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Younger age at initiation of the Human Papillomavirus (HPV) vaccination series is associated with higher rates of on-time completion

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Abstract

Vaccination rates for human papillomavirus (HPV) have remained disappointingly low. It is critical to identify methods to increase on-time vaccine series completion rates (before 13 or 15 years). To determine whether younger age (9 to 10 years of age) at HPV vaccine series initiation was associated with improved on-time completion rates compared to initiation at 11 to 12 years, we examined the prevalence of on-time HPV vaccine series completion rates from August 2006 through December 2012 in a large, population-based cohort of children and adolescents (aged 9.5 to 27 years) residing in Olmsted County, MN on December 31, 2012 (n=36,223). We compared age at vaccine initiation between individuals who successfully completed both 2 and 3 doses of the vaccination series on-time (before age 13.5 or 15.0 years) using multivariate logistic regression. On-time completion of both 2 and 3 doses of the vaccine series by age 13.5 or 15.0 years was significantly associated with initiation at 9 to 10 years as compared to 11 to 12 years after adjusting for sex, race, insurance status, frequent health care visits, and year of first vaccination

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CONFLICT OF INTEREST STATEMENT

Robert M Jacobson serves on safety review committees monitoring studies funded by Merck & Co. regarding human papillomavirus vaccines. The authors declare that there are no other conflicts of interest.

(all $P<.01$). Interventions focused on beginning the vaccination series at 9 to 10 years of age may result in higher rates of timely series completion.

Keywords

Papillomavirus Vaccines; Vaccination; Immunization Programs; Immunization; Patient Acceptance of Health Care; Patient Compliance

INTRODUCTION

Human papillomavirus (HPV) is the most common sexually transmitted disease, with about 14 million incident HPV cases each year, (Centers for Disease Control and Prevention, 2012) and an overall prevalence of approximately 43% among women 14 to 59 years of age. (Hariri et al., 2011) While infection with HPV is asymptomatic, HPV can cause cervical cancer as well as many other anogenital and oropharyngeal cancers. (Chaturvedi et al., 2011; Jayaprakash et al., 2011; Lowy et al., 2008) More than 33,000 new cases of HPV-caused cancers occur in the United States (US) each year. (Centers for Disease Control and Prevention, 2012)

The US Food and Drug Administration has licensed three HPV vaccines, the first two with high efficacy against the two strains of HPV that cause about 70% of cervical cancers (Gardasil® and Cervarix®). (Munoz et al., 2004; Schiffman et al., 2007) The third nonavalent vaccine received approval in December 2014 (Gardasil®9) and could potentially prevent 90% of cervical cancers. (Joura et al., 2015) Completion of the vaccine series prior to initiation of sexual activity is crucial for prevention of cervical cancers, since the vaccine is most effective in persons not previously exposed to HPV. (Herrero et al., 2011; Markowitz et al., 2014) Therefore, Healthy People 2020 has set a target for an 80% completion rate of the 3-dose HPV vaccine series for girls/women by 13 to 15 years of age. (Centers for Disease Control and Prevention, 2012) The rate of vaccine uptake has increased over time; however, the 2014 National Immunization Survey showed that only 39.7% of girls aged 13–17 years had completed the series. (Reagan-Steiner et al., 2015) In addition, only 21.6% of boys of the same age had completed the 3-dose series. (Reagan-Steiner et al., 2015)

