Research Article

Cancer Epidemiology, Biomarkers & Prevention

# Predictors of Human Papillomavirus Vaccination in a Large Clinical Population of Males Aged 11 to 26 years in Maryland, 2012–2013

Megan A. Clarke[1], Francesca Coutinho[1], Darcy F. Phelan-Emrick[1], MaryAnn Wilbur[2], Betty Chou[2], and Corinne E. Joshu[1,3]

## Abstract

**Background:** Despite the recommendation for routine human papillomavirus (HPV) vaccination in males, coverage estimates remain low. We sought to identify predictors of receiving each HPV vaccine dose among a large clinical population of males.

**Methods:** We conducted a cross-sectional analysis of electronic medical records for 14,688 males ages 11 to 26 years attending 26 outpatient clinics (January 2012–April 2013) in Maryland to identify predictors of each HPV vaccine dose using multivariate logistic regression models with generalized estimating equations. All analyses were stratified in accordance with vaccine age recommendations: 11 to 12 years, 13 to 21 years, and 22 to 26 years. Analyses of predictors of receipt of subsequent HPV doses were also stratified by the number of clinic visits ($\leq$3 and >3).

**Results:** Approximately 15% of males initiated the HPV vaccine. Less than half of males eligible received the second and third doses, 49% and 47%, respectively. Non-Hispanic black males (vs. non-Hispanic white) ages 11 to 12 and 13 to 21 years and males with public insurance (vs. private) ages 13 to 21 years had significantly greater odds of vaccine initiation, but significantly decreased odds of receiving subsequent doses, respectively. Attendance to >3 clinic visits attenuated the inverse association between public insurance and receipt of subsequent doses.

**Conclusion:** Overall, rates of HPV vaccine initiation and of subsequent doses were low. While non-Hispanic black and publicly insured males were more likely to initiate the HPV vaccine, they were less likely to receive subsequent doses.

**Impact:** Tailoring different intervention strategies for increasing HPV vaccine initiation versus increasing rates of subsequent doses among males may be warranted. *Cancer Epidemiol Biomarkers Prev; 25(2); 351–8. ©2015 AACR.*



## Introduction

Vaccination against human papillomavirus (HPV) in males is substantially lower compared with other adolescent vaccines. As of 2014, approximately 42% of males ages 13 to 17 years in the United States initiated the HPV vaccine series, as compared with approximately 79% coverage for meningococcal conjugate and 88% coverage for tetanus, diphtheria, and pertussis (1). Completion rates for the HPV vaccine are even lower, with 21.6% of males receiving all three doses in 2014 (1). The HPV vaccine was originally licensed for males in 2009 (2). In October 2011, the Advisory Committee on Immunization Practices (ACIP) recommended routine HPV vaccination for males ages 11 to 12 years, with catch-up vaccination for males ages 13 to 21 years, and permissive vaccination up to 26 years of age (3). Although HPV vaccination coverage among US males has increased, more than half of the target population still remains unvaccinated.

The quadrivalent HPV vaccine (Gardasil, Merck and Co, Inc.) is administered as a 3-dose series, with the second and third doses administered at 2 and 6 months after the first dose, respectively (3). The vaccine protects against high-risk HPV types 16 and 18 and low-risk HPV types 6 and 11, and is most effective when administered prior to HPV exposure before sexual debut (4, 5). Persistent infection with HPV types 16 and 18 is causally associated with a significant proportion of anal, penile, and oropharyngeal cancers in males (6, 7) and cause up to 70% of cervical cancers in females (8). Infection with low-risk HPV types 6 and 11 is responsible for nearly all cases of genital warts (9–11).

Data on determinants of HPV vaccination among males are limited, but suggest a healthcare provider's recommendation as one of the most important predictors of HPV vaccine initiation (12). Additionally, rates of vaccine initiation are generally higher among non-Hispanic black and Hispanic males (vs. non-Hispanic whites) and among males living below the poverty level (vs. at or above the poverty level; refs. 1, 12, 13). Less is known about factors related to HPV vaccine completion among males; however, a few studies have shown that rates are lower among non-Hispanic black and Hispanic males and among uninsured/underinsured male adolescents (1, 12, 13). Frequent contact with the healthcare system has also been cited as an important predictor of completion, particularly among low-income and minority males (12, 14). Most of the evidence on predictors of HPV vaccine initiation and completion among males was generated before the ACIP recommendation in 2011 (15–18), with a majority of studies focusing on vaccine acceptability (14, 19–22). More recent studies, such as the National Immunization Survey-Teen (NIS-Teen), include

[1]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland. [2]Department of Gynecology and Obstetrics, Johns Hopkins University School of Medicine, Baltimore, Maryland. [3]Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, Maryland.

**Corresponding Author:** Megan A. Clarke, Johns Hopkins Bloomberg School of Public Health, 615 North Wolfe Street, Baltimore, MD 21205. Phone: 551-427-5020; Fax: 410-614-2632; E-mail: mclark43@jhu.edu

**doi:** 10.1158/1055-9965.EPI-15-0983

limited age ranges (13–17 years) and do not include males in the target age range (1, 13). To our knowledge, no recent studies have examined predictors of the second dose of the HPV vaccine, despite growing interest in reduced dosing schedules of the HPV vaccine series (23–25). To this end, the purpose of our study was to identify predictors of each dose of the HPV vaccine series among a large, clinical population of males ages 11 to 26 years after the ACIP recommendation, January 2012 through April 2013.

