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# What explains the different rates of human papillomavirus vaccination among adolescent males and females in the United States?



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#### ARTICLE INFO

Article history: Received 2 September 2015 Received in revised form 7 February 2016 Accepted 19 February 2016 Available online 4 March 2016

Keywords: Human papillomavirus Adolescent health Vaccination NIS-Teen Gender interaction

### ABSTRACT

*Purpose:* To identify factors that explain differences in HPV vaccination rates for male and female adolescents and to determine self-reported barriers by parents affecting vaccination decisions. *Methods:* The sample included adolescents 13–17 years old with a vaccination record documented in the 2012 and 2013 National Immunization Survey-Teen dataset. A logistic regression model was developed with 13 socio-demographic factors and survey year, along with significant interaction pairs with gender. *Results:* Subjects included 20,355 and 18,350 adolescent boys and girls, respectively. About half of the females (56%) received at least one dose of HPV vaccine, compared to 28% of males. Several factors differed between males and females, including higher vaccination rates among non-Hispanic Black males and lower vaccination rates for non-Hispanic Black females compared to Whites; and a stronger association with health care provider recommendation among males. The most common parental reasons for not vaccinating their children included 'not recommended by a health care provider' for males (24%), and 'unnecessary' for females (18%).

*Conclusion:* We found a significant gender interaction with several socio-demographic variables in predicting vaccination uptake. These gender differences may be partially an artifact of timing, because male vaccination became routine approximately five years after female vaccination.

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# 1. Introduction

Considerable attention has been given to human papillomavirus (HPV) infection's association with cervical cancer in women [1]. However, HPV is also associated with a variety of other cancers in women and men including anal cancer and a subset of penile and oral cancers. A three-dose series of HPV vaccine was initially recommended for females by the Advisory Committee on Immunization Practices (ACIP) in 2007 [2]. Later in 2011, the ACIP added a recommendation of the quadrivalent HPV vaccine for males aged 11–12 years for routine vaccination as well as at 13–21 years for a catch up vaccination [3]. During the year prior to ACIP's recommendation, only 14% of young males were vaccinated, which was considerably lower than the 44% of adolescent females vaccinated during the same time period [4].

For adolescents aged 18 years and younger, the decision to vaccinate is largely influenced by a parent or caregiver [5]. Therefore, strategies aimed at heightening parental acceptance or attitudes toward vaccination are important for ensuring that vaccines are administered before adolescents becomes sexually active, which is important for realizing the full benefits of the vaccine [6]. Studies have appeared in the literature to show the role of certain factors, including socioeconomic status and ethnicity, in predicting which individuals are vaccinated for HPV. While these studies have been useful in guiding interventions intended to improve adherence to ACIP guidelines, the majority of these studies suffer from poor generalizability because they used samples drawn from small geographic areas in the US or because they have not identified factors that explain why females are more likely to be vaccinated than males [4,7–9]. These limitations form the basis for the present study, which aims to explore which factors explain differences in vaccination rates by gender among adolescents who received at least one HPV vaccine dose in a national sample. In addition, we also explore barriers identified by parents or caregivers that shape a decision to vaccinate a child.

http://dx.doi.org/10.1016/j.pvr.2016.02.001

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# 2.1. Study design

We analyzed data from the National Immunization Survey-Teen (NIS-Teen), which was conducted by the Centers for Disease Control and Prevention (CDC). This survey reports immunization coverage estimates for adolescents aged 13-17 years [10] during the periods between January 2012 and February 2013 (reported in the 2012 NIS-Teen) and between January 2013 and February 2014 (reported in the 2013 NIS-Teen) [11,12]. Since the routine use of HPV vaccine for males was recommended in October 2011 [3], the responses captured in both NIS-Teen surveys reflect its most recent recommendation for the catch up vaccination. Vaccination information was collected in two ways: (1) a Random Digit Dialing (RDD) telephone survey of households with children 13-17 years of age, and (2) a survey mailed to health care providers asking for immunization records of children for whom parents or guardians gave consent to share records with the survey collectors [11,12]. If more than one adolescent between 13 and 17 years was identified in a sampled household, one child was randomly chosen as the subject of the interview [11,12]. Details of NIS-Teen methods including data collection and weights generation were previously published [11-13].