The Advisory Committee on Immunization Practices (ACIP) recommends routine vaccination at 11 to 12 years of age but gives permission for use of the HPV vaccine beginning at 9 years of age. (Markowitz et al., 2014) Several studies indicate that earlier age at vaccination is associated with a stronger immune response, (Block et al., 2006; Giuliano et al., 2007; Reisinger et al., 2007) and the duration of protection of the HPV vaccines is known to be at least 8 to 9 years, with little evidence of waning immunity. (Ferris et al., 2014; Naud et al., 2014) Therefore, vaccination at earlier ages would still confer protection throughout adolescence and early adulthood. Furthermore, earlier initiation of the vaccine offers more time for completion of the series by the recommended ages. Earlier initiation of the vaccine could therefore offer the dual benefit of improved immunity and higher completion rates. It is unclear, however, whether younger age at initiation is associated with higher on-time completion rates of the vaccine series. We therefore hypothesized that initiating the HPV vaccine series at 9 to 10 years of age would be associated with a higher

rate of on-time completion of the 3-dose vaccine series compared to initiating the series at 11 to 12 years.

Finally, persistently poor HPV vaccine series completion rates by 13 to 15 years have prompted several studies examining the efficacy of a 2-dose, rather than a 3-dose series. Two doses of the HPV vaccine produce a non-inferior antibody response in healthy girls aged 9–14 years compared to three doses. (D'Addario et al., 2014) These findings form the basis of the current World Health Organization recommendations for completion of two doses of HPV vaccine among girls 9–13 years of age. (World Health Organization, 2015)

Although the United States has not yet adopted a 2-dose HPV vaccination policy, we also examined the association between age at vaccine initiation and on-time completion of two doses of the vaccine as a secondary outcome.

METHODS

Study Design and Population

We used the Rochester Epidemiology Project (REP) to identify all children and adolescents who were 9.5 to 27 years of age and residing in Olmsted County, Minnesota (MN) on December 31, 2012. Only those ages 9.5 and older (up to 27 years of age) on December 31, 2012 were included in the cohort, as younger children would not have had the opportunity to complete all three doses by December 31, 2012. Briefly, the REP links data on medical care delivered to the population of Olmsted County, MN. Primary care in this community is currently provided by a limited number of health care practitioners. These practitioners share their medical record information through the REP research infrastructure for approved research studies. (St Sauver et al., 2012; St Sauver et al., 2011) The dates of the health care visits to any of these practitioners are linked to addresses at the time of the visit, and this information is used to define who resided in Olmsted County at any given point in time since 1966 (REP Census). The population counts obtained by the REP Census are similar to those obtained by the US Census, indicating that virtually the entire population of the county is captured by the system. (St Sauver et al., 2011) We included in our analyses only those individuals who had given permission for their medical records to be used for research, and this study was approved by the Mayo Clinic and Olmsted Medical Center Institutional Review Boards.

Identification of Vaccines

We searched the REP electronic data to identify all HPV vaccinations received by the study population between August 2, 2006 and December 31, 2012, using the current procedural terminology (CPT) codes 90649 (Gardasil®) and 90650 (Cervarix). Gardasil®9 was not included in this study, because it was not available to this population during the study time frame.

In 2006, some of the health care practitioners in the study region began offering HPV vaccination at 9 to 10 years of age. However, because only some of the health care practitioners changed their practices, most children in the region continued to be eligible for the vaccine only at ages 11 to 12 years. This natural experiment made it possible for us to

compare the on-time vaccination completion rates between children initiating the series at different ages. Children and adolescents were defined as having completed the series if they had received three doses of the HPV vaccine with appropriate spacing by December 31, 2012. Appropriate spacing was defined according to recommendations from ACIP. (Centers for Disease Control and Prevention, 2010a, b) The second dose must have been administered at least 4 weeks (24 days) after the first dose. The third dose must have been administered at least 12 weeks (80 days) after the second dose, and at least 24 weeks (164 days) after the first dose. (Markowitz et al., 2014) A 4-day grace period was permitted at each dose. (Centers for Disease Control and Prevention, 2011) We excluded doses given before 9 years of age (n=7) except for those who received the first dose within 4 days of their 9th birthday (n=5) in accordance with the ACIP General Recommendations on Immunizations regarding minimal intervals and grace periods. (Centers for Disease Control and Prevention, 2011) Children were classified as having completed either 2 doses or the full 3-dose series on-time (by the recommended ages) or not on time.