## Materials and Methods

### Study population

We evaluated electronic medical record (EMR) data from 15,996 males ages 11 to 26 years attending Johns Hopkins Community Physicians (JHCP) clinics from January 2012 through April 2013. JHCP is a university-affiliated practice comprised of 26 primary care outpatient sites in 11 counties in Maryland. Our study population was drawn from the Family Practice, Internal Medicine/Pediatrics (IM/Peds), Internal Medicine, and Pediatrics practice specialties at these facilities. Males who received an HPV vaccine dose outside of a JHCP clinic (coded as "historical" in the EMR; $n = 101$) and those who initiated the HPV vaccine series prior to the start of our study (vaccine dose 1 or 2 date was missing in the EMR but date for vaccine dose 2 or 3, respectively, was not missing; $n = 1{,}207$, 7.6%) were excluded. We created three analytic cohorts to evaluate HPV vaccine initiation, receipt of the second dose of the HPV vaccine, and HPV vaccine completion. Therefore, the analytic cohort for HPV vaccine initiation included 14,688 males who had not received an HPV vaccine dose as of 2012. Based on estimates from US census data, our study population included slightly more non-Hispanic black males and slightly fewer non-Hispanic white males (35.1% and 50.6%, respectively) compared with males of similar ages living in JHCP-affiliated counties in Maryland (27.0% and 59.5% on average, respectively. With respect to insurance status, the proportion of males in our study population (21.2%) was very similar to the average proportion of males with public insurance of similar ages living in JHCP-affiliated counties in Maryland (20.2%). Dates in the EMR data included only visit year (vs. month and year). As such, we could not determine whether males who initiated in 2013 ($n = 346$) or those who received the second dose in 2013 ($n = 202$) had enough time (i.e., 6 months) to complete the series; these males were excluded from the second dose and completion analytic cohorts, respectively. Thus, the analytic cohort for the second dose of the HPV vaccine included the 1,834 males who initiated the HPV vaccine in 2012, and the analytic cohort for the completion analysis included the 702 males who received the second dose in 2012. This study protocol was approved by the Johns Hopkins Medicine Institutional Review Board.

### HPV vaccination outcome definitions

Information on HPV vaccination status was available from the EMR. HPV vaccine "initiation" was defined as receipt of at least one dose of the HPV vaccine, the second dose was defined as receipt of two doses of the HPV vaccine, and HPV vaccine "completion" was defined as receipt of all three doses of the HPV vaccine series.

### Demographic and clinical predictors of HPV vaccination

Demographic and clinical characteristics were available from the EMR. We evaluated age at the first clinic visit during the study period (i.e., "baseline") as a continuous variable and also categorized baseline age according to the ACIP recommendations: 11 to 12 years (target age range for vaccination, "Target"), 13 to 21 years (catch-up age range for vaccination, "Catch-Up," and 22 to 26 years (permissive age for vaccination, "Permissive"). Race/ethnicity was self-identified in the registration files of the EMR and defined as non-Hispanic white, non-Hispanic black, Hispanic, Asian, or other race/ethnicity. Insurance was categorized as private, public, or military. The number of clinic visits during the study period was categorized as $\leq 3$ visits (the minimum number of visits required to complete the HPV vaccine series) vs. >3 visits. JHCP clinic location was defined as urban or suburban using US census data, and JHCP practice specialty was categorized as Family Practice, IM/Peds, Internal Medicine, or Pediatrics. Because males could visit more than one practice specialty type during the study period, we assigned each male the most common practice specialty observed. When we were unable to identify the most common practice specialty because a male attended an equal number of different specialties ($n = 602$, 3.8%), we used the practice specialty at the male's first visit. Among males who were vaccinated, agreement between the assigned practice specialty and the specialty associated with the vaccine visit was 95%.

### Statistical analysis

In this cross-sectional analysis, we calculated means and proportions for demographic and clinical predictors, using descriptive statistics with $t$ tests and Pearson $\chi^2$ tests to assess differences by uptake of each HPV vaccine dose. Multivariable logistic regression models using generalized estimating equations (GEE) were used to calculate adjusted odds ratios (aOR) and 95% confidence intervals of associations of demographic and clinical predictors with each HPV vaccine dose, accounting for clustering within JHCP clinics. All models were stratified by baseline age group and mutually adjusted for continuous baseline age, race/ethnicity, insurance type, number of clinic visits, JHCP clinic location, and JHCP practice specialty. Because additional clinic visits are required for receipt subsequent doses of the HPV vaccine, we conducted a subanalysis to explore whether the number of clinic visits modifies any potential association of race/ethnicity and insurance type with receipt of the second and third doses of the HPV vaccine, respectively. In this analysis, we focused on race/ethnicity and insurance because these factors are known to be differentially associated with healthcare utilization patterns (14). To increase statistical power and adequately test for interaction, we combined the target and catch-up age groups and re-categorized race/ethnicity as non-Hispanic white, non-Hispanic black, and other (Hispanic, Asian/Pacific Islander, and other race/ethnicity). We stratified our models by the number of clinic visits ($\leq 3$ and >3), and tested for statistical interaction using the Wald test. All analyses were conducted using Stata v.13.1 (StataCorp). All tests were two-sided and results were considered statistically significant if $P < 0.05$.

## Results

### HPV vaccine initiation

Of the 14,688 males eligible for the first dose of the HPV vaccine, a total of 2,180 (14.8%) initiated the series. The average baseline age of males eligible for the first dose of the HPV vaccine was $18.0 \pm 4.7$ years, and the majority were non-Hispanic white (50.6%; Table 1). More than half of all males were privately

