/obstetrician/gynecologist. In the multivariable analyses restricted to those with an opportunity visit for vaccination, associations were consistent with those observed in the nonrestricted analyses (Table 3).

DISCUSSION

In this study based on the early postlicensure experience of HPV vaccination in a managed care organization, we found that certain racial/ethnic minorities, lower neighborhood income level, having a male primary care provider, and history of hospitalizations were correlates of lower likelihood of HPV4 initiation. On the other hand, enrollment in state-subsidized programs (Medi-Cal), having a pediatrician as a primary care provider, history of influenza vaccination, and several women's health-related and immune-related conditions were positive predictors for HPV4 initiation. Importantly, these associations could not be explained by the absence or presence of a physician visit (i.e., vaccination opportunity) during the assessment period.

Reports based on the National Immunization Survey-Teen and the California Health Interview Survey suggest that 1 in 4 adolescent girls aged 13–17 years initiated the HPV vaccine in 2007 nationwide and in California, respectively (10, 11). Although our study covered an 18-month period, we calculated the rate of initiation for girls aged 13–17 years in a 12-month period (October 2006–September 2007). This rate was 32%, suggesting somewhat higher HPV vaccine uptake in adolescent girls who were Kaiser Permanente Southern California members than among the general population in California.

Demographics

Our results suggest that the HPV4 vaccine was more likely to be administered to older adolescents than to young girls. This finding was consistent with previous reports on providers' intent for vaccination, which suggested that providers were more likely to recommend HPV vaccination (or any STD vaccine) to older adolescents (12–15). Young black women appeared to be at the greatest risk of underutilizing the HPV4 vaccine compared with their white counterparts. Hispanic ethnicity showed different associations with HPV4 initiation by age group. Although Hispanic girls were more likely to receive the vaccine at the younger age (9–12 years), young women of Hispanic ethnicity were slightly less likely than whites to receive the vaccine. The results for Asian adolescent girls appeared to be somewhat sensitive to the imputation method used (RR = 0.93, 95% CI: 0.91, 0.96 by algorithm vs. RR = 0.98, 95% CI: 0.95, 1.02 by multiple imputation). However, both estimates suggested that if there is a true association between Asian race and HPV4 uptake, its magnitude would likely be small. A previous study reported that black, Hispanic, and white women had similar HPV vaccine acceptability. It is therefore unclear whether the difference observed in our study was due to access to care, cultural attitude toward HPV/cervical cancer/vaccination, and/or physician-patient communication. All of these explanations are plausible. More studies are needed to understand whether there is a racial disparity in HPV vaccination.

Lower neighborhood income level was adversely linked to vaccine initiation, but only to a small magnitude. Some may be due to the presumably equal access in a prepaid managed-care setting. Interestingly, higher neighborhood educational level was inversely linked to vaccine uptake in adolescent girls. This inverse association was slightly stronger for younger girls aged 9–12 years. A study examining mothers' intent to vaccinate their daughters found that

Table 3. Relative Risks[a] for Vaccination Among Those Who Visited a Primary Care Provider or Obstetrician/Gynecologist, Kaiser Permanente Southern California, October 2006–March 2008