Analysis

Characteristics of the study population were described overall, including the proportion of the population that had completed either 2 or 3 doses of the vaccine with appropriate spacing. The population was sub-set to those that had completed either 2 or 3 doses of the vaccine. Timely (or on-time) completion of the series was defined as completion of the vaccine by 13.5 or 15 years. Age 13.5 years was used to allow children who were almost 13 years old at time of initiation to complete the vaccine series within the recommended 6-month window. For example, if a child initiated the series at 12 years, 11 months, it would not be possible to complete the series by age 13.0 years, but the 6 month grace period would allow for completion. Timely completion of the series by age 15 was also assessed in accordance with Healthy People 2020 recommendations. (Centers for Disease Control and Prevention, 2011) A grace period was not applied to completion by age 15 because anyone who initiated the vaccine series prior to age 13 would have ample time to complete the series by age 15.

Sex, race, insurance status, high frequency of health care visits, year of series initiation, and proportion completing the series by 13.5 or 15 years of age (on-time completion) were compared between those that had initiated the series at 9 to 10 years vs. 11 to 12 years using Chi-square, Fisher's exact tests, or Wilcoxon rank-sum tests, as appropriate. The top 25th percentile of health care visits between 2006 and 2012 was used as a marker for high frequency of health care visits. Year of initiation of the vaccine series was examined to account for changing HPV immunization policies between 2006 and 2012.

Finally, the odds of timely completion of both 2- and 3-doses of the vaccine series by age, sex, race, insurance status, number of health care visits, and year of initial vaccination were modeled using logistic regression and summarized using odds ratios (ORs) and corresponding 95% confidence intervals (CIs).

RESULTS

Overall, 37,368 individuals between 9.5 and 27 years of age were identified as residents of Olmsted County, MN on December 31, 2012. Of these, 36,223 (97%) provided authorization for their records to be used in research and were included in this study. Characteristics of the study population are shown in Table 1. A total of 11,534 (31.8%) residents between the ages of 9.5 and 27 years had received at least one dose of the HPV vaccine, and 6,989 (19.3%) had received all three doses with appropriate timing between August 2006 and December 2012. Similarly, 9,283 (25.6%) residents had completed 2 doses of the vaccine series with appropriate timing (Table 1).

We next studied all children that had initiated the series between 9 and 12 years of age and completed 2 or 3 doses of the HPV vaccine series by December 31, 2012 (n=3,210 and 2,338 respectively). Overall, 97.5% of children who initiated their HPV vaccination at 9 to 10 years of age completed all three doses before 13.5 years of age compared to 78.0% who initiated their HPV vaccination at 11 to 12 years of age ($p<.001$; Table 2). Younger age at vaccine initiation was also associated with completion of 2 doses of the vaccine by 13.5 years of age ($p<.001$; Table 2). Similarly, younger age at initiation was also associated with completion of both 2 doses of the vaccine and the full 3 doses of the series before 15 years of age (both $p<.001$; Table 2).

The median duration of time between completion of the first and final dose of the 3-dose series was slightly longer among children that initiated the series at 9 to 10 years compared to children that initiated at 11 to 12 years (9.6 months vs 8.3 months; $p=0.006$). In addition, children that initiated the series at 9 to 10 years of age were more likely to be female, of a minority race or ethnicity, and have governmental insurance compared to children that initiated the series at 11 to 12 years (Table 2). The same characteristics were also associated with on-time completion of 2 doses of the vaccine (Table 2).

We hypothesized that the difference in characteristics between those that initiated the vaccine series at 9 to 10 years compared to 11to 12 years may have accounted for the association between age at vaccine initiation and on-time completion of the series. However, initiation of the vaccine series at 9 to 10 years compared to 11 to 12 years remained significantly associated with on-time completion of the series, even after adjusting for other characteristics (by 13.5 years OR: 12.82, 95% CI: 7.83, 20.99; by 15 years OR: 14.21; 95% CI: 4.97, 40.65; Table 3). Children who initiated the vaccine at 9 to 10 years compared to 11 to 12 years were also more likely to have completed 2 doses of the HPV series on time, even after adjusting for other characteristics (Table 4).

