

Quadrivalent Human Papillomavirus Vaccine Uptake in Adolescent Boys and Maternal Utilization of Preventive Care and History of Sexually Transmitted Infections

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In October 2009, the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (CDC) recommended that quadrivalent human papillomavirus vaccine (HPV4) may be given to males aged 9 to 26 years at the discretion of the patient's health care provider (permissive use) to reduce the likelihood of acquiring genital warts (*condyloma acuminata*).¹ However, uptake among eligible males was low following this recommendation for permissive use, with only an estimated 2% of male adolescents initiating the vaccine.² As the national data indicated that uptake among females remained suboptimal for a few years following the recommendation for routine vaccination in females,³ human papillomavirus (HPV) vaccination of males offers an opportunity to achieve herd immunity in the whole population. On the basis of these considerations and the clinical trial data indicating HPV4's high efficacy for prevention of genital warts and grade 2 or 3 anal intraepithelial neoplasia (AIN2/3, a precursor of anal cancer) in males, in October 2011, the ACIP recommended routine use of HPV4 in boys aged 11 or 12 years. The ACIP also recommended vaccination with HPV4 for males aged 13 through 21 years who have not been vaccinated previously or who have not completed the 3-dose series; men aged 22 through 26 years may be vaccinated.⁴

Parents are involved in deciding whether their adolescent children get vaccinated regardless of whether the vaccine is recommended for routine use, because parental consent is typically required for adolescent HPV vaccination.^{5,6} Previous experience with HPV vaccination in female adolescents suggests that the decision to vaccinate their children with HPV vaccines is often affected by parents' knowledge about HPV infection, attitudes toward the

Objectives. We examined whether maternal utilization of preventive care and history of sexually transmitted infections (STIs) predicted quadrivalent human papillomavirus vaccine (HPV4) uptake among adolescent boys 1 year following the recommendation for permissive use of HPV4 for males.

Methods. We linked maternal information with electronic health records of 254 489 boys aged 9 to 17 years who enrolled in Kaiser Permanente Southern California health plan from October 21, 2009, through December 21, 2010. We used multivariable Poisson regression with robust error variance to examine whether HPV4 initiation was associated with maternal uptake of influenza vaccine, Papanicolaou (Pap) screening, and history of STIs.

Results. We identified a modest but statistically significant association between initiation of HPV4 series and maternal receipt of influenza vaccine (rate ratio [RR] = 1.16; 95% confidence interval [CI] = 1.07, 1.26) and Pap screening (RR = 1.13; 95% CI = 1.01, 1.26). Boys whose mothers had a history of genital warts were more likely to initiate HPV4 (RR = 1.47; 95% CI = 0.93, 2.34), although the association did not reach statistical significance ($P = .1$).

Conclusions. Maternal utilization of preventive care and history of genital warts may influence HPV4 uptake among adolescent boys. The important role of maternal health characteristics and health behaviors needs be considered in intervention efforts to increase vaccine uptake among boys. (*Am J Public Health.* 2013;103:e63–e68. doi:10.2105/AJPH.2013.301495)

vaccine, and parental history of sexually transmitted infections (STIs) or HPV-related disease.^{7,8} In a previous study, we found that mothers' Papanicolaou (Pap) screening behavior was associated with their daughters' uptake of HPV4 in an insured population.⁹ Therefore, we hypothesized that previous maternal utilization of Pap screening might reflect a positive attitude toward prevention of HPV infection. In addition, mothers with a history of STIs, especially genital warts, might be familiar with preventive measures for HPV infection, which might influence their decision to vaccinate their children with HPV4 vaccine. We hypothesized that this influence might be even more important for HPV4 uptake among adolescent boys when the vaccine was initially recommended for permissive use among males in the United States.

In this study, we sought to determine whether initiation of HPV4 in a large cohort of insured boys aged 9 to 17 years was associated with maternal utilization of preventive care and history of STIs during the time period when the vaccine was indicated for permissive use in males.

