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Human papillomavirus vaccination coverage among females and males, National Health and Nutrition Examination Survey, United States, 2007–2016 ⋆

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Abstract

Background—Human papillomavirus (HPV) vaccination has been routinely recommended at age 11–12 years in the United States for females since 2006 and males since 2011. Coverage can be estimated using self/parent-reported HPV vaccination collected in the National Health and Nutrition Examination Survey (NHANES) for a wider age range than other national surveys. We assessed vaccination coverage in 2015–2016, temporal trends by age, and the validity of self/parent-reported vaccination status.

Methods—Participants aged 9–59 years completed an interview collecting demographic and vaccination information. Weighted coverage was estimated for two-year NHANES cycles by age group for 2007–2008 to 2015–2016 for females (N = 14318) and 2011–2012 to 2015–2016 for males (N = 7847). Temporal trends in coverage were assessed from 2007–2008 to 2011–2012 for females and from 2011–2012 to 2015–2016 for both sexes. Sensitivity and specificity of self/parent-reported vaccination were assessed using provider-verified vaccination records from a pilot study in 14–29 year-olds.

Results—In 2015–2016, ≥1 dose coverage among females was highest in 14–19 (54.7%) and 20–24 (56.0%) year-olds and lower in successively older age groups. Among males, ≥1 dose coverage was highest in 14–19 year-olds (39.5%) and lower at older ages. Coverage was similar in 9–13 year-old females and males. Between 2007–2008 and 2011–2012, there were increases among females younger than 30 years. Between 2011–2012 and 2015–2016, there were increases among female age groups including 20–39 year-olds; male coverage increased among ages 9–13, 14–19, and 20–24 years. Self/parent-reported receipt of ≥1 dose had a sensitivity and specificity of 87.0% and 83.3%. Performance was lower for 3 doses.

⋆The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.vaccine.2018.03.083.

Declarations of interest

None.

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Conclusions—While overall HPV vaccination coverage remains low, it is higher in females than males, except in 9–13 year-olds. There have been increases in coverage among many age groups, but coverage has stalled in younger females. Adequate validity was demonstrated for self/parent-reported vaccination of ≥1 dose, but not 3 doses, in a pilot study.

Keywords

Human papillomavirus; HPV vaccine; Vaccination coverage; Temporal trends; National Health and Nutrition Examination Survey

1. Introduction

In the United States, routine vaccination with human papillomavirus (HPV) vaccine has been recommended at age 11–12 years for females since 2006 and for males since 2011. The vaccination series may be initiated at age 9 years. Vaccination is also recommended for females through age 26 years and for males through age 21 years [1,2].

National coverage of HPV vaccination in 13–17 year-olds is monitored through the National Immunization Survey-Teen (NIS-Teen), which is conducted annually and collects provider-verified vaccination history. Data from NIS-Teen have shown increases in HPV vaccination coverage since routine vaccination was recommended, but coverage has lagged behind other adolescent vaccines [3]. The National Health Interview Survey (NHIS) collects self-reported vaccination history from adults ages 18 years and older; published reports have included HPV vaccination coverage among 19–26 year-olds [4].

Parent or self-reported vaccination history is also collected in the National Health and Nutrition Examination Survey (NHANES), which can be used to assess national vaccination coverage across a wider age range than currently reported for other surveys. NHANES began including questions on HPV vaccination among 9–59 year-olds in 2007 for females [5] and 2011 for males [6]. This survey is a continuous, nationally representative survey that can be used to evaluate coverage estimates in two-year data release cycles. While validity assessments have been performed on NIS-Teen's parent-reported vaccination status [7,8], there are no data on the validity of the self/parent-reported vaccination status collected using NHANES. The present study aims to (1) estimate HPV vaccination coverage of ≥1 dose, coverage of 3 doses, and age at vaccination in 2015–2016; (2) assess temporal trends in vaccination coverage by age group from 2007–2008 to 2015–2016 for females and 2011–2012 to 2015–2016 for males; and (3) assess the validity of self/parent-reported vaccination status in NHANES.