DISCUSSION

We found that found that earlier age of initiation (9 to 10 years of age) was associated with higher odds of timely completion of the HPV vaccine series by the ages recommended by ACIP. (Markowitz et al., 2014) Initiating routine HPV vaccination at 9 to 10 years instead of 11 years of age could increase timely completion rates of the HPV vaccine series. However, it is also possible that younger age at vaccine initiation is a surrogate marker for other

factors that should be identified and targeted to improve on-time completion of the HPV vaccine series.

Several studies have found that younger age at initiation is associated with higher overall HPV vaccine completion rates. (Hirth et al., 2012, 2013; Rubin et al., 2012) However, these studies have focused on overall completion rates, rather than completion of the vaccine series by 13 or 15 years of age. Completion of the HPV vaccine series by 13 or 15 years is recommended to ensure optimal protection prior to initiation of sexual activity, and is the basis for the ACIP recommendations. (Markowitz et al., 2014) The HPV vaccine series is not currently routinely recommended for children younger than 11 years of age, but some of the health care practitioners in our community began routinely offering the vaccine at 9 years of age in 2006, while the others continued standard of care by offering the vaccine at 11 years or older. The results of this natural experiment suggested that initiation of the vaccine series prior to age 11 was associated with higher rates of on-time completion of the full 3-dose series by the recommended ages.

We also found that initiating the vaccine at 9 to 10 years versus 11 to 12 years was associated with a higher likelihood of on-time completion of 2 doses of the vaccine. While the HPV vaccine series is not currently licensed for 2 doses in the United States, completion of 2 doses prior to initiation of sexual activity is the current recommendation by the World Health Organization. Multiple European countries have moved to a 2-dose schedule, and preliminary data from international studies indicate that even a single dose may provide acceptable levels of protection. (Kreimer et al., 2015; Sankaranarayanan et al., 2016) Our data are not completely comparable to studies specifically examining a 2-dose series, because the recommended spacing for two doses differs from that of a 3-dose series. (World Health Organization, 2015) However, if the United States adopts a 2-dose schedule in the future, our data suggest that younger age at initiation could also be associated with higher on-time completion rates of a 2-dose series.

Younger age at vaccine initiation could be a marker for several factors that could help improve on-time completion rates. For example, Rubin and colleagues found that patients who had received their vaccines from pediatricians were more likely to complete the HPV series than those who received their vaccines from other specialists. (Rubin et al., 2012) These authors speculate that pediatricians may be more comfortable with recommending vaccines and have better procedures for ensuring follow-up and completion rates. (Rubin et al., 2012) However, a recent report by Dunne and colleagues indicated that vaccine initiation rates were lowest among 11 to 12 year olds compared to those 13 years of age or older in persons continuously enrolled in a large, national private insurance plan, suggesting that vaccination rates are suboptimal even in 11 to 12 year olds. (Dunne et al., 2015) We were not able to examine the specialty of the health care practitioners that administered the vaccines in our population, and it is possible that those initiating at 9 to 10 years were more likely to be seen by a pediatric practice, while those initiating at 11 to 12 years may have been more likely to be seen by other specialties. Both groups, however, are well within the age range of pediatric patient populations. As such, differences in specialty may not account for our findings.