A total of 58 geographic areas comprising all 50 states, the U.S. Virgin Islands, Guam (only available in NIS-Teen 2013), and 6 urban areas (Bexar County, TX; City of Houston, TX; Chicago, IL; District of Columbia; New York City; Philadelphia County, PA) were included. The datasets included 32,825 and 33,949 adolescents from the 2012 and 2013 NIS-Teen dataset respectively, representing a Council of American Research Organization (CASRO) response rate of 55.1% and 51.1% for households contacted on landline telephones and a CASRO response rate of 23.6% and 23.3% for households contacted on their cell-phones, excluding U.S. Virgin islands or Guam [11,12]. Of these 66,774 adolescents (referred to as the source population in the present study), the CDC collected additional data for 38,705 of these adolescents from their health care providers about the status of their vaccine schedule (referred to as the study population in the present study) [11,12].

## 2.2. Measures

The primary variable of interest was whether a teen received at least one HPV vaccination in the series or was not vaccinated at all. Vaccination status was identified from a field in the dataset that specified the subject having an "Up-to-date flag: 1+ human papillomavirus shot, excluding any vaccinations after the interview date." We also examined whether the following sociodemographic factors, as well as survey year, was associated with vaccination status: age of the child at the screener completion date calculated from the best date of birth [11,12]; race/ethnicity; child's insurance coverage; number of visits by the child to a health care provider in the previous year; vaccination status for Tetanus-diphtheria/Tetanus-diphtheria-acellular-pertussis vaccine (Td/Tdap) or Meningococcal vaccine (MCV); a recommendation of HPV vaccine by a health care provider; income of the household; census region; number of children in the household; and mother's age, education level, and marital status.

In the source population, parents or their caregivers whose children did not receive a dose of the vaccine were asked how likely their child would be vaccinated for HPV in the next 12 months. For those who said they were not likely to complete the full vaccine series, reasons for this decision were requested.

## 2.3. Data analysis

We recoded the number of health care visits during the previous year (originally 9 levels) to "none," "1," "2–3," and "4 or more"; insurance type was also re-classified as either "employer or union," "others including Medicaid," or "none," The category "others including Medicaid" includes Medicaid, State Children's Health Insurance Program (S-CHIP), TRICARE, or Indian Health Service. It should be noted that children less than 19 years who are eligible for Medicaid, underinsured, or American Indian/Alaska native descent can access vaccines at no cost from a part of the federally funded Vaccine For Children (VFC) program. Also, children enrolled in either S-CHIP or TRICARE are eligible for CDC recommended free vaccines, including HPV [14,15]. While many commercial plans cover HPV vaccines, the level of benefit coverage for HPV vaccination varies by plan [16]. When the dataset reported that a teen had multiple forms of insurance including "employer or union," and "others including Medicaid," the subject was categorized as "others including Medicaid."

When calculating the descriptive statistics, different weights were used for the study population and the source population. For the primary outcome, the study population with 38,705 house-holds was standardized with survey weights to represent all teens aged 13–17 years old that were reported in the provider dataset. For the secondary outcome, the source population with the 66,774 households was weighted generalizable to all teens aged 13–17 years in U.S. We calculated a Pearson's chi-square to compare vaccination rate, parental willingness to vaccinate, and reasons for declining vaccination by gender.

A logistic regression model was developed to test the hypothesis that an association between socio-demographic factors and HPV vaccination was not mediated by sex. The model adjusted for the complex sample design employed in the survey data (strata, cluster and weight) using PROC SURVEY command in SAS 9.4. To determine effect modification by sex, we examined all interaction pairs between 14 independent variables (13 socio-demographic variables and survey year) and sex. Then, the significant interaction pairs as well as the 14 variables and sex were included in the multivariate analysis. We intended to derive estimates taking fourteen variables into account given that over fitting was not a concern for our study [17]. Therefore, additional model selection (e.g. forward selection, backward elimination, or stepwise) was not employed. For variables with significant gender effects, we reported odds ratios (ORs) stratified by sex, while pooled ORs were generated for variables without gender interactions. Multicollinearity was examined by adding each variable to check whether a meaningful increase in standard error (50%) occurred [18]. All statistical tests were conducted at a significance level of p < 0.05for a two-sided test. The study was approved by the Institutional Review Board at the University of Florida.

# 3. Results

# 3.1. Participant characteristics

Socio-demographic characteristics in the study population were similar for both adolescent males and females. The mean age of the adolescents was 15.0 years. The majority were non-Hispanic whites (55.0%) and had healthcare coverage (93.1%). Most teens had at least one encounter with a healthcare provider during the previous year (83.1%) and were immunized for Td/Tdap (89.6%) or Meningococcus (76.9%). Most mothers were 35 years and older (90.0%), married (65.0%), and had at least some college education (61.6%). The majority of parents or caregivers reported that their household incomes were higher than the poverty threshold level (71.7%) and had fewer than four children (87.3%). More than one-third of the adolescents lived in the South (37.3%) (Table 1). However, the frequency in which HPV

Table 1
Characteristics for adolescents aged 13-17 years, 2012-2013 National Immunization
Survey-Teen (NIS-Teen).

