Predictors of Human Papillomavirus Vaccine Follow-Through Among Privately Insured US Patients

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Objectives. To assess predictors of timely human papillomavirus (HPV) vaccine follow-through among privately insured individuals initiating the 3-dose series.

Methods. Using MarketScan Commercial claims data, we identified 1 332 217 privately insured US individuals aged 9 to 26 years who initiated the bivalent or quadrivalent HPV vaccine series from 2006 to 2014, with follow-up data extending through 2015. The study outcome was receipt of third HPV dose within 12 months of the first, compared by year of initiation. Control variables were age, region, insurance plan type, provider type, and seasonal influenza vaccination.

Results. Timely HPV vaccine follow-through fell over time. The trend was especially pronounced for females (from 67% in 2006 to 38% in 2014), but was also present for males (from 36% in 2011 to 33% in 2014). Similar patterns were present when we controlled for patient and provider characteristics or used alternative definitions of follow-through. Other positive predictors of timely follow-through included receipt of flu vaccine in the prior year and receipt of first HPV vaccine dose from an obstetrician/gynecologist.

Conclusions. HPV vaccine follow-through is low and has declined over time. (*Am J Public Health.* 2018;108:946–950. doi:10.2105/AJPH.2018.304408)

See also Pratt, p. 853.

Persistent infection with the human papillomavirus (HPV) causes virtually all cervical cancers and the majority of anal, penile, and oropharyngeal cancers.[1] In 2006, the US Food and Drug Administration approved the quadrivalent HPV vaccine.[2] It was a breakthrough in cancer prevention, with the original vaccine protecting against 4 strains and the version currently available in the United States protecting against 9 strains of the cancer-causing virus.[1] The US Advisory Committee on Immunization Practices (ACIP) first recommended the vaccine for routine provision to girls in 2006 and expanded this recommendation to boys in 2011.[3,4] Despite recommendations, vaccine uptake has been lower than expected, with the 2016 National Immunization Survey Teen (NIS–Teen) estimating only 32% of boys and 43% of girls aged 13 to 17 years have received the full 3-dose series.[5] Previous estimates suggest that only 69% of adolescent girls and 58% of adolescent boys who initiated HPV vaccine completed all 3 doses,[6] a measure sometimes called "follow-through."[7]

To increase the number of fully vaccinated individuals, it is important to understand both how to increase vaccine series initiation and how to improve timely follow-through. Although HPV vaccine initiation is increasing for both males and females, the NIS–Teen suggests that overall follow-through rates for girls have been largely stagnant whereas rates for boys have increased over time.[6] Limited evidence on timely follow-through, defined as vaccine series completion within 1 year of initiation, suggests this decreased among females in the early years following vaccine introduction (2006–2009).[8,9] A study examining timely follow-through in males found that the transition from permissive to routine vaccination did not affect follow-through for this population.[10]

Predictors of timely follow-through also remain unclear. Findings vary among national samples of privately insured individuals, with early studies showing higher follow-through rates among those aged 9 to 12 years[9,11] and studies of more recent data showing that follow-through is higher among older individuals.[12,13] These studies also find associations by insurance plan type and region of residence, with some variation between studies in the patterns of these regional differences.[9,12] Chou et al. found that patients receiving their first vaccine from a gynecologist had higher follow-through than those who saw a pediatrician[14]; another study using data from a managed care organization found that family medicine providers were associated with the highest follow-through rates[15]; a third study found no difference by provider type.[16] Many of these potential differences among males remain unexplored. For females, a more recent evaluation of these associations is needed.

To better target future programs for increasing HPV vaccination, it is important to understand whether previously observed trends in timely follow-through have

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continued. Furthermore, identifying patient and provider characteristics associated with timely follow-through may point to areas for targeted intervention. To address these research gaps, we used MarketScan, a large administrative claims database for privately insured individuals and their dependents, to examine changes in HPV vaccine follow-through over time, as well as predictors of timely HPV vaccination receipt by gender.