Younger age at vaccine initiation may also be a marker for more frequent use of health care in general. Dunne and colleagues reported that younger girls (11 to 12 years of age) had fewer missed opportunities to receive the HPV vaccine compared to older girls and women between 13 and 26 years of age. (Dunne et al., 2015) Increased health care visits may result in more opportunities for vaccination, and higher overall vaccination completion rates. In support of this hypothesis, we found that children that were in the upper quartile of health care visits for this period were more likely to complete the vaccine series on time. However, younger age at first vaccination remained significant after adjustment for this variable, suggesting that a higher number of visits alone does not account for the effect of earlier age at vaccine initiation on completion of the series.

Because the HPV vaccine is not routinely offered to children younger than 11 years, it is also possible that younger age at vaccine initiation is a marker of parental characteristics. For example, parents who initiated HPV vaccinations for their children at early ages may have been more knowledgeable and enthusiastic about the value of the vaccine, and thus more likely to ensure that their child completed the series. It is not possible in this study to separate possible parental enthusiasm from age at initiation. A randomized controlled trial would allow us to determine whether age at initiation is truly the causal factor, or whether parental enthusiasm is driving our findings.

Finally, children who initiated the vaccine series at a younger age may simply have had more time to complete the full vaccine series. Our data suggest that children that initiated the vaccine at 9 to 10 years did take slightly longer to complete the vaccine series than those that initiated at 11 to 12 years (9.6 months vs 8.3 months). This difference was quite small, but it is possible that just offering parents and children more time to complete the series could help to ensure higher on-time HPV vaccination completion rates.

An important consideration with regard to changing clinical practice to encourage HPV vaccination at an earlier age is that such a change would uncouple HPV vaccination from the Tdap and meningococcal conjugate vaccines (MCV) which are due at 11 years of age. In the initial recommendations for female HPV vaccination, the authors specifically cited the theoretical advantage of consolidating the vaccines to an adolescent platform at 11 years of age ensuring that adolescents receive all three vaccines. (Markowitz et al., 2007) Since then, however, the uptake rates of Tdap and MCV in the US have clearly exceeded the uptake rate of even the first dose of HPV. (Jacobson et al., 2015) Nevertheless, a randomized controlled trial to examine age at vaccine series initiation should also address this theoretical adverse impact.

Strengths of our study include our ability to examine an entire Midwestern population of children and adolescents, and to assess their HPV completion rates while residents of this community. However, we may have missed vaccinations that occurred among members of our population who received their vaccinations from a health care provider that did not participate in the REP. Therefore, our vaccination completion rates may be underestimates of the true HPV vaccine series completion rate in this population. Our results show low rates of completion of the 3-dose series, but completion rates were similar to rates in Minnesota and the rest of the United States in the same time frame, suggesting that we did not miss large

numbers of vaccinations. (Centers for Disease Control and Prevention, 2013; Jacobson et al., 2015) In addition, the factors that impact vaccination rates will vary within different populations and our results may not be generalizable to populations with very dissimilar characteristics. We also note that the odds ratios in this study cannot be interpreted as relative risks because the outcome is not a rare event. Interpretation of the odds ratios as relative risks would likely exaggerate the results. Unfortunately, we were not able to explore health system or parental characteristics that may have been associated with younger age at vaccine initiation in this study. Further research is needed to understand why younger age at vaccine initiation is associated with higher rates of completion to precisely pinpoint factors that can be modified to improve overall vaccine uptake rates.

CONCLUSION

Initiating the HPV vaccine series at 9 to 10 years of age was associated with higher rates of on-time vaccination completion compared to initiating at 11 to 12 years of age. These data suggest that immunization programs that begin vaccination against HPV in children 9 to 10 years could improve the likelihood of on-time HPV series completion, but further studies are necessary to determine if younger age at vaccination alone accounts for improved rates, or if age is a marker for other factors that should be targeted to improve on-time completion.