	Males		Females		
	n	(Weighted %)	n	(Weighted %)	
Total	20,355		18,350		
Year					
2012	10,426	(50.0%)	9320	(49.9%)	
2013	9929	(50.0%)	9030	(50.1%)	
Teen characteristics					
Age (years)					
13	4119	(19.9%)	3802	(20.0%)	
14	4286	(20.6%)	3762	(19.4%)	
15	4048	(20.6%)	3/54	(21.3%)	
16	4098 3804	(19.8%)	3760	(21.8%) (17.5%)	
Pagelothnicity					
White non Hispanic	12 100	(55.0%)	11 9/6	(55.0%)	
Hispanic	13,199	(33.0%)	2505	(33.0%)	
Black non-Hispanic	2072	(22.2%)	2033	(21.0%)	
Other non-Hispanic	2070	(87%)	1876	(9.6%)	
	2070	(01770)	1070	(0.0,0)	
Healthcare coverage	1000	(710)	1115	(6.6%)	
No insurance	11.070	(7.1%)	10.074	(6.6%)	
union	11,070	(40.0%)	10,074	(47.3%)	
Other insurance, including	7857	(46.4%)	7010	(46.0%)	
Medicaid		()		()	
Number of visits to doctors in a	provious	1007			
Number of visits to doctors in a	2354	(18.2%)	2563	(15.6%)	
1	5002	(18.2%)	4960	(15.0%)	
1 2_3	7027	(20.7%)	6573	(36.3%)	
4+	3884	(18.4%)	4242	(21.8%)	
	5001	(101.00)	12.12	(2110/0)	
Received meningococcal vaccine	15 224	(77.0%)	12 707	(70.7%)	
Yes	15,334	(77.0%)	13,/6/	(76.7%)	
110	5021	(23.0%)	4385	(23.3%)	
Received Td/Tdap					
Yes	18,145	(89.7%)	16,376	(89.6%)	
NO	2210	(10.3%)	1974	(10.4%)	
Mother characteristics					
Mother's age (years)					
45+	10,205	(43.9%)	9249	(45.2%)	
35-44	8469	(46.3%)	7609	(44.6%)	
< 35	1681	(9.8%)	1492	(10.3%)	
Mother's education					
College graduate	8736	(35.6%)	7897	(35.0%)	
Some college	5605	(25.6%)	5102	(27.0%)	
High school	3856	(25.0%)	3419	(24.0%)	
Less than high school	2158	(13.9%)	1932	(14.0%)	
Mother's marital status					
Married	14,824	(65.5%)	13,225	(64.5%)	
Not married	5531	(34.5%)	5125	(35.5%)	
Received provider recommendat	ion of HP	V vaccine			
Yes	7400	(35.2%)	12,037	(63.4%)	
No	11,267	(57.2%)	5216	(30.7%)	
Others <sup>a</sup>	1476	(7.6%)	919	(5.9%)	
Household characteristics					
Poverty status					
Below poverty	3449	(24.1%)	3140	(24.4%)	
Above poverty, $\leq$ \$75,000	7493	(38.0%)	6769	(37.7%)	
Above poverty, $>$ \$75,000	8832	(33.6%)	7944	(34.0%)	
Unknown	581	(4.3%)	497	(3.9%)	
Census region					
South	6687	(37.3%)	6169	(37.3%)	
Midwest	4399	(21.7%)	3956	(21.8%)	
Northeast	3904	(16.9%)	3543	(16.9%)	
West	4705	(24.0%)	4100	(24.0%)	
Number of children					
1	7699	(31.9%)	6969	(32.3%)	
2-3	10,648	(55.7%)	9508	(54.7%)	

#### Table 1 (continued)

	Males		Females	
	n	(Weighted %)	n	(Weighted %)
4+	2008	(12.4%)	1873	(13.0%)

*Note:* Weighted percentages may not sum to 100% due to rounding. Raw frequencies may not sum to stated sample size due to missing data. Td/ Tdap=Tetanus-diphtheria/Tetanus-diphtheria-acellular-pertussis vaccine.

<sup>a</sup> Others are when parents or caregivers answer 'Don't know' or 'Refused.'

vaccination was recommended by a healthcare provider was different (p < 0.05) for males (35.2%) and females (63.4%).

# 3.2. HPV vaccination

About half of female adolescents (55.6%, n=10,123) received a HPV vaccination compared to 27.7% (n=5333) of males (p < 0.05). In addition, of those vaccinated, females (65.9%) were more likely to complete the 3-dose series compared to males (37.3%).