	Adolescent Girls Aged 9–17 Years			Young Women Aged 18–26 Years			Subanalysis of Younger Girls Aged 9–12 Years		
	RR[b]	95% CI	*P* Value	RR[b]	95% CI	*P* Value	RR[b]	95% CI	*P* Value
Demographics									
Age, years[c]									
9–10/18	0.45	0.44, 0.46	<0.01	Referent			0.45	0.43, 0.46	<0.01
11–12/19–20	Referent			0.82	0.78, 0.84	<0.01	Referent		
13–14/21–22	1.17	1.15, 1.18	<0.01	0.72	0.69, 0.76	<0.01			
15–16/23–24	1.14	1.12, 1.16	<0.01	0.67	0.64, 0.71	<0.01			
17/25–26	0.94	0.91, 0.96	<0.01	0.31	0.29, 0.33	<0.01			
Race/ethnicity									
White	Referent			Referent			Referent		
Black	0.93	0.90, 0.95	<0.01	0.82	0.77, 0.88	<0.01	0.97	0.92, 1.03	0.34
Hispanic	1.04	1.03, 1.06	<0.01	0.95	0.91, 0.99	0.01	1.09	1.06, 1.13	<0.01
Asian	0.93	0.91, 0.96	<0.01	0.95	0.90, 1.01	0.12	0.98	0.93, 1.04	0.56
Other/unknown	0.87	0.85, 0.89	<0.01	0.95	0.92, 0.99	<0.01	0.91	0.87, 0.95	<0.01
Census tract educational level[d]	0.99	0.98, 0.99	<0.01	1.03	1.02, 1.03	<0.01	0.97	0.96, 0.98	<0.01
Census tract household income[e]	1.02	1.01, 1.02	<0.01	1.03	1.02, 1.03	<0.01	1.01	1.00, 1.02	<0.01
Medi-Cal enrollee[f]	1.19	1.19, 1.21	<0.01	1.02	0.92, 1.12	0.74	1.18	1.14, 1.22	<0.01
Provider characteristics									
Specialty									
Pediatrics	Referent			Referent			Referent		
Family medicine	0.81	0.79, 0.83	<0.01	1.06	1.01, 1.11	0.03	0.84	0.79, 0.88	<0.01
Internal medicine	0.93	0.87, 1.00	0.04	0.91	0.86, 0.97	<0.01	0.57	0.24, 1.34	0.20
Other	1.10	1.04, 1.15	<0.01	0.91	0.81, 1.03	0.14	1.13	1.02, 1.25	0.02
Gender									
Female	Referent			Referent			Referent		
Male	0.92	0.91, 0.93	<0.01	0.84	0.81, 0.86	<0.01	0.96	0.94, 0.98	<0.01
Health care utilization									
Primary care provider visit (per visit)	1.03	1.03, 1.03	<0.01	1.02	1.02, 1.02	<0.01	1.02	1.02, 1.03	<0.01
Hospitalization (per visit)	0.86	0.83, 0.89	<0.01	0.83	0.79, 0.88	<0.01	0.90	0.85, 0.95	<0.01
Emergency department visit (per visit)	1.01	1.00, 1.02	<0.01	0.97	0.96, 0.99	<0.01	1.00	0.98, 1.02	0.91
Influenza vaccination	1.20	1.18, 1.22	<0.01	1.34	1.28, 1.39	<0.01	1.21	1.18, 1.25	<0.01
Women's health-related medical history									
Sexually transmitted diseases				1.13	1.04, 1.24	<0.01			
Pap test				1.25	1.21, 1.30	<0.01			
Obstetric history				0.53	0.50, 0.56	<0.01			
Immune-related medical conditions									
Asthma and/or allergy	1.01	0.99, 1.03	0.55	1.07	1.02, 1.13	<0.01	1.00	0.97, 1.04	0.82
Drug allergies/ adverse reaction	1.05	1.03, 1.07	<0.01	1.07	1.04, 1.11	<0.01	1.03	0.99, 1.07	0.10

Abbreviations: CI, confidence interval; Pap, Papanicolaou; RR, relative risk.
[a] The multivariable model was also adjusted for provider medical center and girls'/women's length of health plan membership (relative risks not shown).
[b] A relative risk of >1 suggests a greater chance of vaccination compared with the reference group.
[c] The first value(s) applies to the age category 9–17 years; the second applies to the category 18–26 years.
[d] Relative risks for neighborhood educational level are for a 10% increase in the percentage of adults with a high school diploma in the census tract where the subject resided.
[e] Relative risks for neighborhood income level are for a $10,000 increase in median census tract household income in the census tract where the subject resided.
[f] Medi-Cal refers to California's Medicaid health care program.

mothers who had less than a high school degree were more likely to favor their daughters receiving the HPV vaccine (16). It is therefore possible that parental acceptability of HPV vaccine may be higher among parents with lower educational levels, independent of income level. On the other hand, higher neighborhood educational level was associated with higher vaccine initiation in young women. These contrasting findings may be explained by the role of parental decision in adolescents' vaccination.

Provider characteristics

Adolescent girls with a pediatrician primary care provider were more likely to receive the vaccine than patients of family or internal medicine physicians. This observation may reflect different patterns of integration of HPV vaccine into clinical practice by different specialties. Interestingly, male primary care providers appeared less likely than female primary care providers to prescribe HPV4 vaccination. This finding was particularly the case for young women (RR = 0.84, 95% CI: 0.82, 0.97 for having a male primary care provider). Riedesel et al. (15) conducted a national survey of family physicians and found that female providers were more likely than male providers to recommend the HPV vaccine (15). Our observations were consistent with this finding. However, alternative explanations other than physician attitude are also plausible. For example, patients' and providers' comfort level in communicating about HPV transmission and HPV vaccine could also play a role in a patient's decision making about vaccination. For adolescent girls, our previous findings suggested that the mother's attitude about preventive measures was a predictor for her daughter's HPV4 uptake (17). Parental attitude, likely to affect both the choice of health care provider gender and HPV vaccination for their adolescent daughter, may also possibly explain the inverse association seen. These results suggest that the impacts of providers' attitudes about implementation of a HPV vaccination program deserve further study.

Health care utilization

Those with higher historical levels of health care utilization, specifically primary care visits, were more likely to initiate HPV4 vaccination. This finding was true for even those who had at least one vaccination opportunity (i.e., a primary care provider/obstetrician/gynecologist visit) during the assessment period. It is possible that more frequent interactions between providers, parents, and patients facilitate the decision to vaccinate. Hospitalizations were inversely associated with HPV4 initiation, however. This observation could be due to the fact that hospitalized patients may have been overwhelmed by their medical conditions and were less likely to attend to their other preventive care needs (18). Emergency room visits were not strongly related to HPV4 uptake in adolescent girls and were negatively associated with HPV4 uptake in young women. Again, young women who attend emergency rooms more frequently might be sicker and hence less attentive than their healthier peers to preventive care.