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HIGHLIGHTS

- Vaccination rates for the human papillomavirus (HPV) vaccine have remained disappointingly low.
- **Younger age at vaccine series initiation was associated with higher on-time completion rates of both 2 and 3 doses of the HPV vaccine.**
- **Beginning the series at 9 to 10 years may improve rates of on-time completion of the HPV vaccine series.**

TABLE 1

Characteristics of children and adolescents 9.5 to 27 years of age residing in Olmsted County, MN on December 31, 2012

Characteristic	N=36,223
Sex	
Boys/Men	16,906 (46.7)
Girls/Women	19,317 (53.3)
Age as of 12/31/2012 (years)	
9.5–<11	2,912 (8.0)
≥11–<13	3,648 (10.1)
≥13–<16	5,434 (15.0)
≥16–<22	11,316 (31.2)
≥22–<27	10,635 (29.4)
27	2,278 (6.3)
Race	
White	28,268 (78.0)
Asian	1,706 (4.7)
Black or African American	2,388 (6.6)
Other or unknown	3,861 (10.7)
Insurance status[a]	
No/unknown	6,437 (17.8)
Commercial	22,921 (63.3)
Government	4,589 (12.7)
Other	2,276 (6.3)
Completion of 2 doses of the HPV vaccine[b]	**9,283 (25.6)**
Duration between first and second dose (months), median (IQR)[c]	2.7 (2.1, 5.4)
Completion of 3 doses of the HPV vaccine[b]	**6,989 (19.3)**
Duration between first and third dose (months), median (IQR)[c]	2.5 (2.1, 4.5)

Abbreviations: IQR, interquartile range

Results presented as N (%) unless otherwise noted.

[a] Insurance status closest to August 2, 2006.

[b] Receipt of doses with appropriate timing (The second dose must have been administered at least 4 weeks (24 days) after the first dose. The third dose must have been administered at least 12 weeks (80 days) after the second dose, and at least 24 weeks (164 days) after the first dose. A 4-day grace period was permitted at each dose.)

TABLE 2

Comparison of characteristics between those initiating the HPV vaccine series at 9–10 years compared to 11–12 years

Characteristic	9–10 years	11–12 years	P[a]
Completed 3 doses of the vaccine[b]	**N=725**	**N=1,613**	
Duration between first and third dose (months), median (IQR)	9.6 (6.7, 17.0)	8.3 (6.5, 14.7)	0.006
Completed 3 doses of the vaccine by age 13.5	707 (97.5)	1,258 (78.0)	<0.001
Completed 3 doses of the vaccine by age 15	722 (99.6)	1,517 (94.0)	<0.001
Sex			0.008
Boys	16 (2.2)	72 (4.5)	
Girls	709 (97.8)	1,541 (95.5)	
Race			<0.001
White	537 (74.1)	1,365 (84.6)	
Asian	54 (7.4)	59 (3.7)	
Black or African American	59 (8.1)	60 (3.7)	
Other or unknown	75 (10.3)	129 (8.0)	
Insurance status[c]			<0.001
No/unknown	22 (3.0)	246 (15.3)	
Commercial	568 (78.3)	1,191 (73.8)	
Government	122 (16.8)	151 (9.4)	
Other	13 (1.8)	25 (1.5)	
Number of clinic visits > upper 25th percentile[d]	218 (30.1)	468 (29.0)	0.60
Year of first vaccination			0.12
2006	89 (12.3)	187 (11.6)	
2007	159 (21.9)	414 (25.7)	
2008	131 (18.1)	273 (16.9)	
2009	111 (15.3)	226 (14.0)	
2010	110 (15.2)	192 (11.9)	
2011	95 (13.1)	246 (15.3)	
2012	30 (4.1)	75 (4.6)	
Completed 2 doses of the vaccine[e]	N=951	N=2,259	
Duration between first and second dose (months), median (IQR)	2.9 (2.1, 7.0)	2.7 (2.1, 5.7)	0.007
Completed 2 doses of the vaccine by age 13.5	946 (99.5)	2,071 (91.7)	<0.001
Completed 2 doses of the vaccine by age 15	950 (99.9)	2,210 (97.8)	<0.001
Sex			<0.001
Boys	55 (5.8)	211 (9.3)	
Girls	896 (94.2)	2,048 (90.7)	
Race			<0.001
White	692 (72.8)	1,883 (83.4)	
Asian	67 (7.0)	94 (4.2)	