2. Materials and methods

2.1. Data source and analytic sample

NHANES is an ongoing cross-sectional survey administered by the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention (CDC) and designed to be nationally representative of the non-institutionalized, civilian population living in the United States. Detailed survey methods are described previously [9]. Briefly, participants completed an in-home interview that included the collection of demographic

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and vaccination information. Informed consent was obtained from all participants or their guardians. A proxy completed the interview for participants under the age of 16 years or who were unable to complete the interview themselves. Data collection was approved by the NCHS Research Ethics Review Board. Data from the following cycles were used: 2007–2008 (females only), 2009–2010 (females only), 2011–2012, 2013–2014, and 2015–2016.

Average in-home interview response rates for each NHANES cycle ranged from 62.6% in 2015–2016 to 79.7% in 2009–2010 for females and from 60.1% in 2015–2016 to 72.7% in 2011–2012 in males. A total of 14,865 females and 8525 males were interviewed. Of these, 14,318 (96.3%) females and 7847 (92.0%) males had information on HPV vaccination and were included in the study.

Receipt of ≥1 dose was defined based on a response of Yes/No to “Have you ever received one or more doses of the HPV vaccine?” Receipt of 3 doses was categorized based on self-reported number of doses. In total, 116 females and 100 males reported having received ≥1 dose but were missing number of doses. They were excluded from estimations of 3 dose coverage. Age was categorized as 9–13, 14–19, 20–24, 25–29, 30–34, 35–39, and 40–59 years old. Age at vaccination was assessed by self/parent-reported age at receipt of first vaccine dose.

In 2016, we conducted a pilot study to determine the feasibility of incorporating provider verification of vaccination status into NHANES for 14–29 year-olds. This pilot study was conducted at a limited number of NHANES locations in 2016 and is not nationally representative. During the interview, participants were asked to sign an authorization for the disclosure of vaccination records. If signed, participants were asked to provide contact information for all healthcare providers since 2006. Providers were sent information on the pilot study and NHANES, authorization to disclose vaccination records, and a vaccination questionnaire collecting HPV vaccination administration dates and whether the provider administered the vaccination. A dose was considered valid if an administration date was available, regardless of location of administration.

2.2. Data analysis

We estimated ≥1 dose and 3 dose HPV vaccination coverage by age group in 2015–2016. All estimates were weighted using the interview sample weights to account for unequal probability of selection and non-response. Estimates were calculated using complex survey design methods [10]. Coverages of ≥1 dose and 3 doses in males were compared to females in each age group using a *t*-test. We estimated the median and interquartile range (IQR) of age at vaccination by age group and sex. Due to small sample sizes resulting from low coverage and non-response for age at first dose, median age at vaccination is not reported for males ≥25 years.

To evaluate trends in coverage over time, we assessed coverage among 9–39 year-olds in 2007–2008 to 2015–2016 for females and 2011–2012 to 2015–2016 for males; 40–59 year-olds were excluded due to very low coverage. Trends in weighted vaccination coverage across survey cycle were assessed using the stratum-adjusted Cochran-Mantel-Haenszel statistic for trend. To account for a nonlinear pattern in coverage among females across all

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survey cycles, trends in females were assessed separately for 2007–2008 to 2011–2012 and 2011–2012 to 2015–2016.

Provider-verified data from the pilot study were used to calculate the sensitivity, specificity, and Cohen's kappa statistic (agreement) of self/parent-reported receipt of ≥1 dose and 3 doses, using provider-verified vaccination as the gold standard. This was performed using data from 14–29 year-olds, as well as restricted to 14–19 year-olds. All pilot study data estimates were unweighted since the pilot was not designed to be nationally representative. Confidence intervals (CI) for sensitivity and specificity were calculated using the Clopper-Pearson estimation method.

Data management and analysis were performed in SAS 9.3 (SAS Institute, Cary, NC) and SAS-callable SUDAAN 11.0 (RTI International, Research Triangle Park, NC). All statistical tests with a 2-tailed p-value < 0.05 were considered statistically significant. Estimates with a relative standard error (RSE) >30% are noted.