METHODS

We identified eligible boys through electronic membership records available at Kaiser Permanente Southern California (KPSC) health plan, the largest managed care organization in southern California. As of 2012, KPSC serves more than 3.5 million racially/ethnically diverse members (37% White, 40% Hispanic, 10% African American, 10% Asian/Pacific Islander, and 3% other races). Members of

KPSC are broadly representative of the socioeconomic diversity of the southern California census population.¹⁰ All child and adolescent members of KPSC are fully covered for the cost of childhood vaccines. Following the licensure among males, eligible KPSC male members can receive HPV4 at a physician visit with a small copayment or at a nurse visit without a copayment.

We identified 297 703 boys aged 9 to 17 years who were enrolled in the KPSC health plan during the study inclusion period (October 21, 2009–December 21, 2010) and had no record of HPV4 vaccination prior to October 21, 2009. Kaiser Permanente members may apply for health care coverage for their immediate family members (i.e., spouse, domestic partner, and children). Each boy who enrolled in a family health plan as a “child” was linked to a potential mother through a validated algorithm to identify a female member who (1) enrolled in the same family health plan; (2) was listed as the plan subscriber, spouse, or domestic partner in the family health plan; and (3) was 13 to 60 years older than the boy (to rule out potential sisters and grandmothers). We were able to establish a total of 254 489 (85.5%) mother–son pairs through health plan records that were included in the analyses. We excluded 43 214 boys whose maternal information could not be linked through health plan records from the analyses.

We monitored the boys from the time they entered the study (i.e., baseline: at membership enrollment, 9th birthday, or October 21, 2009, whichever came last) until HPV4 initiation, membership disenrollment, 18th birthday, or December 21, 2010, whichever came first. We defined HPV4 recipients as boys who received their first dose of HPV4 between October 21, 2009 and December 21, 2010.

Data Collection

We defined maternal preventive care utilization as maternal influenza vaccination (general preventive care) up to 1 year prior to baseline or Pap screening (HPV-specific preventive care) up to 3 years prior to baseline. We obtained influenza vaccination records of the mothers and boys up to 1 year prior to baseline and the HPV4 vaccination records of the boys during the follow-up period from the Kaiser Immunization Tracking System,

which contains health plan members’ unique medical record numbers and detailed immunization history. We ascertained maternal history of Pap screening and test results up to 3 years prior to baseline through the electronic database of laboratory procedures. Using codes from the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)*,¹¹ we identified maternal history of genital warts and other selected STIs (including syphilis, gonorrhea, chlamydia, genital herpes, and trichomoniasis) any time prior to baseline from diagnoses recorded at any outpatient or inpatient medical encounter.

We obtained the age, race/ethnicity, and spoken language of the mothers and boys and the marriage status of the mothers through the membership files. We identified the specialty of each boy’s primary care physician through the KPSC provider database. To obtain neighborhood education and median income levels as a proxy for the family’s socioeconomic status (SES), we mapped the home address to US census block groups. We also used enrollment in a Medicaid program as a proxy for SES.

Statistical Analyses

We compared distribution of the boys’ demographic and SES variables by HPV4 initiation status. We used the unpaired *t* test (for continuous variables; e.g., age) and the χ^2 test (for categorical variables) to compare the distribution of baseline characteristics of the boys included in analyses and those who were excluded, and between vaccine recipients and nonrecipients. We used multivariable Poisson regression with robust error variance to estimate the association between boys’ initiation of HPV4 series and maternal history of Pap test, STIs, and influenza vaccination, with adjustment for mothers’ and boys’ demographic variables (age at baseline, race/ethnicity, preferred spoken language), duration of boys’ health plan membership, boys’ influenza vaccination status, boys’ primary care physician specialty, families’ SES proxy, and maternal marital status. We examined all the main predictors of interest and covariates in the same multivariable regression model. To assess the association between maternal abnormal Pap result and initiation of HPV4 series, we conducted a separate multivariable analysis among a subgroup of boys whose mothers had at least

1 Pap test up to 3 years prior to baseline. Because some boys were from the same family and linked to the same mother, we further adjusted for family cluster effects in all multivariable analyses using generalized estimating equations.