Characteristic	9–10 years	11–12 years	P[a]
Completed 3 doses of the vaccine[b]	**N=725**	**N=1,613**	
Black or African American	87 (9.1)	90 (4.0)	
Other or unknown	105 (11.0)	192 (8.5)	
Insurance status[c]			<0.001
No/unknown	28 (2.9)	352 (15.6)	
Commercial	726 (76.3)	1,642 (72.7)	
Government	174 (18.3)	222 (9.8)	
Other	23 (2.4)	43 (1.9)	
Number of clinic visits > upper 25th percentile[d]	269 (28.3)	606 (26.8)	0.40
Year of first vaccination			0.02
2006	98 (103)	203 (9.0)	
2007	167 (17.6)	470 (20.8)	
2008	145 (15.2)	325 (14.4)	
2009	128 (13.5)	267 (11.8)	
2010	131 (13.8)	256 (11.3)	
2011	160 (16.8)	371 (16.4)	
2012	122 (12.8)	367 (16.2)	

Abbreviations: IQR, interquartile range

Results presented as N (%) unless otherwise noted

[a] Chi-square or Fisher's exact P value reported for categorical variables and Wilcoxon rank-sum P value reported for continuous variables

[b] Population includes those that completed the 3-dose series. Receipt of doses with appropriate timing (The second dose must have been administered at least 4 weeks (24 days) after the first dose. The third dose must have been administered at least 12 weeks (80 days) after the second dose, and at least 24 weeks (164 days) after the first dose. A 4-day grace period was permitted at each dose.)

[c] Insurance status closest to August 2, 2006.

[d] Upper quartile of the number of visits based on clinic visits from August 2, 2006 through December 31, 2012 for patients who initiated the HPV vaccine at 9–10 or 11–12 years of age.

[e] Population includes those that completed the 2-dose series. Receipt of doses with appropriate timing. The second dose must have been administered at least 4 weeks (24 days) after the first dose. A 4-day grace period was permitted at each dose.

TABLE 3

Associations between age at vaccine initiation and timely completion of the 3-dose HPV vaccine series

Characteristic	Unadjusted		Adjusted[a]	
Completion of the vaccine by age 13.5	**OR (95% CI)**	**P**	**OR (95% CI)**	**P**
Age at initiation		<0.001		<0.001
11–12	Reference		Reference	
9–10	11.08 (6.84, 17.96)		12.82 (7.83, 20.99)	
Sex		0.01		0.25
Boys	Reference		Reference	
Girls	0.31 (0.12, 0.77)		0.57 (0.22, 1.48)	
Race		0.17		0.22
White	Reference		Reference	
Asian	1.10 (0.64, 1.89)		0.86 (0.48, 1.54)	
Black or African American	0.68 (0.43, 1.08)		0.61 (0.35, 1.06)	
Other	0.74 (0.52, 1.07)		0.74 (0.49, 1.12)	
Insurance status[b]		0.009		0.01
No/unknown	Reference		Reference	
Commercial	1.45 (1.05, 2.02)		1.12 (0.79, 1.58)	
Government	0.96 (0.63, 1.45)		0.62 (0.38, 1.00)	
Other	0.79 (0.36, 1.78)		0.55 (0.23, 1.31)	
Number of clinic visits > upper 25th percentile[c]	1.22 (0.95, 1.57)	0.12	1.43 (1.09, 1.88)	0.01
Year of first vaccination	1.27 (1.18, 1.36)	<0.001	1.29 (1.20, 1.39)	<0.001
Completion of the vaccine by age 15	OR (95% CI)	P	OR (95% CI)[d]	P
Age at initiation		<0.001		<0.001
11–12	Reference		Reference	
9–10	15.23 (4.81, 48.22)		14.21 (4.97, 40.65)	
Sex		0.14		0.63
Boys	Reference		Reference	
Girls	0.12 (0.01, 2.01)[d]		0.50 (0.03, 8.37)	
Race		0.72		0.36
White	Reference		Reference	
Asian	0.67 (0.30, 1.48)		0.52 (0.23, 1.18)	
Black or African American	1.26 (0.45, 3.51)		1.34 (0.46, 3.94)	
Other	1.08 (0.51, 2.26)		1.23 (0.57, 2.66)	
Insurance status[b]		0.22		0.02
No/unknown	Reference		Reference	
Commercial	1.15 (0.61, 2.15)		1.00 (0.53, 1.88)	
Government	0.87 (0.39, 1.91)		0.47 (0.20, 1.10)	
Other	0.40 (0.12, 1.31)		0.26 (0.08, 0.87)	
Number of clinic visits > upper 25th percentile[c]	1.67 (1.02, 2.75)	0.04	2.21 (1.33, 3.69)	0.002