3. Results

3.1. Coverage and age at vaccination in 2015-2016

Coverage with ≥1 dose among females in 2015–2016 was highest in 14–19 (54.7%) and 20–24 (56.0%) year-olds and lower in each successively older age group (Table 1). Among males, ≥1 dose coverage was highest in 14–19 year-olds (39.5%) and lower in older age groups. Among 9–13 year-olds, females (22.4%) and males (24.2%) had similar ≥1 dose coverage. Coverage was also similar, but very low, in 40–59 year-old females and males; neither sex would have been age-eligible for vaccination. Females had significantly higher ≥1 dose coverage than males in all other age groups.

Coverage of 3 doses among females was highest and similar in 14–19 and 20–24 year-olds (32.5%) and, among males, highest in 14–19 year-olds (20.3%). In 9–13 year-olds, females (8.7%) and males (8.2%) had similar coverage. Coverage among 35–39 and 40–59 year-olds was also similar in females and males; both age groups had very low coverage. Females had significantly higher 3 dose coverage than males in all other age groups.

In 2015–2016, among females (n = 554) and males (n = 268) ages 9–59 who reported age at first HPV vaccination, 21.5% and 42.9% were vaccinated before age 13 years, 72.1% and 53.6% were vaccinated at age 13–26 years, and 6.3% and 3.5% were vaccinated at age 27 years or older. The median (IQR) age at vaccination by age group is presented for 9–59 year-old females and 9–24 year-old males (n = 243) in Table 2. A majority of 14–19 year-old females reported receipt of their first dose near the age of the routine recommendation, 11–12 years; their median (IQR) age at vaccination was 12.8 (11.8–13.9) years. Age at vaccination was higher in each successively older age group. Among 30–34 year-old females, the oldest age group entirely covered under the catch-up recommendation based on age in 2006, the median age at first dose was 24.9 (22.0–25.9) years. In 9–13 and 14–19 year-olds, age at vaccination was comparable in females and males.

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3.2. Temporal trends in coverage by age group

Trends in coverage were examined for 9–39 year-olds by age group. For females, ≥1 dose coverage increased significantly from 2007–2008 to 2011–2012 in 9–13, 14–19, 20–24, and 25–29 year-olds and from 2011–2012 to 2015–2016 in 20–24, 25–29, 30–34, and 35–39 year-olds (Fig. 1 and Supplemental Table 1). For males, ≥1 dose coverage increased significantly from 2011–2012 to 2015–2016 in 9–13, 14–19, and 20–24 year-olds.

Coverage of 3 doses of HPV vaccine had similar trends as ≥1 dose coverage across age groups for both sexes (Fig. 2 and Supplemental Table 2). Among females, receipt of 3 doses showed a significant positive trend from 2007–2008 to 2011–2012 in 9–13, 14–19, 20–24, and 25–29 year-olds and from 2011–2012 to 2015–2016 in 25–29, 30–34, and 35–39 year-olds. Among males, there were significant positive trends in receipt of 3 doses from 2011–2012 to 2015–2016 in 9–13 and 14–19 year-olds.

3.3. Validity of self/parent-reported vaccination status

The pilot study included 235 14–29 year-olds. Of all participants, 182 (77.4%) provided authorization to contact providers, 128 (70.3%) of which had information from provider-returned vaccination records. Of those with provider-returned records, 106 (82.8%) had information on receipt of ≥1 dose and 103 (80.5%) had information on receipt of 3 doses from the NHANES immunization questionnaire and were used in validity analyses.

Among participants with provider-returned records and information from the NHANES immunization questionnaire, reported receipt of ≥1 dose from the NHANES questionnaire had a sensitivity of 87.0% (95% CI: 73.7–95.1) and a specificity of 83.3% (95% CI: 71.5–91.7). Agreement was 0.70 (95% CI: 0.56–0.83). Reported receipt of 3 doses had a lower sensitivity (66.7%; 95% CI: 44.7–84.4) and agreement (0.51; 95% CI: 0.31–0.70), but the specificity was comparable (86.1%; 95% CI: 76.5–92.8).