**Table 1.** Demographic and clinical characteristics of males ages 11 to 26 years attending JHCP clinics from 2012 to 2013 by HPV vaccine dose eligibility

| | Vaccine dose eligibility | | |
|---|---|---|---|
| | **HPV vaccine initiation** | **HPV vaccine 2nd dose** | **HPV vaccine completion** |
| Total | 14,688 | 1,834 | 702 |
| Total vaccinated, *n* (%) | 2,180 (14.8) | 904 (49.1) | 331 (47.2) |
| Mean baseline age (SD) | 18.0 (4.7) | 14.9 (3.2) | 14.7 (3.2) |
| Age group, *n* (%) | | | |
| Target | 2,471 (16.8) | 493 (26.9) | 197 (28.1) |
| Catch-up | 8,011 (54.5) | 1,270 (69.2) | 472 (67.2) |
| Permissive | 4,206 (28.6) | 71 (3.9) | 33 (4.7) |
| Race/ethnicity, *n* (%) | | | |
| non-Hispanic White | 7,432 (50.6) | 585 (31.9) | 291 (41.4) |
| non-Hispanic Black | 5,163 (35.1) | 1,062 (57.9) | 328 (46.7) |
| Hispanic | 684 (4.7) | 66 (3.6) | 32 (4.6) |
| Asian | 454 (3.1) | 29 (1.6) | 13 (1.9) |
| Other | 955 (6.5) | 92 (5.0) | 38 (5.4) |
| Insurance type, *n* (%) | | | |
| Private | 8,688 (59.1) | 709 (38.7) | 310 (44.2) |
| Public | 3,114 (21.2) | 797 (43.5) | 226 (32.2) |
| Military | 2,494 (17.0) | 318 (17.3) | 162 (23.1) |
| Missing | 392 (2.7) | 10 (0.5) | 4 (0.5) |
| Number of clinic visits, *n* (%) | | | |
| 1–3 visits | 12,325 (83.9) | 1,296 (70.7) | 346 (49.3) |
| >3 visits | 2,363 (16.1) | 538 (29.3) | 356 (50.7) |
| JHCP clinic location, *n* (%) | | | |
| Suburban | 10,955 (74.6) | 939 (51.2) | 436 (61.1) |
| Urban | 3,730 (25.4) | 895 (48.8) | 266 (37.9) |
| JHCP practice specialty, *n* (%) | | | |
| Family practice | 5,643 (38.4) | 494 (26.9) | 230 (32.8) |
| IM/Peds | 1,021 (7.0) | 115 (6.3) | 41 (5.8) |
| Internal medicine | 3,553 (24.2) | 72 (3.9) | 29 (4.1) |
| Pediatrics | 4,471 (30.4) | 1,153 (62.9) | 402 (57.3) |

Abbreviation: IM/Peds, internal medicine/pediatrics.

insured and the majority attended $\leq$3 clinic visits during the study period (Table 1).

Multivariable aORs for HPV vaccine initiation by age group are shown in Table 2. In the target age group, non-Hispanic black males had 39% greater odds of initiating the HPV vaccine compared with non-Hispanic white males ($P = 0.02$); and males with public insurance had 45% greater odds of HPV vaccine initiation compared with males with private insurance ($P = 0.02$). Attending >3 clinic visits during the study period was associated with over a 2-fold increase in odds of HPV vaccine initiation compared with $\leq$3 visits during the study period ($P < 0.001$), and visiting a clinic in an urban location was associated with over a 3-fold increase in odds of HPV vaccine initiation compared with clinics in a suburban location ($P < 0.01$).

In the catch-up age group, similar to males in the target age group, non-Hispanic black race/ethnicity, public insurance, attending >3 clinic visits during the study period, and urban clinic location were significantly associated with increased odds of HPV vaccine initiation ($P < 0.01$, respectively). Additionally in the catch-up age group, older age at baseline was significantly associated with a 14% decrease in odds of HPV vaccine initiation ($P < 0.001$) and Internal Medicine practice specialty was significantly associated with a 73% decrease in odds of HPV vaccine initiation compared with Family Medicine practice specialty ($P < 0.001$).

Similar to males in both the target and catch-up age groups, non-Hispanic black race/ethnicity in the permissive age group and attending >3 clinic visits during the study period were significantly associated with increased odds of HPV vaccine initiation ($P < 0.001$, respectively). Like males in the catch-up age group, older age at baseline and Internal Medicine practice specialty were significantly associated with decreased odds of HPV vaccine initiation ($P = 0.05$ and $P = 0.02$, respectively). Additionally, in the permissive age group, males with military insurance had nearly two-and-a-half times the odds of initiating the HPV vaccine compared with males with private insurance ($P = 0.04$).

### Second dose of the HPV vaccine

Of the 1,834 eligible males (those who received their first HPV vaccine dose in 2012), a total of 904 (49.1%) received the second dose of the HPV vaccine. Males eligible for the second dose of the HPV vaccine tended to be younger, and a higher proportion were non-Hispanic black and privately insured compared with males eligible for initiation (Table 1).

Multivariable aORs for the second dose of the HPV vaccine by age group are shown in Table 3. Results for the permissive age group are not shown due to limited statistical power. In the target age group, non-Hispanic black males, Hispanic males, and males who identified as other race/ethnicity had 27%, 61%, and 74% decreased odds, respectively, of receiving the second dose of the HPV vaccine compared with non-Hispanic white males ($P \leq 0.05$, respectively). Attending >3 clinic visits during the study period was significantly associated with a 4-fold increase in odds of receiving the second dose compared with $\leq$3 visits ($P < 0.001$).

In the catch-up age group, similar to males in the target age group, non-Hispanic black race/ethnicity was significantly associated with decreased odds of receiving the second dose of the HPV vaccine ($P = 0.02$), and attending >3 clinic visits during the study period was associated with nearly a 6-fold increase in odds of receiving the second dose of the HPV vaccine in the catch-up age group ($P < 0.001$). Additionally, males with public insurance had