Prior to model building, we identified significant interactions between sex and the following variables for HPV vaccination initiation: survey year (p < 0.001), age (p = 0.004), race/ethnicity (p < 0.001), health care coverage (p = 0.021), recommendation for immunization by provider (p < 0.001) and mother's education level (p=0.041). Thus, the final model included these six interaction terms, survey year, 13 socio-demographic variables and sex, resulting in a c statistic=0.831. Six factors differed significantly between males and females. Males were more likely to be vaccinated in 2013 (34.6%) compared to 2012 (20.8%) (mOR: 1.79 [CI: 1.55–2.07]), while an increase in rate was not observed in females (fOR: 1.06 [CI: 0.94-1.20], 53.8% in 2012 and 57.3% in 2013). When the odds for vaccination between males and females at different ages were compared, the only age category that significantly differed by sex was for the 17 year olds. At the age of 17, the odds for a female being vaccinated (fOR: 2.12 [CI: 1.73-2.59]) was higher compared to males (mOR: 1.27 [CI: 1.02-1.59]). With regards to race and ethnicity, the odds of non-Hispanic black males receiving a vaccination was 77% higher compared to White males; on the other hand, the odds of non-Hispanic Black females receiving a vaccination were 16% lower compared to white females. Both males and females insured via "other insurance including Medicaid" were more likely to receive vaccination than those with "employer or union insurance," and the association was stronger for males than females (male OR: 1.54 [CI: 1.31-1.82]; female OR: 1.17 [CI: 1.01-1.36]). The influence of provider recommendation was also more pronounced among the males compared to females (Table 2).

Among variables not showing significant interactions with sex, the administration of meningococcal vaccination was most strongly associated with HPV vaccination (OR=6.10, CI=5.23-7.13). Vaccination rates were also higher in adolescents who received Td/Tdap vaccine (OR=1.69, CI=1.38-2.08), who visited doctors at least once in a previous year (1 time OR=1.28, CI=1.09-1.49; 2-3 times OR=1.42, CI=1.23-1.64; 4+ times OR=1.38, CI=1.18-1.62), whose mothers were aged <35 years old (compared to >45 years old, OR=1.28, CI=1.06-1.55) and who lived in the West (compared to the South, OR=1.45, CI=1.26-1.67). On the contrary, teens living in a household above the poverty level but below \$75,000 (compared to households below poverty, OR=0.64, CI=0.55-0.74) or above \$75,000 (OR=0.67, CI=0.56-0.79) were less likely to have the child vaccinated (Table 3).

### Table 2

Multivariate logistic regression analyses for HPV vaccine initiation among adolescents aged 13–17 years, 2012–2013 National Immunization Survey-Teen (NIS-Teen): variables with significant interactions.

Variables with significant interactions	ions Multivariate				Difference by gender	
	Males	( <i>n</i> =20,355)	Females ( <i>n</i> =18,350)			
	OR	95% CI	OR	95% CI		
Year 2012 2013	1 1.79	[Reference] (1.55–2.07)**	1 1.06	[Reference] (0.94–1.20)	$mOR > fOR^{**}$	
Teen's age (years)						
13 14 15 16 17	1 1.27 1.28 1.30 1.27	[Reference] (1.02–1.59)° (1.02–1.61)° (1.04–1.61)° (1.02–1.59)°	1 1.14 1.35 1.60 2.12	[Reference] (0.96–1.36) (1.13–1.63) (1.33–1.94) (1.73–2.59)	mOR < fOR**	
Teen's race/ethnicity White, non-Hispanic Hispanic Black, non-Hispanic Other, non-Hispanic	1 2.12 1.77 1.14	[Reference] (1.72-2.61)** (1.44-2.19)** (0.90-1.44)	1 1.28 0.84 1.17	[Reference] (1.05–1.55) <sup>°</sup> (0.68–1.03) (0.96–1.44)	$mOR > fOR^{**}$ $mOR > fOR^{**}$	
Healthcare coverage Through parent employer or union No Insurance Other insurance, including Medicaid	1 1.34 1.54	[Reference] (0.91–1.97) (1.31–1.82)**	1 0.91 1.17	[Reference] (0.68–1.21) (1.01–1.36) <sup>°</sup>	$mOR > fOR^{**}$	
Received provider recommendation of F No Yes	IPV vacci 1 8.61	ne [Reference] (7.36–10.08) <sup>**</sup>	1 3.23	[Reference] (2.82–3.71)**	$mOR > fOR^{**}$	
Mother's education level College graduate Some college High school Less than high school	1 0.68 0.93 1.28	[Reference] (0.57–0.81)** (0.75–1.14) (0.97–1.69)	1 0.87 1.30 1.99	[Reference] (0.75–1.02) (1.09–1.55)** (1.56–2.53)**	$\begin{array}{l} mOR < fOR^{^\circ} \\ mOR < fOR^{^\circ} \\ mOR < fOR^{^\circ} \end{array}$	

*Note:* Variables in Tables 2 and 3 were investigated in a same logistic regression model. OR: odds ratio. CI: confidence interval. mOR: males OR. fOR: females OR.  $_{*p}^{*} < 0.05$ .

p < 0.01.