RESULTS

We compared the demographic characteristics of the 254 489 boys included in the analyses with those of the 43 214 boys (14.5%) excluded from the analyses. Compared with those excluded from the analyses because their mothers’ information could not be identified through health plan records, the boys who were included were more likely to be non-Hispanic White and less likely to be Hispanic. A greater proportion of the included boys resided in neighborhoods with higher levels of income and educational attainment; they were less likely to be enrolled in a Medicaid program and had been enrolled in the health plan for a significantly longer period prior to baseline (Table 1).

Among the boys included in the analyses, 4055 (1.6%) initiated HPV4 between October 21, 2009, and December 21, 2010. Table 2 shows the vaccine initiation by the baseline characteristics of the boys and mothers. Uptake was higher among boys who were Hispanic, who had a pediatrician as primary care physician, who resided in neighborhoods with lower levels of income and educational attainment, and who had been enrolled in a Medicaid program prior to baseline. Compared with nonrecipients, vaccine recipients were slightly older (average age = 13.7 vs 12.8 years) and had longer membership at baseline (7.9 years vs 7.3 years). The initiation rate was higher among boys whose mothers had received influenza vaccine within the year prior to baseline (2.0% vs 1.5%). More mothers of HPV4 recipients received Pap screening within 3 years prior to baseline than did the mothers of nonrecipients (78.2% vs 76.3%), although the proportion with abnormal Pap results did not differ significantly (18.6% vs 17.4%). Most of the mothers (97.2%) had no history of STIs. There was no substantial difference in prevalence of recorded history of genital warts and other selected STIs between mothers of HPV4 recipients and those of nonrecipients.

TABLE 1—Comparison of Baseline Characteristics of Boys Included in and Excluded From the Study Sample: Kaiser Permanente Southern California, October 21, 2009–December 21, 2010

	Included (n = 254 489), Mean \pm SD or No. (%)	Excluded (n = 43 214), Mean \pm SD or No. (%)	Total (n = 297 703), Mean \pm SD or No. (%)
Age,* y	12.8 \pm 2.7	12.7 \pm 2.7	12.8 \pm 2.7
Race/ethnicity*			
Non-Hispanic White	43 272 (17.0)	3843 (8.9)	47 115 (15.8)
Non-Hispanic Black	17 934 (7.0)	3472 (8.0)	21 406 (7.2)
Hispanic	116 146 (45.6)	24 235 (56.1)	140 381 (47.2)
Asian/Pacific Islander	15 267 (6.0)	2041 (4.7)	17 308 (5.8)
Other/unknown	61 870 (24.3)	9623 (22.2)	71 493 (24.0)
Ever enrolled in Medicaid programs*			
Yes	37 725 (14.8)	29 348 (67.9)	67 073 (22.5)
No	216 729 (85.2)	13 861 (32.1)	230 590 (77.5)
Neighborhood median annual income, ^{a,*} \$			
Missing	13 152 (5.2)	7132 (16.5)	20 284 (6.8)
< 25 000	6197 (2.4)	1552 (3.6)	7749 (2.6)
25 000–39 999	37 059 (14.6)	8056 (18.6)	45 115 (15.2)
40 000–59 999	71 672 (28.2)	13 048 (30.2)	84 720 (28.5)
60 000–79 999	61 070 (24.0)	8077 (18.7)	69 147 (23.2)
\geq 80 000	65 339 (25.7)	5349 (12.4)	70 688 (23.7)
Neighborhood education level ^{a,*}			
Missing	13 152 (5.2)	7132 (16.5)	20 284 (6.8)
\geq 75% of adults had high school diploma	129 413 (50.9)	14 248 (33.0)	143 661 (48.3)
50%–74% of adults had high school diploma	72 903 (28.6)	13 362 (30.9)	86 265 (29.0)
< 50% of adults had high school diploma	39 021 (15.3)	8472 (19.6)	47 493 (16.0)
Membership in KPSC,* y	7.3 \pm 4.9	3.3 \pm 3.7	6.7 \pm 4.9

Note. KPSC = Kaiser Permanente Southern California. Percentages may not add up to 100% because of missing data or rounding.