A sensitivity analysis was performed restricted to 14–19 year-olds to determine if the validity analysis was sensitive to participant age. Among participants who granted permission to contact providers, 14–19 year-olds were more likely to have providers return records than 20–29 year-olds (81.5% vs. 58.9%). When restricting to 14–19 year-olds (n = 62; n = 60 for analysis of validity of receipt of 3 doses), reported receipt of ≥1 dose had a sensitivity of 86.1% (95% CI: 70.5–95.3), comparable to 14–29 year-olds, and a specificity of 96.2% (95% CI: 80.4–99.9), higher than in 14–29 year-olds. Agreement (0.81; 95% CI: 0.66–0.95) was also higher in the restricted analysis. Reported receipt of 3 doses showed a lower sensitivity (55.6%; 95% CI: 30.8–78.5) and agreement (0.46; 95% CI: 0.21–0.71) but similar specificity (88.1%; 95% CI: 74.4–96.0) to the validity analysis among 14–29 year-olds.

4. Discussion

This is the first report of HPV vaccination coverage from a national US survey across an age range spanning from preadolescence through decades of adulthood. In 2015–2016, we found similar ≥1 dose coverage in 14–19 and 20–24 year-old females (54.7% and 56.0%). For males, the highest ≥1 dose coverage was in 14–19 year-olds (39.5%). Coverage for females

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was higher than males in nearly every age group. However, coverage was similar for 9–13 year-olds, suggesting sex differences in coverage may diminish in the future.

In the United States, HPV vaccination coverage at the routine age (i.e., 11–12 years old) has been below the Healthy People 2020 coverage goal of 80% [11,12]. Females 13–26 years old may be vaccinated as part of catch-up vaccination [2]. Therefore, coverage for each age group, especially among 14–19 and 20–24 year-olds currently, is a combination of both routine and catchup vaccination. There is evidence from NIS-Teen that vaccination at the routine age has been increasing across birth cohorts, but there is still a substantial proportion of females initiating the vaccine series after age 11–12 years [11]. Similarly, in NHANES, while most 20–24 year-old females in 2015–2016 reported receiving their first vaccine dose in their teens (median: 15.2 years), most 14–19 year-olds reported receiving their first dose near the routine target age (median: 12.8 years).

Estimated HPV vaccination coverage of ≥1 dose, based on data in NHANES, increased in both females and males following routine recommendations. Among females younger than 20 years old, reported coverage increased significantly during the survey cycles immediately following the routine recommendation but has stalled more recently, similar to data from NIS-Teen [3]. This suggests the need for additional efforts to increase coverage at the recommended age [13]. Coverage among females in their 20s has continued to increase since the routine recommendation. Among females in their 30s, increases in coverage began in 2011, primarily due to females vaccinated as part of catch-up vaccination aging into these age groups. Increases in coverage among males were limited to age groups included in the routine and catch-up recommendations (i.e., 9–24 year-olds). With time, increases in vaccination coverage should be seen in older females and males as younger vaccinated persons age into older groups.

NIS-Teen is the main national survey used to monitor HPV vaccination coverage and estimates coverage annually among 13–17 year-olds. In 2015, the estimated coverages for ≥1 dose and 3 doses were 62.8% and 41.9% for females and 49.8% and 28.1% for males [14]. Coverage estimates in 2016 were higher [3]. For comparison, 13–17 year-olds in NHANES in 2015–2016 had lower coverage, with coverage estimates for ≥1 dose and 3 doses of 54.6% and 32.1% for females and 40.6% and 20.7% for males. Variations in coverage estimates may be due to methodological differences between the two surveys. NIS-Teen uses provider-verified vaccination to estimate coverage. It samples from all 50 states and uses random digit dialing to identify parents/guardians of eligible adolescents to collect information on providers [15]. NHANES uses self/parent-reported vaccination, samples from 30 counties per two-year cycle, and interviews the participant themselves or, depending on age, their parent/guardian. Additionally, NIS-Teen has a lower overall response rate compared to NHANES [15].