METHODS

The Truven Health Analytics MarketScan Commercial Claims and Encounters database includes administrative claims for more than 50 million privately insured individuals and their dependents living in the United States. Using outpatient and pharmacy claims from 2006 to 2014, we identified individuals aged 9 to 26 years who had received at least 1 dose of HPV vaccine, as indicated by a Current Procedural Terminology Code or National Drug Code (n = 3 534 828; Figure A, available as a supplement to the online version of this article at http://www.ajph.org). Initial HPV doses were primarily quadrivalent vaccines, with bivalent HPV vaccines making up less than 1% of all doses. Almost none were nonavalent HPV vaccine doses because this vaccine was not introduced in the United States until 2015. For individuals whose follow-up period extended to 2015, identification of follow-through doses included all 3 HPV vaccines. To ensure a reasonably complete vaccination history, we excluded individuals who were not continuously enrolled in their health plans for 12 months prior to and following their first recorded HPV vaccine dose (n = 2 092 362). Analyses also excluded individuals missing data on provider type for their first HPV vaccine doses (4% of sample; n = 54 795) and those who were missing values for any covariates (3% of sample; n = 41 676). Finally, because the Advisory Committee on Immunization Practices gave a permissive recommendation of HPV vaccination for males in 2009, but recommended routine administration starting only in 2011,[4] we excluded males who initiated the vaccine series prior to 2011 (1% of sample; n = 13 778).

Measures

Outcome. The study outcome was receipt of 3 doses of HPV vaccine within 12 months of initiation.

Covariates. We identified patient age, region (i.e., Northeast, West, North Central, South), and insurance plan type at the time of the individual's first HPV vaccination. Insurance plan types included preferred provider organization, health maintenance organization (HMO), consumer-directed or high-deductible health plan, and other. We also identified whether the patient had received a seasonal influenza vaccine in the year prior to HPV vaccination as an indicator of prior preventive service use.

Using codes on the vaccination claim, we categorized the type and specialty of the provider who delivered the first HPV vaccine dose as follows: physician-family medicine, physician-obstetrics/gynecology, physician-pediatrics (nonspecialty), and midlevel provider (including nurse practitioner, physician assistant, and nursing services). Lastly, "other provider" included multispecialty physician groups, internal medicine physicians, medical doctors without other classification, and a number of other specialties; each of these groups made up 5% or less of total vaccines administered.

Data Analysis

Given differences in vaccination recommendations by gender, we report cohort characteristics and other findings separately by gender. We report the study outcome first as an unadjusted percentage of individuals completing 3 doses of HPV vaccine within 1 year of their first dose. We examined bivariate regressions for each covariate of interest to assess the unadjusted effect of these factors. We then used multivariate logistic regression to predict the adjusted probability of vaccine follow-through by year, while holding all other covariates constant. We obtained confidence intervals through 100 bootstrapped replications of the model using recycled prediction, with significance assessed using a Wald test.

We performed 2 sensitivity analyses to examine the robustness of these findings. To understand the impact of restricting follow-up time to 1 year, we repeated analyses of 3-dose follow-through with follow-up time extended to 18 months following HPV vaccine initiation. To examine whether follow-through patterns differ for 2 and 3 doses, we report on receipt of a second dose of HPV vaccine within 12 months of initiation. We performed analyses using SAS version 9.4 (SAS Institute, Cary, NC) with 2-tailed tests and a critical α of 0.05.

RESULTS

We identified 1 332 217 individuals aged 9 to 26 years who had received at least 1 dose of HPV vaccine between 2006 and 2014 and met all inclusion criteria. Of those with a first HPV vaccine dose, 70% of females and 62% of males received a second HPV vaccine dose within 1 year of initiation; 45% of females and 35% of males received all 3 doses within 1 year (Table 1). Providers most likely to administer the first HPV vaccine dose were pediatricians (48% of females, 67% of males) and family physicians (20% of females, 15% of males). For females, obstetricians/gynecologists (OB/GYNs) delivered 12% of initial HPV vaccine doses.

Females initiating the vaccine in 2006 had high rates of follow-through (66.8%), which declined sharply each year in 2007 (59.0%), 2008 (50.8%), and 2009 (42.1%) in unadjusted analyses (Table 2). This decline slowed, but continued, after 2010, reaching a low of 38.2% in 2014. For males, the decline over time was smaller, with follow-through at 36.1% in 2011 and 33.1% by 2014.

Females who received their first HPV vaccine dose from OB/GYNs were more likely to receive 3 doses within 1 year than were those seeing a pediatrician (54.7% vs 44.3%, $P < .001$; Table 2). Females initiating with midlevel providers were least likely to follow through (41.4%). Similarly, males who received their first HPV vaccine dose from a midlevel provider were less likely to receive the full series than were males who saw a pediatrician (31.3% vs 36.1%, $P < .001$).