#### 3.3. Willingness to vaccinate and reasons for refusals

Parents of female adolescents who had not been vaccinated stated they were either very likely or somewhat more likely to vaccinate their children (39.4%, n=6106) compared to parents of males (35.5%, n=8925) (p < 0.05). For those parents who reported they were not likely to complete the vaccination for their child, the most common reasons differed by gender. In the case of adolescent males, 23.7% of parents said a HPV vaccination was never recommended by their health care providers, while 17.6% of parents of females said the vaccination was unnecessary. Since the vaccination rate was lower among males, we show the parental reasons for declining vaccination stratified by gender (Table 4). Three barriers were mentioned by both parents of males and females, but each of the reasons was found to be statistically significant by gender (p < 0.05).

# 4. Discussion

In this national sample of adolescents, based on data collected between 2012 and 2014, HPV vaccination rate differs by gender. While vaccination rates increased over this two-year period for males, they were relatively unchanged for females. The increase in vaccination rate for males in this study is likely influenced by the 2011 ACIP recommendation, which shifted the key message to providers and to the general population from "may be given to males" to "males should receive the vaccination." A similar rapid increase in vaccination rates for adolescent females was also noted in 2008 following the CDC recommendation that all female adolescents be given the immunization (from 25.1% in 2007 to 48.7% in 2010) [19]. Our finding that HPV vaccination coverage rate is higher among female versus male teens and that male coverage increased during the period from 2012 to 2013 was also reported by Elam-Evans et al. [20]. We also found differences for non-vaccination by gender similar to those reported by the CDC [19] and Stokley et al. [21] Our study, however, builds on these works by revealing specific variables associated with vaccination coverage by gender.

First, we observed a significant interaction between gender and age. While vaccination rates for females increase as girls became older, the vaccination rate for males stayed stable across the 14–17 year age range. The difference, however, between 17 year old males and females may simply reflect more years of eligibility among 17 year old females, because females aged 17 in 2013 would have had six years in which they were age-eligible and HPV vaccination was a routine recommendation [2]. Why we found a delay in vaccinating females from the recommended age (11–12) may also be related to parents' concern about their daughters becoming sexually active after being vaccinated, which is suggested by the interviews with parents and caregivers [22].

#### Table 3

Multivariate logistic regression analyses for HPV vaccine initiation among adolescents aged 13–17 years, 2012–2013 National Immunization Survey-Teen (NIS-Teen): variables with non-significant interactions.

Variables with non-significant interactions	Multivariate ( $n=38,705$ )		
	OR	95% CI	
Teen characteristics Number of visits to doctors in a previous ye None 1 2-3	ear 1 1.28 1.42	[Reference] (1.09–1.49) (1.23–1.64)	
4+ Received meningococcal vaccine No Yes	1.38 1 6.10	(1.18–1.62) [Reference] (5.23–7.13)**	
Received Td/Tdap No Yes	1 1.69	[Reference] (1.38–2.08)**	
Mother characteristics Mother's age (years) 45+ 35-44 <35	1 1.08 1.28	[Reference] (0.97–1.19) (1.06–1.55)**	
Mother's marital status Married Not married	1 1.22	[Reference] (1.09–1.36)**	
Household characteristics Poverty status Below poverty Above poverty, ≤ \$75,000 Above poverty, > \$75,000	1 0.64 0.67	[Reference] (0.55–0.74)** (0.56–0.79)**	
Census region South Midwest Northeast West	1 1.03 1.07 1.45	[Reference] (0.92–1.15) (0.95–1.20) (1.26–1.67)**	
Number of children 1 2–3 4+	1 1.04 0.96	[Reference] (0.94–1.16) (0.80–1.14)	

*Note:* Variables in Tables 2 and 3 were investigated in a same logistic regression model. Td/Tdap=Tetanus-diphtheria/Tetanus-diphtheria-acellular-pertussis vaccine. OR: odds ratio. CI: confidence interval.

<sup>\*\*</sup> *p* < 0.01.