Data on HPV vaccination coverage in adults is collected by NHIS. For 19–26 year-olds, ≥1 dose coverages for 2015 and 2016 were 41.6% and 48.5% in females and 10.1% and 13.5% in males [4,16]. These point estimates are lower than point estimates for 19–26 year-olds using NHANES, where coverage of ≥1 dose was 53.9% for females and 21.3% for males. Compared to NIS-Teen, NHIS is more methodologically similar to NHANES. NHIS uses

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self-reported vaccination, samples from a limited number of locations each year, and collects data using an in-home face-to-face interview [17]. Variations in coverage between NHIS and NHANES may be due to other differences. NHIS includes over 85,000 participants to provide estimates for each survey year while NHANES includes approximately 10,000 for every two-year cycle. Additional research is needed to understand the effect of methodological differences between these surveys on national coverage estimates.

A novel aspect of the current study is the validity assessment of self/parent-reported vaccination in 14–29 year-olds in NHANES using data from a feasibility pilot study with provider-verified vaccination records. A previous validity assessment comparing parent-reported HPV vaccination of ≥1 dose to provider-reported vaccination in NIS-Teen has shown minimal net bias in national coverage estimates [8] and 86% sensitivity, 87% specificity, and 73% agreement [7]. These are very comparable to our reported 87% sensitivity, 83% specificity, and 70% agreement for receipt of ≥1 dose. A validity assessment of receipt of 3 doses was also performed using NIS-Teen data, where findings were more optimistic with 72% sensitivity, 91% specificity, and 64% agreement [7] compared to our reported 67% sensitivity, 86% specificity, and 51% agreement. Restricting the validity analysis to 14–19 year-olds in the NHANES pilot showed similar specificity for receipt of 3 doses, but sensitivity and agreement were lower. These results suggest NHANES data are more valid for assessing receipt of ≥1 dose than receipt of 3 doses. Therefore, analyses, such as assessment of vaccine effectiveness, by number of doses may be misleading. Of note, the pilot study suggested that incorporating provider verification of vaccination records into NHANES would be challenging and likely not feasible using the design of the pilot study.

This study was subject to several limitations. First, with the exception of the data from the pilot study, vaccination status was collected using self/parent-report. However, coverage estimates in age groups who were not eligible for vaccination were very low, as expected based on recommended age for vaccination. Additionally, based on the validity analysis from our pilot study and previous assessments of self/parent-reported vaccination, reported receipt of ≥1 dose has adequate sensitivity, specificity, and agreement, suggesting minimal bias in estimates of coverage of ≥1 dose. There is more concern of recall bias for estimates of coverage of 3 doses. Second, the pilot study sample was not nationally representative and small; only 54.5% of participants had provider-returned records. Third, many coverage estimates were unstable. This was expected as coverage was low immediately following the start of the vaccination program and several groups were not age-eligible for vaccination.

In addition to providing vaccination coverage estimates, vaccination data can be combined with other data collected using NHANES. HPV DNA testing in self-collected vaginal swabs was incorporated into NHANES for females in 2003–2004 and continues to be collected. These data have provided some of the strongest data demonstrating impact of the HPV vaccination program in the United States in ecologic analyses [18-20]. HPV DNA testing in self-collected genital swabs was introduced for males in 2013–2014 [21]. In addition to evaluation of ecologic changes over time after introduction of HPV vaccine, vaccine effectiveness has been estimated for ≥1 dose of HPV vaccine using data from NHANES. Our findings suggest that the validity of the self/parent-reported data is sufficient for ≥1 dose

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but not for measures based on number of doses; data on individual number of doses should be interpreted with caution.

Data on overall HPV vaccination coverage across a wide age range in NHANES will provide useful information for assessment of the immunization program and can complement other coverage surveys. NHANES coverage estimates can also assist in interpreting data from monitoring projects that continue to evaluate the impact of the vaccination program in target as well as older age groups, where later endpoints (i.e., precancers, cancers) can be studied [22-24].