For both males and females, receipt of a flu vaccine in the previous year was associated with higher HPV vaccine follow-through, and living in the South or West was associated with lower follow-through (Table 2). Insurance plan type was associated with HPV vaccine follow-through, with

TABLE 1—Characteristics of Age-Eligible, Privately Insured Persons Initiating Human Papillomavirus (HPV) Vaccine, by Gender: United States, 2006–2014

Characteristic	Females (n = 937 555), % (No.)	Males (n = 394 662), % (No.)
Received 3 HPV vaccine doses	45 (425 689)	35 (139 870)
Received 2 HPV vaccine doses	70 (659 351)	62 (244 571)
Year of initiation		
2006	2 (17 960)	. . .
2007	18 (172 489)	. . .
2008	12 (114 602)	. . .
2009	11 (100 601)	. . .
2010	8 (75 893)	. . .
2011	12 (116 448)	13 (52 728)
2012	12 (115 727)	29 (114 938)
2013	14 (128 752)	34 (132 829)
2014	10 (95 043)	24 (94 167)
Initiating provider		
Pediatrician	48 (448 386)	67 (263 955)
Family physician	20 (183 828)	15 (58 446)
Obstetrician/gynecologist	12 (111 949)	. . .
Midlevel provider	2 (20 255)	2 (6 049)
Other provider/unknown	18 (173 137)	17 (66 212)
Age at initiation, y		
9–10	2 (19 036)	1 (4 925)
11–12	25 (232 790)	25 (97 140)
13–17	39 (368 489)	47 (24 731)
18–26	33 (317 240)	27 (68 724)
Region		
Northeast	16 (154 941)	23 (98 303)
North Central	26 (247 987)	23 (96 945)
South	37 (342 802)	22 (95 343)
West	20 (191 825)	30 (127 420)
Insurance plan design		
PPO	60 (562 990)	58 (248 941)
HMO	18 (167 407)	17 (71 962)
CDHP	9 (81 813)	14 (57 708)
Other types	13 (125 345)	11 (47 909)
Seasonal influenza vaccine in previous year	15 (142 293)	24 (94 596)

Note. CDHP = consumer-directed health plan; HMO = health maintenance organization; PPO = preferred provider organization. Midlevel providers included nurse practitioners and physician assistants.

those in HMO plans less likely to follow through all 3 doses than were those in preferred provider organization plans (females, 42.4% vs 46.2%; males, 31.7% vs 36.3%; $P < .001$). For females, but not for males, those in high-deductible health plans were less likely to follow through than were those in preferred provider organizations (44.2% vs 46.2%, $P < .001$).

After adjustment for demographic characteristics, insurance plan type, and past year flu vaccination (Table 2), differences in follow-through rates over time widened, with a 30.3-percentage-point decline for females from 2006 to 2014 ($P < .001$) and a 3.6-percentage-point decline for males from 2011 to 2014 ($P < .001$). For females, the adjusted probability of follow-through remained highest for those who saw an OB/GYN (55.4%; 95% confidence interval [CI] = 54.7%, 56.1%) and lowest for those who saw a midlevel provider (42.3%; 95% CI = 41.0%, 43.5%). For males, follow-through remained highest for those seeing a pediatrician (35.8%; 95% CI = 35.4, 36.1) and lowest for those seeing a midlevel provider (31.9%; 95% CI = 30.2, 34.5).

Sensitivity analyses extending the follow-up for 3-dose HPV vaccine to receipt within 18 months yielded largely similar findings, although unadjusted follow-through rates appeared to stabilize for females after 2009, with around 50% of those who initiated the vaccine series completing over the 18-month follow-up (Table A, available as a supplement to the online version of this article at http://www.ajph.org). In sensitivity analyses of receipt of 2 doses within 1 year, the persistent decline remained, with 2-dose follow-through for females falling from 87.2% in 2006 to 67.5% in 2014 and 2-dose follow-through for males falling from 62.7% in 2011 to 59.0% in 2014 (Table B, available as a supplement to the online version of this article at http://www.ajph.org).

DISCUSSION

Increases in HPV vaccine initiation are well documented,[17] but researchers have paid little attention to changes in HPV vaccine series completion. Completion of the recommended 3 doses within 1 year declined sharply over time in our analysis of a large cohort of privately insured US individuals who initiated the HPV vaccine series. Adjusting for age, region, insurance type, administering physician, and prior flu vaccine only increased the magnitude of these differences. Our findings suggest that series completion merits a renewed focus by vaccination programs.