^aCensus block data.

* $P < .01$.

In multivariable analyses (Table 3), we observed a modest association between the likelihood of initiation of HPV4 series and maternal history of influenza vaccination (rate ratio [RR] = 1.16; 95% confidence interval [CI] = 1.07, 1.26; $P < .001$) and Pap test (RR = 1.13; 95% CI = 1.01, 1.26; $P = .03$) after adjustment for demographics of mothers and boys, family SES proxy, boys' primary care physician specialty, influenza vaccination status and membership length of boys, and maternal marital status. Maternal history of diagnosed genital warts appeared to be associated with initiation of HPV4 series (RR = 1.47; 95% CI = 0.93, 2.34; $P = .1$). However, maternal history of other STIs was not predictive of initiation of HPV4 series (RR = 1.00; 95% CI = 0.80, 1.24; $P = .97$). Among a subgroup of 194 205 boys whose mothers had received at least 1 Pap screening up to 3 years prior to

baseline, we observed a modest association between maternal history of an abnormal Pap test result and HPV4 initiation (RR = 1.09; 95% CI = 0.99, 1.20; $P = .09$; Table 3). The positive association between maternal history of influenza vaccination and initiation of HPV4 series remained statistically significant (RR = 1.16; 95% CI = 1.06, 1.27; $P = .001$) in the subgroup analysis.

DISCUSSION

We found that over 1 year after the national recommendation of permissive use for males, only 1.6% of adolescent boys aged 9 to 17 years enrolled in KPSC had initiated HPV4 vaccine. This figure was noticeably lower than the 37% of girls in KPSC of the same age group who had initiated HPV vaccine 18 months after its licensure.¹² The uptake rate observed

in this insured population is similar to the coverage rate in a national sample of adolescent boys aged 13 to 17 years in 2010 (1.4%), based on the National Immunization Survey-Teen data.¹³

The recommendation for permissive use could have discouraged health care providers and parents from vaccinating adolescent boys. The cost of the vaccine was also perceived as a barrier to HPV4 uptake as some private health insurance plans did not cover the cost of the vaccine because the recommendation was for permissive (rather than routine) use. A postlicensure survey among a national sample of mothers with sons aged 9 to 18 years identified cost of the vaccine as a barrier to HPV vaccine acceptability, and reported that 47% of the mothers were willing to vaccinate their sons if the vaccine were free.¹⁴ Therefore, it was projected that a recommendation of

TABLE 2—Quadrivalent Human Papillomavirus Vaccine (HPV4) Initiation Status by Baseline Characteristics of Boys and Their Mothers: Kaiser Permanente Southern California, October 21, 2009–December 21, 2010

Baseline Characteristics	Boys With HPV4 Initiation, No. (%) ^a	Total Eligible Boys, No. (%) ^b
Total	4055 (1.6)	254 489 (100)
	Boys	
Race/ethnicity		
Non-Hispanic White	610 (1.4)	43 272 (17.0)
Non-Hispanic Black	277 (1.5)	17 934 (7.0)
Hispanic	2224 (1.9)	116 146 (45.6)
Asian/Pacific Islander	228 (1.5)	15 267 (6.0)
Other/unknown	716 (1.2)	61 870 (24.3)
Preferred spoken language		
English	3112 (1.5)	203 124 (79.8)
Spanish	879 (2.3)	38 629 (15.2)
Other	64 (0.5)	12 736 (5.0)
Ever enrolled in Medicaid programs		
Yes	797 (2.1)	37 725 (14.8)
No	3258 (1.5)	216 729 (85.2)
Neighborhood median annual income, ^c \$		
< 25 000	147 (2.4)	6 197 (2.4)
25 000–39 999	744 (2.0)	37 059 (14.6)
40 000–59 999	1233 (1.7)	71 672 (28.2)
60 000–79 999	880 (1.4)	61 070 (24.0)
≥ 80 000	899 (1.4)	65 339 (25.7)
Neighborhood education level ^c		
≥ 75% of adults had high school diploma	1845 (1.4)	129 413 (50.9)
50%–74% of adults had high school diploma	1229 (1.7)	72 903 (28.6)
< 50% of adults had high school diploma	829 (2.1)	39 021 (15.3)
Influenza vaccination in prior year	1408 (2.2)	62 660 (24.6)
	Mothers	
Race/ethnicity		
Non-Hispanic White	758 (1.4)	55 686 (21.9)
Non-Hispanic Black	289 (1.3)	21 757 (8.5)
Hispanic	2208 (1.9)	117 839 (46.3)
Asian/Pacific Islander	316 (1.5)	21 335 (8.4)
Other/unknown	484 (1.3)	37 872 (14.9)
Preferred spoken language		
English	2721 (1.5)	187 548 (73.7)
Spanish	949 (2.2)	42 675 (16.8)
Other	47 (1.6)	2915 (1.1)
Marital status		
Married, domestic partner, or common law	2532 (1.3)	199 418 (78.4)
Divorced, separated, or widowed	202 (2.3)	8952 (3.5)
Single	626 (1.6)	39 912 (15.7)
Other or unknown	695 (11.2)	6207 (2.4)
Influenza vaccination in prior year	1040 (2.0)	52 191 (20.5)