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

HPV	human papillomavirus
NHANES	National Health and Nutrition Examination Survey
NIS-Teen	National Immunization Survey-Teen
NHIS	National Health Interview Survey
NCHS	National Center for Health Statistics
CDC	Centers for Disease Control and Prevention
IQR	interquartile range

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CI	confidence interval
RSE	relative standard error

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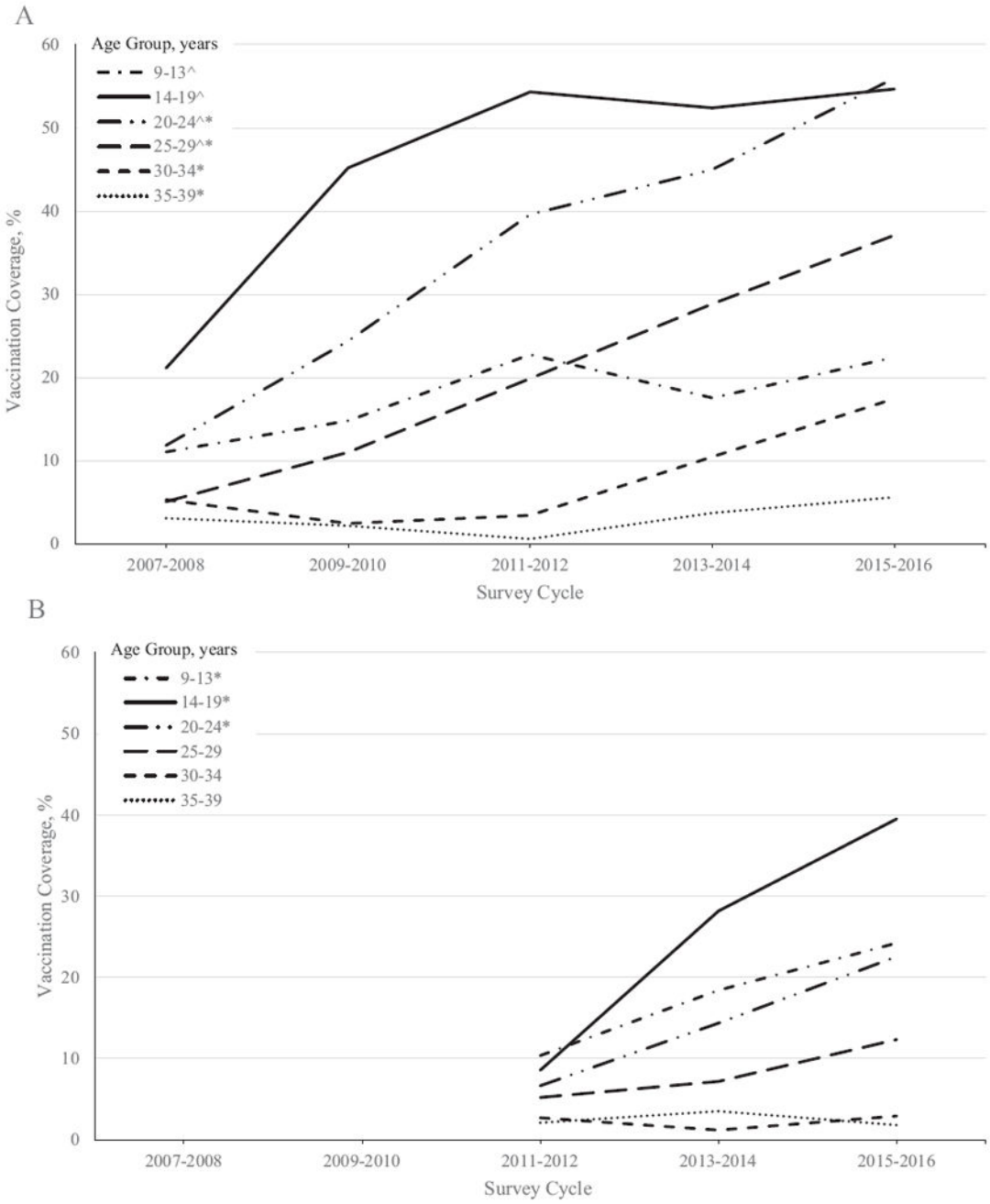

Fig. 1.