**Table 2.** Associations of demographic and clinical characteristics with HPV vaccine initiation by age group among 14,688 males attending JHCP clinics from 2012 to 2013

| | Target (11–12 years) | | | Catch-up (13–21 years) | | | Permissive (22–26 years) | | |
|---|---|---|---|---|---|---|---|---|---|
| | HPV vaccine initiation | | | HPV vaccine initiation | | | HPV vaccine initiation | | |
| | Yes ($n = 617$) | No ($n = 1,854$) | aOR (95% CI) | Yes ($n = 1,483$) | No ($n = 6,528$) | aOR (95% CI) | Yes ($n = 80$) | No ($n = 4,126$) | aOR (95% CI) |
| Mean baseline age (SD) | 11.43 (0.5) | 11.42 (0.5) | 1.07 (0.82–1.40) | 15.80 (2.2) | 17.15 (2.6) | 0.86 (0.84–0.89) | 23.53 (1.3) | 24.03 (1.4) | 0.84 (0.72–0.97) |
| Race/ethnicity, *n* | | | | | | | | | |
| non-Hispanic White | 187 | 943 | 1.0 (Reference) | 469 | 3,400 | 1.0 (Reference) | 39 | 2,394 | 1.0 (Reference) |
| non-Hispanic Black | 368 | 660 | 1.39 (1.06–1.84) | 866 | 2,165 | 1.39 (1.12–1.74) | 32 | 1,072 | 1.93 (1.20–3.09) |
| Hispanic | 20 | 65 | 1.36 (0.79–2.35) | 54 | 312 | 1.04 (0.76–1.42) | 5 | 228 | 1.58 (0.42–5.89) |
| Asian | 11 | 57 | 1.15 (0.69–1.90) | 21 | 198 | 0.85 (0.46–1.57) | 2 | 165 | 0.76 (0.18–3.26) |
| Other | 31 | 129 | 1.16 (0.77–1.75) | 73 | 453 | 1.01 (0.76–1.33) | 2 | 267 | 0.50 (0.12–2.11) |
| Insurance type, *n* | | | | | | | | | |
| Private | 193 | 896 | 1.0 (Reference) | 588 | 3,692 | 1.0 (Reference) | 59 | 3,260 | 1.0 (Reference) |
| Public | 312 | 457 | 1.45 (1.07–1.96) | 625 | 1,237 | 1.21 (1.05–1.39) | 9 | 474 | 0.61 (0.28–1.37) |
| Military | 112 | 493 | 1.25 (1.03–1.51) | 261 | 1,466 | 1.06 (0.91–1.25) | 10 | 152 | 2.46 (1.06–5.71) |
| Number of clinic visits, *n* | | | | | | | | | |
| 1–3 visits | 429 | 1,528 | 1.0 (Reference) | 1,103 | 5,562 | 1.0 (Reference) | 51 | 3,652 | 1.0 (Reference) |
| >3 visits | 188 | 326 | 2.39 (1.84–3.11) | 380 | 966 | 2.19 (1.76–2.73) | 29 | 474 | 4.08 (2.20–7.56) |
| JHCP clinic location, *n* | | | | | | | | | |
| Suburban | 299 | 1,474 | 1.0 (Reference) | 765 | 5,298 | 1.0 (Reference) | 63 | 3,056 | 1.0 (Reference) |
| Urban | 318 | 380 | 3.27 (1.53–6.99) | 718 | 1,229 | 3.84 (2.23–6.61) | 17 | 1,068 | 0.98 (0.35–2.76) |
| JHCP specialty, *n* | | | | | | | | | |
| Family practice | 120 | 613 | 1.0 (Reference) | 423 | 2,873 | 1.0 (Reference) | 43 | 1,571 | 1.0 (Reference) |
| IM/Peds | 39 | 125 | 1.17 (0.73–1.88) | 86 | 515 | 1.00 (0.74–1.34) | 7 | 249 | 0.97 (0.35–2.66) |
| Internal medicine | 5 | 4 | 1.43 (0.78–2.63) | 55 | 1,187 | 0.27 (0.15–0.47) | 29 | 2,273 | 0.47 (0.22–0.98) |
| Pediatrics | 455 | 1,112 | 0.81 (0.51–1.28) | 919 | 1,953 | 1.28 (0.95–1.73) | 1 | 33 | 1.77 (0.23–13.37) |

NOTE: All models mutually adjusted for all variables listed in the table.
Abbreviation: IM/Peds, internal medicine/pediatrics.

27% decreased odds of receiving the second dose of the HPV vaccine compared with males with private insurance ($P = 0.02$) and IM/Peds practice specialty was significantly associated with a 48% decrease in odds of receiving the second dose of the HPV vaccine compared with Family Practice specialty ($P = 0.04$).

In the target and catch-up age groups, non-Hispanic black males with $\leq$3 visits had lower odds (aOR 0.62; 95% CI, 0.4–0.9) of receiving the second dose of the HPV vaccine compared with their non-Hispanic white male counterparts. This association was nearly equivalent for non-Hispanic black males with

**Table 3.** Associations of demographic and clinical characteristics with the second dose of HPV vaccine by age group among 1,834 males attending JHCP clinics from 2012 to 2013

| | Target (11–12 years) | | | Catch-up (13–21 years) | | |
|---|---|---|---|---|---|---|
| | 2nd dose HPV vaccine | | | 2nd dose HPV vaccine | | |
| | Yes ($n = 261$) | No ($n = 232$) | aOR (95% CI) | Yes ($n = 603$) | No ($n = 667$) | aOR (95% CI) |
| Mean baseline age (SD) | 11.43 (0.5) | 11.46 (0.5) | 0.86 (0.65–1.13) | 15.55 (2.1) | 15.97 (2.2) | 0.95 (0.88–1.02) |
| Race/ethnicity, *n* | | | | | | |
| non-Hispanic White | 104 | 43 | 1.0 (Reference) | 257 | 147 | 1.0 (Reference) |
| non-Hispanic Black | 132 | 160 | 0.63 (0.40–1.00) | 283 | 458 | 0.65 (0.46–0.92) |
| Hispanic | 8 | 10 | 0.39 (0.17–0.89) | 21 | 23 | 0.72 (0.33–1.54) |
| Asian | 6 | 4 | 0.50 (0.17–1.46) | 10 | 7 | 1.11 (0.52–2.40) |
| Other | 11 | 15 | 0.26 (0.09–0.81) | 32 | 32 | 0.71 (0.37–1.37) |
| Insurance type, *n* | | | | | | |
| Private | 100 | 61 | 1.0 (Reference) | 266 | 230 | 1.0 (Reference) |
| Public | 104 | 142 | 0.77 (0.43–1.39) | 195 | 347 | 0.73 (0.56–0.96) |
| Military | 57 | 29 | 1.03 (0.60–1.79) | 138 | 86 | 0.78 (0.52–1.16) |
| Number of clinic visits, *n* | | | | | | |
| 1–3 visits | 136 | 194 | 1.0 (Reference) | 326 | 596 | 1.0 (Reference) |
| >3 visits | 125 | 38 | 4.01 (3.22–4.99) | 277 | 71 | 5.82 (4.13–8.20) |
| JHCP clinic location, *n* | | | | | | |
| Suburban | 149 | 89 | 1.0 (Reference) | 374 | 273 | 1.0 (Reference) |
| Urban | 112 | 143 | 1.08 (0.35–3.34) | 229 | 394 | 0.77 (0.46–1.31) |
| JHCP specialty, *n* | | | | | | |
| Family practice | 64 | 37 | 1.0 (Reference) | 205 | 149 | 1.0 (Reference) |
| IM/Peds | 19 | 13 | 0.63 (0.34–1.19) | 32 | 44 | 0.52 (0.28–0.97) |
| Internal medicine | 0 | 3 | 1.00 (1.00–1.00) | 17 | 28 | 0.65 (0.31–1.40) |
| Pediatrics | 178 | 179 | 0.57 (0.30–1.06) | 349 | 446 | 1.07 (0.74–1.54) |