History of influenza vaccination was one of the strongest predictors for uptake of HPV vaccine in both age groups. This result suggests that subjects initiating HPV4 vaccination also tend to utilize other preventive measures. Our previous study found that a mother's Pap screening behavior, an indicator for her attitude about prevention, was consistently associated with HPV4 uptake in her adolescent daughters (17). These findings together support the notion that women's attitudes about preventive measures may play an important role in decision making about HPV vaccination.

Women's health-related medical history

Women with an obstetric history were significantly less likely to initiate HPV4. The results for Pap screening, STDs, and contraceptive use in general indicate that young women who were sexually active otherwise were more likely to receive the vaccine. However, more specific data on women's sexual history are needed to help interpret these results. It is also somewhat reassuring that those at increased risk of repeated/new HPV infections (i.e., those with a history of STDs) did not seem to be at risk of undervaccination, although only diagnosed STDs were assessed in this study.

Immune-related medical history

Those who had the selected immune-related conditions were not less likely to receive the vaccine. These findings on immune-related conditions have implications for the generalizability of ongoing studies of postlicensure safety surveillance for the HPV4 vaccine. Autoimmune conditions are particular outcomes of interest regarding safety surveillance for the vaccine. If girls/women prone to these outcomes were refusing the vaccines, the findings from the safety surveillance study may not be readily generalizable to those at higher baseline risk. Our findings suggest that subjects who might be at greater risk of immune-related adverse outcomes (19, 20) were not underrepresented among vaccine recipients in this early experience of HPV vaccination, which should provide some reassurance about the generalizability of the vaccine safety surveillance study in this regard.

There are several potential limitations to consider when interpreting the results of this study. First, race/ethnicity data were lacking for approximately 50% of the subjects. To address this issue, we implemented a previously validated, highly predictive imputation algorithm for race/ethnicity, which reduced the missing data issue to about 20% of the subjects. However, this imputation approach likely led to underestimated variance and confidence intervals. Rubin's multiple imputation method (7) provided additional insight into the appropriate confidence intervals, yielding generally similar findings on race/ethnicity despite the small shift in the point estimate for Asian adolescent girls. Our results were also similar to those obtained without any imputation for race/ethnicity. We combined race and ethnicity into one variable because of our imputation algorithm, which did not enable us to examine the association for Hispanic ethnicity separately from race. Therefore, further examination of the association between race/ethnicity and vaccine uptake is warranted.

Second, several limitations are associated with the use of electronic records. For example, information on sexual behaviors (e.g., whether the women have been sexually active) was not available to help interpret the results of women's health-related medical history. Therefore, many of our results should be interpreted as hypothesis generating rather than hypothesis testing. Furthermore, health care delivered outside Kaiser Permanente Southern California facilities, such as in free STD clinics and Planned Parenthood clinics, would not be captured. It is possible that teenagers seeking oral contraceptives or STD treatment may visit those free service clinics rather than their primary care physicians, resulting in some degree of misclassification. Girls/young women might also have access to the vaccine in other health care settings such as university health care centers. Although the magnitude of misclassification regarding vaccine uptake is unclear, it is likely that most members would choose to receive the vaccine at Kaiser Permanente Southern California because vaccination is covered at no additional charge for them.

Lastly, because of the large sample size, there may be associations that are statistically significant but not clinically meaningful in magnitude. Hence, our discussion has focused on associations likely to be of clinical and public health interest. Also note that generalizability of these results outside Kaiser Permanente Southern California managed care settings needs to be further assessed. For example, socioeconomic status might have a more profound impact on HPV4 uptake among underinsured and/or unemployed populations.

Despite these potential limitations, our study has several important strengths, including a population-based study design that minimized selection bias, use of electronic medical records that avoided recall bias, the measure of vaccine uptake behavior rather than intent to vaccinate, and a large sample size of 285,265 females. To conclude, we found that certain racial/ethnic minorities (particularly blacks), those who reside in neighborhoods with a lower average income, those with a male or nonpediatrician primary care provider, and those with histories of several hospitalizations were less likely to initiate HPV4. Those with a history of STDs or immune-related conditions were not less likely to have received the vaccine, suggesting no concern about underrepresentation of these groups among current vaccine recipients. This information should prove helpful in developing HPV immunization programs in managed care organizations because the safety profile and long-term efficacy of the HPV vaccine are continuing to be evaluated. Specifically, focus groups can be conducted and education materials can be developed tailored to subgroups underutilizing the vaccine and to enhance physician communication about HPV vaccination.

ACKNOWLEDGMENTS

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This work was supported by a research grant from Merck & Co, Inc. (EPI08014.036.02). C. Chao, J. M. Slezak, and S. J. Jacobsen received research funding from Merck & Co., Inc. to work on this study and a related study.

S. J. Jacobsen has been an unpaid consultant for Merck & Co., Inc. C. Velicer is an employee of Merck & Co., Inc.

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