Human papillomavirus vaccination coverage of ≥1 dose by age group and survey cycle for females (A) and males (B). Coverage estimates are weighted and based on self/parent report. ^p for trend < 0.05 for 2007–2008 to 2011–2012; *p for trend < 0.05 for 2011–2012 to 2015–2016. Estimates with a relative standard error (RSE) between 30% and 50%: females: 2007–2008: ages 25–29, 35–39 years; 2009–2010: ages 30–34, 35–39 years; 2015–2016: ages 35–39 years; males: 2011–2012: ages 20–24, 25–29 years; 2013–2014: ages 25–29, 35–39 years; 2015–2016: ages 30–34, 35–39 years. Estimates with a RSE over 50%:

females: 2011–2012: ages 30–34, 35–39 years; males: 2011–2012: ages 30–34, 35–39 years; 2013–2014: ages 30–34 years.

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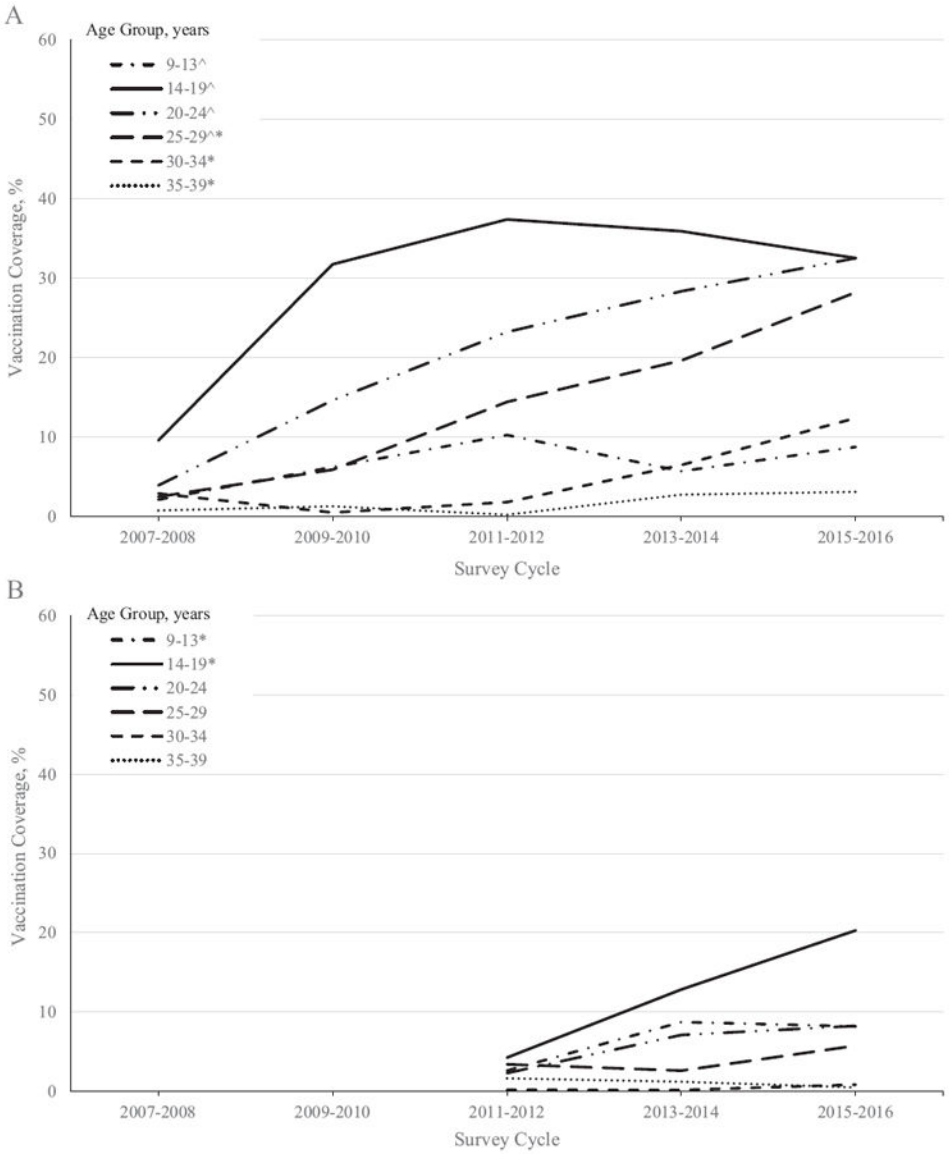

Fig. 2.