NOTE: All models mutually adjusted for all variables listed in the table. Results for the permissive age group are not shown due to limited statistical power.
Abbreviation: IM/Peds, internal medicine/pediatrics.

>3 visits (aOR 0.66, 95% CI, 0.4–1.1). Similar patterns were observed for males in the combined "Other" race/ethnicity category (data not shown). The number of clinic visits did not modify the association between race/ethnicity and receipt of the second dose of the HPV vaccine ($P_{interaction} = 0.07$). In contrast, in the target and catch-up age groups, publicly insured males with ≤3 visits had significantly lower odds of receiving the second dose of the HPV vaccine (aOR 0.67; 95% CI, 0.5–0.9) compared with their privately insured counterparts; however, this association was attenuated for publicly insured males with >3 visits (aOR 1.05; 95%, 0.7–1.6). There was no significant difference in the odds of receipt of the second dose of the HPV vaccine when comparing males with military insurance to their privately insured counterparts, irrespective of the number of clinic visits (≤3 visits: aOR 0.85; 95% CI, 0.6–1.2 vs. >3 visits: aOR 0.81; 95% CI, 0.3–1.9). The number of clinic visits modified the association between insurance type and receipt of the second dose of the HPV vaccine ($P_{interaction} = 0.001$).

### HPV vaccine completion

Of the 702 eligible males (those who received their second HPV vaccine dose in 2012), a total of 331 (47.2%) completed the series during the study time frame. Males eligible for the third dose of the HPV vaccine tended to be younger, and a higher proportion were non-Hispanic black and privately insured compared with males eligible for initiation (Table 1).

Multivariable aORs for HPV vaccine completion by age group are shown in Table 4. Results for the permissive age group are not shown due to limited statistical power. In the target age group, attending >3 clinic visits during the study period was significantly associated with over a three-and-a-half-fold increase in odds of HPV vaccine completion compared with ≤3 visits ($P < 0.001$) and visiting a clinic in an urban location was significantly associated with a 43% decrease in odds of HPV vaccine completion compared with suburban locations ($P < 0.01$).

In the catch-up age group, similar to males in the target age group, attending >3 clinic visits during the study period was significantly associated with over a three-and-a-half-fold increase in odds of HPV vaccine completion ($P < 0.001$). Additionally, males with public insurance had 50% decreased odds of HPV vaccine completion compared with males with private insurance ($P = 0.05$).

In the target and catch-up age groups, non-Hispanic black males with ≤3 visits had lower odds (aOR 0.53; 95% CI, 0.2–1.3) of completing the HPV vaccine compared with their non-Hispanic white male counterparts. This association was nearly equivalent for non-Hispanic black males with >3 visits (aOR 0.69; 95% CI, 0.3–1.5). Similar patterns were observed for males in the combined "Other" race/ethnicity category (data not shown). The number of clinic visits did not modify the association between race/ethnicity and HPV vaccine completion ($P_{interaction} = 0.14$). In contrast, in the target and catch-up age groups, publicly insured males with ≤3 visits had significantly lower odds of completing the HPV vaccine (aOR 0.46; 95% CI, 0.3–0.6) compared with their privately insured counterparts; however, this association was attenuated for publicly insured males with >3 visits (aOR 0.72; 95% 0.3–1.7). There was no significant difference in the odds of completing the HPV vaccine when comparing males with military insurance to their privately insured counterparts, irrespective of the number of clinic visits (≤3 visits: aOR 0.76; 95% CI, 0.3–1.7 vs. >3 visits: aOR 0.89; 95% CI, 0.5–1.5). The number of clinic visits modified the association between insurance type and completing the HPV vaccine ($P_{interaction} = 0.0001$).