Two hypotheses may explain the declining follow-through in HPV vaccination. First, the characteristics of individuals initiating the vaccine may be changing in ways not captured in our study. Although not specific to the privately insured, studies describing US HPV vaccination patterns over time show that vaccine initiation has increased at a higher rate over time among racial/ethnic minorities and those of low socioeconomic status than among their majority or high–socioeconomic status counterparts.[18,19] As evidence also suggests that these groups are also less likely to follow through with all 3 vaccine doses,[20] this could be 1 source of the decline observed here.

TABLE 2—Correlates of Human Papillomavirus (HPV) Vaccine Follow-Through Within 1 Year (3 Doses): United States, 2006–2014

	Females (n = 937 555)		Males (n = 394 662)	
Characteristic	Unadjusted %	Adjusted % (95% CI)	Unadjusted %	Adjusted % (95% CI)
Year of initiation				
2006 (Ref)	66.8	67.2 (65.7, 68.7)	. . .	. . .
2007	59.0***	59.6*** (59.1, 60.1)	. . .	. . .
2008	50.8***	51.7*** (51.0, 52.4)	. . .	. . .
2009	42.1***	42.5*** (41.8, 43.1)	. . .	. . .
2010	40.1***	39.9*** (39.2, 40.6)	. . .	. . .
2011	40.0***	40.1*** (39.5, 40.7)	36.1	36.3 (35.7, 37.6)
2012	40.2***	40.2*** (39.6, 40.7)	36.6	36.9*** (36.2, 37.5)
2013	39.9***	39.0*** (38.5, 39.5)	35.9	35.7*** (35.1, 36.2)
2014	38.2***	36.9*** (36.2, 37.5)	33.1***	32.7*** (32.1, 33.4)
Initiating provider				
Pediatrician (Ref)	44.3	43.7 (43.4, 44.0)	36.1	35.8 (35.4, 36.1)
Family physician	44.1	44.9*** (44.4, 45.4)	33.8***	35.2*** (34.3, 36.1)
Obstetrician/gynecologist	54.7***	55.4*** (54.7, 56.1)	...	...
Midlevel provider	41.4***	42.3*** (41.0, 43.5)	31.3***	31.9*** (30.2, 34.5)
Other provider	44.1	44.2*** (43.7, 44.6)	34.5***	34.8*** (33.9, 35.6)
Age at initiation, y				
9–10 (Ref)	46.1	46.9 (45.5, 48.3)	37.1	36.8 (33.8, 39.8)
11–12	43.4***	46.7 (46.3, 47.1)	35.8	35.8*** (35.2, 36.4)
13–17	46.5	46.8 (46.5, 47.1)	36.8	36.6 (36.1, 37.1)
18–26	45.6	42.7*** (42.3, 43.1)	32.6***	33.1*** (32.5, 33.7)
Region				
Northeast (Ref)	49.6	50.9 (50.4, 51.4)	39.8	39.9 (39.2, 40.5)
North Central	49.2*	48.4*** (47.9, 48.8)	37.1***	36.6*** (35.9, 37.2)
South	44.6***	43.7*** (43.4, 44.1)	32.4***	32.3*** (31.6, 32.8)
West	38.4***	40.0*** (39.5, 40.5)	33.4***	34.1*** (33.3, 34.8)
Insurance plan design				
PPO (Ref)	46.2	46.0 (45.7, 46.3)	36.3	36.3 (35.9, 36.7)
HMO	42.4***	42.9*** (42.4, 43.4)	31.7***	32.2*** (31.3, 33.1)
CDHP	44.2***	47.7*** (47.0, 48.5)	36.6	36.9*** (36.1, 37.7)
Other types	46.7	44.4*** (43.8, 45.0)	35.1***	34.2*** (33.3, 35.1)
Seasonal influenza vaccine in previous year				
Yes (Ref)	53.1	55.0 (54.4, 55.6)	45.7	45.3 (44.5, 46.1)
No	44.0***	43.7*** (43.4, 43.9)	32.2***	32.3*** (32.0, 32.7)

Note. CDHP = consumer-directed health plan; CI = confidence interval; HMO = health maintenance organization; PPO = preferred provider organization. Adjusted estimates are average predicted probabilities adjusting for all other variables in the table. Midlevel providers included nurse practitioners and physician assistants.