We also found a significant interaction between race/ethnicity of the adolescent and gender, especially among non-Hispanic Black adolescents. Non-Hispanic Black males were more likely to be vaccinated, while non-Hispanic Black females were less likely to be vaccinated compared to Whites. Similar findings have been also reported in other studies for males [4,23,24] and females [25,26]. One explanation for a higher vaccination rate among Black males was suggested by Perkins et al. [27], who noted that Black or Latino parents are more amenable than Whites to vaccinate their sons against HPV. Perkins et al. also found that Black and Latino parents believed that vaccine mandates would prevent their children from having the unintended consequences of unprotected sex [27]. This finding is noteworthy since the incidence rate of penile cancer is higher among Blacks and Hispanics [28] compared with Whites and non-Hispanics. Also, non-White adolescent males were more likely to have sexual intercourse before 13 years: Black male (24%), Hispanic male (9.2%) and White male (4.4%) [29]. On the other hand, one potential explanation for our finding that non-Hispanic Black females are less likely to be vaccinated may be that concern about the vaccine's safety is pronounced in some Black mothers of girls [22].

#### Table 4

Main reasons of not vaccinating adolescents aged 13-17 years by a gender, 2012-2013 National Immunization Survey-Teen (NIS-Teen).

	Male ( <i>n</i> =18,269)			Female ( <i>n</i> =12,115)		
	Rank	Count	(Weighted %)	Rank	Count	(Weighted %)
Not recommended	1	4268	(23.7%)	2	1918	(16.4%)
Not needed or not necessary	2	3645	(19.9%)	1	2244	(17.6%)
Lack of knowledge	3	2853	(15.9%)	3	1583	(13.4%)
Not sexually active	4	1364	(7.4%)	5	1051	(8.3%)
Safety concern/side effects	5	1008	(5.6%)	4	1544	(12.8%)
Not a school requirement	6	657	(3.6%)	9	310	(2.9%)
Child is male	7	640	(3.6%)	-	-	-
Not appropriate age	8	536	(2.8%)	6	528	(4.1%)
Family/parental decision	9	456	(2.7%)	7	463	(3.6%)
Costs	10	298	(1.8%)	12	197	(1.7%)

*Note:* Table shows raw frequencies and weighted proportions. Each of the reasons was found to be statistically significant by gender (p < 0.05). HCP: health care provider

A health care provider's recommendation to vaccinate for HPV was more strongly associated with males being vaccinated compared to females. Our finding may very well be an artifact of the more recent introduction of the guidelines for male vaccination compared to those for females [2,3]. It is possible that this finding merely reflects an openness among parents of males who may have been relatively unaware of HPV vaccination for their male children until it was recommended by their healthcare provider; which may contrast with a closed mindset – either positive or negative – among parents of female children. Because HPV vaccination has been highly publicized by the media, in both positive and negative ways, many parents of females may be coming to the physician with their minds already made up to either accept or reject vaccination, thus the doctor's recommendation may very well have become less influential.

Regardless of gender, adolescents who received a meningococcal or Td/Tdap vaccine were likely to also have HPV vaccination. This finding was not unexpected since quadrivalent HPV vaccine may be given concomitantly with Tdap or meningococcal vaccine [30]. Other studies have also reported associations between receiving Tdap and/ or MCV and HPV [31]. Finally, adolescents living in poverty had higher vaccination coverage based on provider report. This finding may have been influenced by the availability of full coverage of HPV vaccine for children enrolled in government insurance or entitlement programs, while children enrolled in commercial health plans may have had higher out-of-pocket expenses; however, the cost of the vaccine was rarely mentioned by our subjects as a barrier to vaccination. Also, we were not able to determine what proportion of plans were not covering vaccination during the study period.

This study has both strengths and limitations. This large national level sample included families reached by either a landline phone or by cellphone, thus offering greater generalizability compared to previous studies [11,26]. The primary outcome was measured from immunization records and is believed to provide a more accurate measure of vaccination compared to shot cards or parent recall [32,33]. However, the following limitations should be considered when interpreting these findings. First, our findings did not include children 11 or 12 years old. Due to the cross-sectional nature of data collection, we recommend against using this study's findings to predict vaccination beyond the time it was measured for each subject. Also, we pooled NIS-Teen data 2012 and 2013, thus the association reported in this study might not be directly applicable for each year. Other potentially important variables, such as whether a subject was enrolled in particular entitlement programs (e.g.

Vaccines for Children) and subject's health perceptions about their perceived susceptibility, severity, or benefits of vaccination [23,26,34], were not included in NIS Teen 2012–2013, which may have limited the predictive ability of the model. However, we were able to investigate certain subsets of VFC eligibility such as uninsured or Medicaid covered adolescents. Lastly, despite incorporation of weights in the model, nonresponse bias might remain. Nevertheless, our study included variables at the adolescent, mother, and household level to control multiple unmeasured factors possibly related to HPV vaccination.