**Table 4.** Associations of demographic and clinical characteristics with HPV vaccine completion by age group among 702 males attending JHCP clinics from 2012 to 2013

| | Target (11–12 years) | | | Catch-up (13–21 years) | | |
|---|---|---|---|---|---|---|
| | HPV vaccine completion | | | HPV vaccine completion | | |
| | Yes ($n = 86$) | No ($n = 111$) | aOR (95% CI) | Yes ($n = 228$) | No ($n = 244$) | aOR (95% CI) |
| Mean baseline age (SD) | 11.45 (0.5) | 11.41 (0.5) | 1.27 (0.72–2.23) | 15.47 (2.1) | 15.55 (2.0) | 1.01 (0.91–1.12) |
| Race/ethnicity, *n* | | | | | | |
| non-Hispanic White | 40 | 38 | 1.0 (Reference) | 116 | 83 | 1.0 (Reference) |
| non-Hispanic Black | 36 | 60 | 0.63 (0.31–1.29) | 87 | 130 | 0.54 (0.25–1.19) |
| Hispanic | 4 | 4 | 1.01 (0.38–2.73) | 10 | 11 | 0.57 (0.17–1.88) |
| Asian | 3 | 2 | 1.95 (0.17–23.02) | 2 | 6 | 0.24 (0.06–0.99) |
| Other | 3 | 7 | 0.36 (0.11–1.21) | 13 | 14 | 0.62 (0.31–1.26) |
| Insurance type, *n* | | | | | | |
| Private | 35 | 42 | 1.0 (Reference) | 112 | 95 | 1.0 (Reference) |
| Public | 29 | 45 | 1.10 (0.74–1.63) | 55 | 94 | 0.50 (0.25–1.01) |
| Military | 22 | 23 | 1.14 (0.69–1.86) | 58 | 55 | 0.67 (0.43–1.04) |
| Number of clinic visits, *n* | | | | | | |
| 1–3 visits | 29 | 72 | 1.0 (Reference) | 78 | 157 | 1.0 (Reference) |
| >3 visits | 57 | 39 | 3.69 (2.00–6.82) | 150 | 87 | 3.56 (2.34–5.40) |
| JHCP clinic location, *n* | | | | | | |
| Suburban | 54 | 62 | 1.0 (Reference) | 151 | 144 | 1.0 (Reference) |
| Urban | 32 | 49 | 0.57 (0.38–0.85) | 77 | 100 | 1.42 (0.64–3.12) |
| JHCP specialty, *n* | | | | | | |
| Family practice | 18 | 32 | 1.0 (Reference) | 82 | 83 | 1.0 (Reference) |
| IM/Peds | 7 | 7 | 1.51 (0.49–4.69) | 11 | 13 | 0.82 (0.37–1.80) |
| Internal medicine | 0 | 0 | — | 7 | 7 | 1.10 (0.32–3.83) |
| Pediatrics | 61 | 72 | 2.15 (0.93–5.00) | 128 | 141 | 1.34 (0.81–2.20) |

NOTE: All models mutually adjusted for all variables listed in the table. Results for the permissive age group are not shown due to limited statistical power.
Abbreviation: IM/Peds, internal medicine/pediatrics.

## Discussion

In this large clinical population of over 14,500 males ages 11 to 26 years, the overall proportion of HPV vaccine initiation was low, with approximately 15% of males receiving at least one dose of the vaccine between January 2012 and April 2013. We observed differences in rates of initiation by age group; approximately 25% of males in the target age group initiated the HPV vaccine, while 18.5% and 2% of males in the catch-up and permissive age groups initiated the HPV vaccine, respectively. Our rates of initiation were lower than those reported from the NIS-Teen, which estimated that 35% of males ages 13 to 17 years initiated the HPV vaccine in the United States in 2013 (21% in 2012; ref. 13). In our study, among all males who initiated the HPV vaccine in 2012, 49% received the second dose, and among those who received the second dose in 2012, 47% completed the HPV vaccine series. Our rates of completion were comparable with those reported for the general US male population in the NIS-Teen study, which estimated that 48% of males who initiated the HPV vaccine (45.1% in 2012; ref. 13) completed the series in 2013.

Among all age groups, we found that non-Hispanic black males were more likely to initiate the HPV vaccine compared with non-Hispanic white males. Irrespective of race/ethnicity, males in the target and catch-up age groups who were publicly insured were also more likely to initiate the HPV vaccine. These findings are in line with previous studies among both males and females, suggesting higher HPV vaccine initiation rates among non-Hispanic black and publicly insured populations (1, 12, 13). Although cost has been previously cited as a barrier to HPV vaccination (26–29), efforts over the past several years have focused on improving HPV vaccine reimbursement (30). For low-income children, the Vaccine For Children (VFC) program provides access to the HPV vaccine for Medicaid and underinsured children less than 18 years of age (31). In the private sector, the Affordable Care Act requires most private insurance plans to cover the HPV vaccine at no cost to patients up to 18 years of age (32). We also observed that males in the permissive age group with military insurance were more likely to initiate the HPV vaccine compared with males with private insurance. HPV vaccination is a covered benefit for males ages 11 to 26 years under military insurance plans (33). Given that cost should not be a barrier going forward, interventions targeting parents and/or providers to increase HPV vaccine initiation may be warranted.

In contrast to our findings for HPV vaccine initiation, we found that non-Hispanic black males (vs. non-Hispanic white) in both the target and catch-up age groups and males with public insurance (vs. private insurance) in the catch-up age group were less likely to receive subsequent doses of the HPV vaccine. These findings are comparable with previous studies reporting lower completion rates among non-Hispanic black and publicly insured/underinsured populations (12). It is unclear why the same males who are more likely to initiate the vaccine series are less likely to receive subsequent doses. Our data indicated that for non-Hispanic black males, returning for additional clinic visits did not explain this disparity; however, for publicly insured males, those who attended >3 clinic visits during the study period were equally likely to complete the HPV vaccine series compared with males with private insurance. These findings suggest that provider alerts and/or patient reminder systems may facilitate HPV series completion for all males, and could be particularly effective among minority and publicly insured male patients.

We also found important clinical predictors associated with HPV vaccination in our study. Among all age groups, attending >3 clinic visits was associated with increased odds of HPV vaccine initiation and with receipt of subsequent doses. These findings are similar to other studies reporting that males require more primary care visits to complete HPV vaccine series (14, 34). We also found that males in the catch-up and permissive age groups who primarily attended Internal Medicine clinics (vs. Family Practice) were less likely to initiate the HPV vaccine; however, once they initiated, they were equally likely to receive subsequent doses. Together, these findings have important implications for clinical intervention strategies. For example, broad interventions encouraging routine healthcare visits may promote HPV vaccine initiation and completion among all age-eligible males, whereas more targeted interventions focused on increasing vaccine initiation among patients of Internal Medicine physicians may be needed for increasing coverage in males who require catch-up HPV vaccination.