Human papillomavirus vaccination coverage of 3 doses by age group and survey cycle for females (A) and males (B). Coverage estimates are weighted and based on self/parent report. ˆp for trend < 0.05 for 2007–2008 to 2011–2012; *p for trend < 0.05 for 2011–2012 to 2015–2016. Estimates with a relative standard error (RSE) between 30% and 50%: females: 2007–2008: ages 9–13, 14–19, 20–24, 30–34 years; 2009–2010: ages 35–39 years; 2015–2016: ages 35–39 years; males: 2011–2012: ages 20–24 years; 2013–2014: ages 20–24 years; 2015–2016: ages 20–24, 25–29 years. Estimates with a RSE over 50%: females: 2007–2008: ages 25–29, 35–39 years; 2009–2010: ages 30–34 years; 2011–2012: ages 30–34, 35–39 years; males: 2011–2012: ages 9–13, 25–29, 30–34, 35–39 years; 2013–2014: ages 25–29, 30–34, 35–39 years; 2015–2016: ages 30–34 years.

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Table 1

Human papillomavirus vaccination coverage of ≥1 dose and 3 doses by sex and age group, 2015–2016.

Age group, years	Coverage of ≥1 dose			Coverage of 3 doses		
	Weighted % (95% CI)			Weighted % (95% CI)		
	Females	Males	p-value*	Females	Males	p-value*
	N = 2800	N = 2497		N = 2766	N = 2442	
9–13	22.4 (17.2–28.6)	24.2 (19.7–29.4)	0.58	8.7 (4.9–14.9)	8.2 (5.4–12.3)	0.84
14–19	54.7 (47.7–61.5)	39.5 (29.0–51.0)	0.02	32.5 (25.6–40.4)	20.3 (13.7–29.0)	<0.01
20–24	56.0 (45.9–65.6)	22.6 (15.4–31.8)	<0.01	32.5 (23.4–43.2)	8.3 (3.8–17.1)†	<0.01
25–29	37.1 (30.3–44.4)	12.3 (6.5–22.1)	<0.01	28.2 (21.0–36.7)	5.8 (2.1–15.0)†	<0.01
30–34	17.4 (11.9–24.8)	2.9 (1.3–6.5)†	<0.01	12.4 (7.5–19.8)	0.9 (0.2–3.1)‡	<0.01
35–39	5.6 (2.9–10.6)†	1.8 (0.7–4.7)†	0.02	3.1 (1.3–7.3)†	0.5 (0.3–0.9)	0.06
40–59	1.6 (0.8–3.0)	1.1 (0.5–2.3)†	0.41	0.3 (0.1–0.8)†	0.6 (0.1–2.7)‡	0.53

Coverage estimates are based on self/parent report.

CI, confidence interval.

*p-value from *t*-test comparing coverage in males and females.

†30% < relative standard error (RSE) ≤ 50%.

‡RSE > 50%.

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Table 2

Age at receipt of first human papillomavirus vaccine dose by sex and age group, 2015–2016.

	Age at vaccination, years Weighted median (IQR)	
Age group, years	**Females N = 554**	**Males N = 243**
9–13	10.8 (10.1–11.8)	11.0 (10.2–11.5)
14–19	12.8 (11.8–13.9)	12.6 (11.6–13.9)
20–24	15.2 (13.5–16.9)	16.6 (12.8–17.9)
25–29	17.7 (16.0–21.5)	–
30–34	24.9 (22.0–25.9)	–
35–39	27.9 (27.0–33.7)	–
40–59	39.4 (35.8–46.3)	–

IQR, interquartile range.