# 5. Conclusion

HPV Vaccination rates for both adolescent males and females have increased compared to previous reports. Even after strong recommendations to vaccinate adolescent males, vaccination rates remain lower for males compared to females. We found a significant gender interaction with several socio-demographic variables in predicting vaccination, including age, race/ethnicity, mother's education level, healthcare coverage and providers' recommendations to vaccinate. However, these gender differences may be partially an artifact of timing, because male vaccination became routine approximately five years after female vaccination.

# Sources of funding

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

#### **Disclosure of potential conflicts**

Dr. Eworuke disclosed that this work was completed while all authors were affiliated with the University of Florida. The views expressed were those of the authors and not necessarily those of the US Department of Health and Human Services or the FDA.

#### References

- J.M. Palefsky, Human papillomavirus-related disease in men: not just a women's issue, J. Adolesc. Health 46 (2010) S12–S19.
- [2] Centers for Disease Control and Prevention (CDC), Quadrivalent human papillomavirus vaccine recommendations of the advisory committee on immunization practices (ACIP), 2007, Morb. Mortal. Wkly. Rep. 56 (2007) 1–24.
- [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, Morb. Mortal. Wkly. Rep. 60 (2011) 1705–1708.
- [4] M.B. Gilkey, J.L. Moss, A.L. McRee, N.T. Brewer, Do Correl. HPV 30 (2012) 5928–5934.
- [5] J.D. Allen, M.K. Othus, R.C. Shelton, Y. Li, N. Norman, L. Tom, et al., Parental decision making about the HPV vaccine, Cancer Epidemiol. Biomark. Prev. 19 (2010) 2187–2198.
- [6] Centers for Disease Control and Prevention (CDC), HPV Vaccine-Questions & Answers Web sites, Available at: (http://www.cdc.gov/vaccines/vpd-vac/hpv/ vac-faqs.htm) (accessed 22.02.14).
- [7] R.B. Perkins, G. Apte, C. Marquez, C. Porter, M. Belizaire, J.A. Clark, et al., Factors affecting human papillomavirus vaccine use among White, Black and Latino parents of sons, Pediatr. Infect. Dis. J. 32 (2013) e38–e44.
- [8] J.R. Cates, N.T. Brewer, K.I. Fazekas, C.E. Mitchell, J.S. Smith, Racial differences in HPV knowledge, HPV vaccine acceptability, and related beliefs among rural, southern women, J Rural. Health. 25 (2009) 93–97.
- [9] T.L. Thomas, O. Strickland, R. Diclemente, M. Higgins, An opportunity for cancer prevention during preadolescence and adolescence: stopping human

papillomavirus (HPV)-related cancer through HPV vaccination, J. Adolesc. Health 52 (2013) S60–S68.