^aThe data represent the number of HPV4 recipients and the initiation rate in each subgroup (percentage of eligible boys in subgroup who initiated the vaccine).

^bThe data represent the total number and percentage of eligible boys within major group. The percentages may not add up to 100% because of missing data or rounding.

^cCensus block data.

routine vaccination would remove the cost barrier and increase the coverage of HPV4 among males. However, the health plan members in this study were eligible for HPV4 without out-of-pocket cost except for a small copay for a provider visit, and vaccines can be given at no-cost nurse visits, which would even further minimize the impact of cost on vaccine uptake. Our findings suggest that factors other than the cost of vaccine played a role in parents' decision-making about their sons' HPV4 vaccination.

We identified a modest association between initiation of HPV4 series and maternal preventive care utilization indicated by influenza vaccination and Pap screening. This finding is consistent with our hypothesis that mothers who utilized preventive care may be more likely to have their sons vaccinated with HPV4. It is also consistent with the results in our earlier study among girls in the same age group during the year after HPV4 was approved for routine vaccination for females. However, the influence of maternal receipt of Pap test on initiation of HPV4 series appeared to be relatively weaker among boys than among girls (odds ratio = 1.14 vs 1.48, respectively).⁹ Previous studies have suggested that parents and health care providers are more likely to favor vaccination for females than for males.^{15,16} There was also a significant discrepancy between parents' general support of male HPV4 vaccination and their intention to have their own sons vaccinated.⁶

We observed that initiation of HPV4 series was positively associated with maternal history of genital warts. Although the association was not statistically significant, an ad hoc power calculation suggested that we may not have had adequate power to detect a significant association (power was 51% for RR = 1.5) because of the very small number of mothers with genital warts in this study population. We also observed a modest association between maternal history of abnormal Pap test results and initiation of HPV4 series. Although we did not directly measure knowledge and acceptance of vaccine among mothers, it is plausible to assume that mothers with a history of genital warts may have increased awareness of HPV and acceptance of the HPV vaccine. Our findings are in agreement with the results from previous studies that suggested that intention to vaccinate children is often tied to maternal

TABLE 3—Associations Between Boys' Initiation of Quadrivalent Human Papillomavirus Vaccine (HPV4) and Selected Maternal Characteristics: Kaiser Permanente Southern California, October 21, 2009–December 21, 2010

Maternal Characteristics	No. of Boys With HPV4 Initiation (%) ^a	Adjusted Rate Ratio ^b (95% CI)
Received influenza vaccine ^c		
No	3015 (1.5)	1.00 (Ref)
Yes	1040 (2.0)	1.16 (1.07, 1.26)
Received Pap screening ^d		
No	883 (1.5)	1.00 (Ref)
Yes	3172 (1.6)	1.13 (1.01, 1.26)
Abnormal Pap result ^e		
No	2581 (1.6)	1.00 (Ref)
Yes	591 (1.8)	1.09 (0.99, 1.20)
History of STIs ^f		
No history of STIs	3937 (1.6)	1.00 (Ref)
History of genital warts	23 (2.3)	1.47 (0.93, 2.34)
History of other STIs	95 (1.6)	1.00 (0.80, 1.24)

Note. CI = confidence interval; Pap = Papanicolaou; STI = sexually transmitted infection.