To our knowledge, this is one of the first and largest studies of demographic and clinical predictors of HPV vaccination among age-eligible males after the ACIP began routinely recommending the vaccine in 2011 (12). Our study is unique in that we assessed independent predictors of each dose of the HPV vaccine, and contributes to the literature by identifying predictors of the second dose of the vaccine. Additional strengths include our diverse study population in terms of patient age, race/ethnicity, insurance, and practice specialties. However, some important limitations are worth noting. First, our study population was selected from clinics affiliated with a single academic-institution in Maryland, representing a small proportion of all males in the 11- to 26-year-old age range in the underlying counties. Although males attending JHCP clinics appear to be similar to males in the same age range within their respective counties with respect to race/ethnicity and insurance type, our results may not be generalizable to non-academic practice settings or other geographic regions. Second, because we assigned each male a practice specialty type based on his most common visit or first visit (if most common was not available), it is possible that we misclassified practice specialty type; however, we would expect such misclassification to be non-differential by vaccine status. Third, we did not have exact visit date, and therefore were limited in our ability to determine dosing intervals and assess timing of each vaccine dose. Finally, we used data obtained from the medical record, which is subject to the limitations of databases that were not designed for research purposes (e.g., a limited number of predictor variables, lack of data on potential confounders such as parent perceptions, provider recommendation to vaccinate, etc.). With this type of EMR, it is difficult to know how many males received services exclusively at JHCP. The rate of vaccination was low in our study population and consistent with the literature regarding HPV vaccination in males during this time period, which suggests that the number of males who may have been misclassified as unvaccinated is relatively low.

In conclusion, our study indicates that a substantial proportion of age-eligible males attending primary care clinics did not receive the HPV vaccine during visits with their healthcare provider. Consistent with the literature, we found important disparities in HPV vaccine completion by race/ethnicity and insurance status. Moreover, we provide new evidence demonstrating that these disparities are as equally important for receipt of the second dose of the HPV vaccine. These findings point toward a need for

understanding barriers to receiving subsequent doses of the HPV vaccine and focused interventions among minority and publicly insured males to ensure HPV vaccine series completion. Further, our data suggest that interventions may need to be targeted by provider specialty and warrant future research on provider-level factors associated with HPV vaccination.

## Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

## Authors' Contributions

**Conception and design:** D.F. Phelan-Emrick, M.A. Wilbur, B. Chou
**Development of methodology:** B. Chou
**Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.):** D.F. Phelan-Emrick, M.A. Wilbur
**Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis):** M.A. Clarke, F. Coutinho, D.F. Phelan-Emrick, C.E. Joshu
**Writing, review, and/or revision of the manuscript:** M.A. Clarke, F. Coutinho, D.F. Phelan-Emrick, M.A. Wilbur, B. Chou, C.E. Joshu
**Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases):** D.F. Phelan-Emrick, B. Chou
**Study supervision:** B. Chou, C.E. Joshu

## Acknowledgments

The authors thank the Optimizing Cancer Screening Working Group, also known as the Johns Hopkins Program to Individualize Cancer Screening (*in*CAS), for their support of this study. They also thank the Research Staff at Johns Hopkins Community Physicians for their expert assistance with this project.

## Grant Support

This work was supported by P30 CA006973. M.A. Clarke was additionally supported by the National Cancer Institute, T32 CA009314.

Received September 9, 2015; revised December 8, 2015; accepted December 14, 2015; published OnlineFirst December 23, 2015.