- [10] Centers for Disease Control and Prevention (CDC), About the National Immunization Survey Websites, Available at: <a href="http://www.cdc.gov/nchs/nis/about\_nis.htm">http://www.cdc.gov/nchs/nis/about\_nis.htm</a>) (accessed 12.05.14).
- [11] U.S. Department of Health and Human Services (DHHS), National Center for Health Statistics, The 2012 National Immunization Survey-Teen, Centers for Disease Control and Prevention, Hyattsville, MD, 2013.
- [12] U.S. Department of Health and Human Services (DHHS), National Center for Health Statistics, The 2013 National Immunization Survey-Teen, Centers for Disease Control and Prevention, Hyattsville, MD, 2014.
- [13] N. Jain, J.A. Singleton, M. Montgomery, B. Skalland, Determining accurate vaccination coverage rates for adolescents: the National Immunization Survey-Teen 2006, Public Health Rep. 124 (2009) 642–651.
- [14] Centers for Disease Control and Prevention (CDC), Finding and Paying for Vaccines web sites, Available at: (http://www.cdc.gov/vaccines/adults/findpay-vaccines.html) (accessed 28.06.14).
- [15] Association of Maternal and Child Health Programs (AMCHP), The HPV Vaccine: Background, Coverage & Benefits. AMCHP FACT SHEET, Association of Maternal and Child Health Programs, Washington, DC, 2007.
- [16] National Cancer Institute (NCI), Human Papillomavirus (HPV) Vaccines Websites, Available at: <a href="http://www.cancer.gov/cancertopics/causes-prevention/risk/infectious-agents/hpv-vaccine-fact-sheet">http://www.cancer.gov/cancertopics/causes-prevention/ risk/infectious-agents/hpv-vaccine-fact-sheet</a> (accessed 23.04.14).
- [17] P. Peduzzi, J. Concato, E. Kemper, T.R. Holford, A.R. Feinstein, A simulation study of the number of events per variable in logistic regression analysis, J Clin. Epidemiol. 49 (1996) 1373–1379.
- [18] C. Salmond, Fitting complex models using Health Survey data, Available at: (http://www.otago.ac.nz/wellington/otago020178.pdf) (accessed 20.10.14).
- [19] Centers for Disease Control and Prevention (CDC), Human papillomavirus vaccination coverage among adolescent girls, 2007–2012, and postlicensure vaccine safety monitoring, 2006–2013–United States, 2013, Morb. Mortal. Wkly. Rep. 62 (2013) 591–595.
- [20] L.D. Elam-Evans, D. Yankey, J. Jeyarajah, J.A. Singleton, R.C. Curtis, J. MacNeil, et al., National, regional, state, and selected local area vaccination coverage among adolescents aged 13--17 years—United States, 2013, Morb. Mortal. Wkly. Rep. 63 (2014) 625–633.
- [21] S. Stokley, J. Jeyarajah, D. Yankey, M. Cano, J. Gee, J. Roark, et al., Human papillomavirus vaccination coverage among adolescents, 2007–2013, and postlicensure vaccine safety monitoring, 2006–2014–United States, Morb. Mortal. Wkly. Rep. 63 (2014) 620–624.
- [22] L.A. Marlow, J. Wardle, J. Waller, Attitudes to HPV vaccination among ethnic minority mothers in the UK: an exploratory qualitative study, Hum. Vaccin. 5 (2009) 105–110.
- [23] P.L. Reiter, M.B. Gilkey, N.T. Brewer, HPV vaccination among adolescent males: results from the National Immunization Survey-Teen, Vaccine 31 (2013) 2816–2821.
- [24] A.F. Dempsey, A. Butchart, D. Singer, S. Clark, M. Davis, Factors associated with parental intentions for male human papillomavirus vaccination: results of a national survey, Sex. Transm. Dis. 38 (2011) 769–776.
- [25] A.N. Polonijo, R.M. Carpiano, Social inequalities in adolescent human papillomavirus (HPV) vaccination: a test of fundamental cause theory, Soc. Sci. Med. 82 (2013) 115–125.
- [26] C.G. Dorell, D. Yankey, T.A. Santibanez, L.E. Markowitz, Human papillomavirus vaccination series initiation and completion, 2008–2009, Pediatrics 128 (2011) 830–839.
- [27] R.B. Perkins, H. Tipton, E. Shu, C. Marquez, M. Belizaire, C. Porter, et al., Attitudes toward HPV vaccination among low-income and minority parents of sons; a gualitative analysis, Clin. Pediatr. 52 (2013) 231–240.
- [28] Centers for Disease Control and Prevention (CDC), Human papillomavirusassociated cancers—United States, 2004–2008, Morb. Mortal. Wkly. Rep. 61 (2012) 258–261.
- [29] L. Kann, S. Kinchen, S.L. Shanklin, K.H. Flint, J. Kawkins, W.A. Harris, et al., Youth risk behavior surveillance–United States, 2013, MMWR Surveill. Summ. 63 (Suppl. 4) (2014) 1–168.
- [30] GARDASIL [package insert], Merck & Co, Whitehouse Station, NJ, 2011.
- [31] R.B. Perkins, S.B. Brogly, W.G. Adams, K.M. Freund, Correlates of human papillomavirus vaccination rates in low-income, minority adolescents: a multicenter study, J. Womens Health 21 (2012) 813–820.
- [32] C.G. Dorell, N. Jain, D. Yankey, Validity of parent-reported vaccination status for adolescents aged 13–17 years: National Immunization Survey-Teen, 2008, Public Health Rep. 126 (Suppl. 2) (2011) 60–69.
- [33] R.P. Ojha, J.E. Tota, T.N. Offutt-Powell, J.L. Klosky, R. Ashokkumar, J.G. Gurney, The accuracy of human papillomavirus vaccination status based on adult proxy recall or household immunization records for adolescent females in the United States: results from the National Immunization Survey-Teen, Ann. Epidemiol. 23 (2013) 281–285.
- [34] SJ. Hanley, E. Yoshioka, Y. Ito, R. Konno, Y. Hayashi, R. Kishi, et al., Acceptance of and attitudes towards human papillomavirus vaccination in Japanese mothers of adolescent girls, Vaccine 30 (2012) 5740–5747.