^aThe percentage represents the HPV4 initiation rate among each subgroup.

^bThe multivariable model controlled for boys' age, race/ethnicity, spoken language, membership length, influenza vaccination status in the year prior to baseline, primary care provider specialty, enrollment status in Medicaid programs, and neighborhood education and median annual household income levels, as well as maternal age, race/ethnicity, spoken language, and marital status.

^cMother received influenza vaccine within a year prior to baseline.

^dMother received at least 1 Pap screening up to 3 years prior to baseline.

^eAnalysis was restricted to 194 205 boys whose mothers had at least 1 Pap screening up to 3 years prior to baseline.

^fMother had a clinical diagnosis of genital warts or other STIs (including syphilis, gonorrhea, chlamydia, genital herpes, and trichomoniasis) recorded in medical records some time prior to baseline.

perceived risk and history of STIs¹⁷ and that women who have had an HPV-associated infection are more likely to accept HPV vaccine.¹⁸

Several limitations should be considered when interpreting our findings. We were not able to identify the mothers of all eligible boys in our sample. Boys included in the analyses were more likely to have a higher SES than excluded boys. The racial/ethnic distribution of boys included in the analyses was also different from that of excluded boys. This potential selection bias because of unavailability of data might have affected the generalizability of our findings. However, the HPV4 initiation rates among the included and excluded boys were similar (1.63% for all eligible boys and 1.60% for the included boys). Given that we were able to include 85% of all eligible boys and that there were a large number of boys in each racial/ethnic and SES group included in the analyses, the difference in racial/ethnic and SES distribution between the included and excluded boys is unlikely to have fully accounted for the observed association

between maternal factors and boys' HPV4 uptake. Another limitation is that we used census data as a proxy for family SES, which may not accurately reflect the actual individual SES. In addition, information on some variables such as maternal history of STIs may be incomplete if the mothers experienced STIs prior to their enrollment in KPSC health plan. Some variables that previous studies have reported as having a strong association with HPV vaccine uptake, such as doctor's recommendation, were not measured in this study.

Despite these limitations, this study had a number of strengths, including use of a large electronic medical record system to ascertain immunization records, which minimized recall bias inherent in most observational studies that rely on self-reported data. The availability of longitudinal health records allowed us to efficiently assess association between maternal history of STIs and Pap test results with sons' HPV4 uptake among a large racially/ethnically diverse population. In addition, it is important to examine correlates for the actual uptake

of HPV4 among adolescent boys rather than those for acceptability and willingness to vaccinate, since previous studies suggest that intent does not always lead to behavior.¹⁹

Our findings suggest that maternal utilization of general and HPV-specific preventive care and history of genital warts may influence uptake of HPV4 among adolescent boys. The identified association underscores the importance of targeting maternal health behaviors toward preventive care in enhancing HPV4 uptake in adolescent boys. Further investigations are needed to examine uptake and its correlates after the recent ACIP recommendation for routine use of HPV4 among adolescent boys. ■

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Contributors

R. C. Hechter and S. J. Jacobsen both led the study conceptualization and design. R. C. Hechter supervised the data collection and analyses and wrote the initial draft of the article. C. Chao, L. S. Sy, B. K. Ackerson, and J. M. Slezak assisted with analysis plan and edited the drafts. M. A. Sidell performed data collection and analyses. All authors contributed substantially to the interpretation of data and critical review, assisted in editing and revising drafts, and approved the final version of the article.

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Human Participant Protection

The study protocol was reviewed and approved by the Kaiser Permanente Southern California institutional review board, with a waiver of requirement for informed consent.

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