## References

1. Reagan-Steiner S, Yankey D, Jeyarajah J, Elam-Evans LD, Singleton JA, Curtis CR, et al. National, regional, state, and selected local area vaccination coverage among adolescents aged 13–17 years—United States, 2014. MMWR Morb Mortal Wkly Rep 2015;64:784–92.
2. Centers for Disease Control and Prevention (CDC). FDA licensure of quadrivalent human papillomavirus vaccine (HPV4, Gardasil) for use in males and guidance from the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 2010;59:630–2.
3. Centers for Disease Control and Prevention (CDC). Recommendations on the use of quadrivalent human papillomavirus vaccine in males–Advisory Committee on Immunization Practices (ACIP), 2011. MMWR Morb Mortal Wkly Rep 2011;60:1705–8.
4. Kjaer SK, Sigurdsson K, Iversen OE, Hernandez-Avila M, Wheeler CM, Perez G, et al. A pooled analysis of continued prophylactic efficacy of quadrivalent human papillomavirus (Types 6/11/16/18) vaccine against high-grade cervical and external genital lesions. Cancer Prev Res 2009;2:868–78.
5. Paavonen J, Jenkins D, Bosch FX, Naud P, Salmeron J, Wheeler CM, et al. Efficacy of a prophylactic adjuvanted bivalent L1 virus-like-particle vaccine against infection with human papillomavirus types 16 and 18 in young women: an interim analysis of a phase III double-blind, randomised controlled trial. Lancet 2007;369:2161–70.
6. Li N, Franceschi S, Howell-Jones R, Snijders PJ, Clifford GM. Human papillomavirus type distribution in 30,848 invasive cervical cancers worldwide: variation by geographical region, histological type and year of publication. Int J Cancer 2011;128:927–35.
7. Bosch FX, Burchell AN, Schiffman M, Giuliano AR, de Sanjose S, Bruni L, et al. Epidemiology and natural history of human papillomavirus infections and type-specific implications in cervical neoplasia. Vaccine 2008;26:K1–16.
8. de Sanjose S, Quint WG, Alemany L, Geraets DT, Klaustermeier JE, Lloveras B, et al. Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. Lancet Oncol 2010;11:1048–56.
9. Gillison ML, Chaturvedi AK, Lowy DR. HPV prophylactic vaccines and the potential prevention of noncervical cancers in both men and women. Cancer 2008;113:3036–46.
10. Gillison ML. Human papillomavirus-related diseases: oropharynx cancers and potential implications for adolescent HPV vaccination. J Adolesc Health 2008;43:S52–60.
11. Chaturvedi AK, Engels EA, Pfeiffer RM, Hernandez BY, Xiao W, Kim E, et al. Human papillomavirus and rising oropharyngeal cancer incidence in the United States. J Clin Oncol 2011;29:4294–301.
12. Holman DM, Benard V, Roland KB, Watson M, Liddon N, Stokley S. Barriers to human papillomavirus vaccination among US adolescents: a systematic review of the literature. JAMA Pediatr 2014;168:76–82.
13. Elam-Evans LD, Yankey D, Jeyarajah J, Singleton JA, Curtis RC, MacNeil J, et al. National, regional, state, and selected local area vaccination coverage among adolescents aged 13–17 years–United States, 2013. MMWR Morb Mortal Wkly Rep 2014;63:625–33.
14. Rand CM, Szilagyi PG, Albertin C, Auinger P. Additional health care visits needed among adolescents for human papillomavirus vaccine delivery within medical homes: a national study. Pediatrics 2007;120:461–6.
15. Perkins RB, Apte G, Marquez C, Porter C, Belizaire M, Clark JA, et al. Factors affecting human papillomavirus vaccine use among white, black and Latino parents of sons. Pediatr Infect Dis J 2013;32:e38–44.
16. Reiter PL, Oldach BR, Randle KE, Katz ML. Acceptability of HPV vaccine for males and preferences for future education programs among Appalachian residents. Am J Mens Health 2014;8:167–74.
17. Reiter PL, McRee AL, Pepper JK, Chantala K, Brewer NT. Improving human papillomavirus vaccine delivery: a national study of parents and their adolescent sons. J Adolesc Health 2012;51:32–7.
18. Donahue KL, Stupiansky NW, Alexander AB, Zimet GD. Acceptability of the human papillomavirus vaccine and reasons for non-vaccination among parents of adolescent sons. Vaccine 2014;32:3883–5.
19. Reiter PL, McRee AL, Pepper JK, Gilkey MB, Galbraith KV, Brewer NT. Longitudinal predictors of human papillomavirus vaccination among a national sample of adolescent males. Am J Public Health 2013;103:1419–27.
20. Du P, Camacho F, McCall-Hosenfeld J, Lengerich E, Meyers CM, Christensen ND. Human papillomavirus vaccination among adults and children in 5 US States. J Public Health Manag Pract 2015 Jun 1 [Epub ahead of print].
21. Dempsey A, Cohn L, Dalton V, Ruffin M. Patient and clinic factors associated with adolescent human papillomavirus vaccine utilization within a university-based health system. Vaccine 2010;28:989–95.
22. Reiter PL, Gilkey MB, Brewer NT. HPV vaccination among adolescent males: results from the National Immunization Survey-Teen. Vaccine 2013;31:2816–21.
23. Kreimer AR, Struyf F, Del Rosario-Raymundo MR, Hildesheim A, Skinner SR, Wacholder S, et al. Efficacy of fewer than three doses of an HPV-16/18 AS04-adjuvanted vaccine: combined analysis of data from the Costa Rica Vaccine and PATRICIA trials. Lancet Oncol 2015;16:775–86.
24. Romanowski B, Schwarz TF, Ferguson LM, Peters K, Dionne M, Schulze K, et al. Immunogenicity and safety of the HPV-16/18 AS04-adjuvanted vaccine administered as a 2-dose schedule compared with the licensed 3-dose schedule: results from a randomized study. Hum Vaccin 2011;7:1374–86.
25. Dobson SR, McNeil S, Dionne M, Dawar M, Ogilvie G, Krajden M, et al. Immunogenicity of 2 doses of HPV vaccine in younger adolescents vs 3 doses in young women: a randomized clinical trial. JAMA 2013;309:1793–802.
26. Berenson AB, Rahman M. Gender differences among low income women in their intent to vaccinate their sons and daughters against human papillomavirus infection. J Pediatr Adolesc Gynecol 2012;25:218–20.

27. Oldach BR, Katz ML. Ohio Appalachia public health department personnel: human papillomavirus (HPV) vaccine availability, and acceptance and concerns among parents of male and female adolescents. J Community Health 2012;37:1157–63.
28. Quinn GP, Murphy D, Malo TL, Christie J, Vadaparampil ST. A national survey about human papillomavirus vaccination: what we didn't ask, but physicians wanted us to know. J Pediatr Adolesc Gynecol 2012;25:254–8.
29. Sanders Thompson VL, Arnold LD, Notaro SR. African American parents' HPV vaccination intent and concerns. J Health Care Poor Underserved 2012;23:290–301.
30. National Vaccine Advisory Committee. Financing vaccination of children and adolescents: National Vaccine Advisory Committee recommendations. Pediatrics 2009;124:S558–62.
31. VFC Program [Internet]. Atlanta, GA: Centers for Disease Control; 2015 [updated February 19, 2015; cited 2015 Jun 19]. Available from: http://www.cdc.gov/features/vfcprogram/#vfclist.
32. The Affordable Care Act and Immunization [Internet]. Washington DC: U.S. Department of Health and Human Services; 2012 [updated January 20, 2012; cited 2015 Jun 19]. Available from: http://www.hhs.gov/healthcare/facts/factsheets/2010/09/The-Affordable-Care-Act-and-Immunization.html.
33. TRICARE Retail Vaccination Program [Internet]: Department of Defense, Defense Health Agency; 2015 [cited 2015 Jun 19]. Available from: https://www.express-scripts.com/TRICARE/news/Vaccine_List.pdf.
34. Allison MA, Dunne EF, Markowitz LE, O'Leary ST, Crane LA, Hurley LP, et al. HPV vaccination of boys in primary care practices. Acad Pediatr 2013;13:466–74.