*$P < .05$; **$P < .01$; ***$P < .001$.

Second, patient and provider perceptions of the importance of vaccine completion may be changing over time. Providers and patients may feel low urgency about timely completion of the HPV vaccine, which may result in delayed completion.[21–23] Although our data only extend through 2015, we acknowledge that providers may have anticipated the change to a 2-dose series that took place in 2016[24] and shifted their vaccination patterns preemptively. We find this unlikely to fully explain our results, however, as completion of 2 doses within 1 year also consistently declined in our study. Further examination of provider and patient perceptions of vaccine completion may help in understanding the drivers of low follow-through rates.

Updated US recommendations amended HPV vaccination doses and schedule for adolescents younger than 15 years.[24] Requiring 2 rather than 3 doses may result in an increase in series completion for those younger than 15 years. However, although it is tempting to use historical 2-dose data to speculate on what the magnitude of this change will be, the simultaneous changing of number of doses and timing of the second dose weakens the ability of prior vaccination patterns to project future trends.

Estimates of follow-through presented here (45% for females, 35% for males) are lower than commonly cited estimates of follow-through among vaccine initiators reported by the 2015 NIS–Teen (69% for females, 45% for males).[17] This difference is likely explained by our estimation of follow-through within 1 year rather than at any time, as done by NIS–Teen. Thus, for example, a youth aged 17 years in the NIS–Teen had 6 or more years to get the vaccine, which would lead to higher estimates than in our constrained 1-year follow-up. Sensitivity analysis extending the follow-up period to 18 months found that the early decline in completion stabilized after 2009; this suggests that follow-through may be increasingly delayed over time rather than decreasing altogether, but that even in a fairly long follow-up period, series completion is low.

It is also important to note that our sample included only privately insured individuals who were continuously insured for 1 year before and after their initial HPV vaccine dose. Therefore, the generalizability of the findings to Medicaid, uninsured, or transiently insured populations is not known. However, it is telling that timely follow-through rates are so low even within this relatively advantaged group.

In addition to changes over time, we found that receipt of the first HPV vaccine dose from an OB/GYN was associated with being more likely to receive the full series compared with initiating with any other provider type; however, the vast majority of HPV vaccinations are not initiated by OB/GYNs. For both males and females, follow-through was lowest among those initiating

HPV vaccines with nurse practitioners and physician assistants. HPV vaccine follow-through varied by patient age and region, which is consistent with previous findings.[12,13]

Limitations

Our study has several limitations worthy of mention. Although our analysis controlled for patient characteristics including age, receipt of flu vaccine, and insurance plan type, we did not have access to data on other potentially important patient characteristics. Further research should consider to what extent differences in HPV vaccine follow-through are attributable to patient factors, provider factors, system-level factors, or a combination of these. Our use of administrative claims included only vaccines obtained through insurance; patients paying out-of-pocket would not be observed. However, we anticipate that most individuals would use their insurance benefits for such transactions, particularly after the inclusion of HPV vaccines as a preventative service offered without cost sharing for patients with commercial insurance. Finally, our study used a retrospective cohort design, precluding strong inferences about causal effects among variables.

Conclusions

Low rates of HPV vaccine initiation and follow-through have left a generation of young people unnecessarily at risk for cancer, precancer, and other HPV-related sequelae. Although HPV vaccine initiation is improving over time, only 45% of females and 35% of males in our study completed the HPV series within 1 year of initiation. Furthermore, timely follow-through declined over time. Increasing follow-through will help to increase the number of fully protected individuals and is an important step to reaching the nation's goals for HPV vaccination. We found that vaccine follow-through was highest among patients initiating HPV vaccine through an OB/GYN and lowest among those initiating through a nurse practitioner or physician assistant. Patients in HMO insurance plans also had lower follow-through than did those with other insurance plan types. Programs seeking to improve vaccination should emphasize the importance of timely follow-through and should target the full range of providers who deliver HPV vaccines. AJPH

CONTRIBUTORS

J. C. Spencer led data analysis and writing and conceptualized the study. N. T. Brewer, J. G. Trogdon, and S. B. Wheeler made substantial contributions to the final analysis, interpretation of findings, and revision of the manuscript. S. B. Dusetzina supervised analysis and initial manuscript drafts and contributed to conceptualization of the study.

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HUMAN PARTICIPANT PROTECTION

Because this study used secondary, de-identified data, it was exempt from review by the University of North Carolina institutional review board.

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