Characteristic	Unadjusted		Adjusted[a]	
Completion of the vaccine by age 13.5	**OR (95% CI)**	**P**	**OR (95% CI)**	**P**
Year of first vaccination	1.58 (1.36, 1.83)	<0.001	1.61 (1.38, 1.88)	<0.001

[a] Adjusted for all variables in the table.

[b] Insurance status closest to August 2, 2006.

[c] Upper quartile of the number of visits based on clinic visits from August 2, 2006 through December 31, 2012 for patients who initiated the HPV vaccine at 9–10 or 11–12 years of age.

[d] Firth's bias correction applied due to zero cell issue.

TABLE 4

Associations between age at vaccine initiation and timely completion of 2 doses of the HPV vaccine

Characteristic	Unadjusted		Adjusted[a]	
Completion of the vaccine by age 13.5	**OR (95% CI)**	**P**	**OR (95% CI)**	**P**
Age at initiation		<0.001		<0.001
11–12	Reference		Reference	
9–10	17.17 (7.04, 41.87)		22.09 (8.96, 54.50)	
Sex		0.004		0.03
Boys	Reference		Reference	
Girls	0.05 (0.01, 0.39)		0.11 (0.02, 0.79)	
Race		0.01		0.02
White	Reference		Reference	
Asian	1.14 (0.55, 2.37)		0.98 (0.46, 2.08)	
Black or African American	0.44 (0.27, 0.72)		0.40 (0.23, 0.72)	
Other	0.87 (0.53, 1.43)		0.93 (0.55, 1.59)	
Insurance status[b]		0.04		0.03
No/unknown	Reference		Reference	
Commercial	1.22 (0.79, 1.90)		0.91 (0.58, 1.44)	
Government	0.70 (0.41, 1.20)		0.47 (0.26, 0.85)	
Other	1.48 (0.43, 5.05)		1.02 (0.29, 3.59)	
Number of clinic visits > upper 25th percentile[c]	1.51 (1.06, 2.17)	0.02	1.89 (1.29, 2.77)	0.001
Year of first vaccination	1.32 (1.22, 1.43)	<0.001	1.31 (1.20, 1.43)	<0.001
Completion of the vaccine by age 15	OR (95% CI)	P	OR (95% CI)	P
Age at initiation		0.003		0.002
11–12	Reference		Reference	
9–10	21.04 (2.90, 152.43)		22.62 (3.09, 165.44)	
Sex		0.14		0.61
Boys	Reference		Reference	
Girls	0.22 (0.03, 1.62)		1.77 (0.20, 15.59)	
Race		0.24		0.13
White	Reference		Reference	
Asian	0.44 (0.17, 1.14)		0.34 (0.13, 0.92)	
Black or African American	1.24 (0.30, 5.20)		1.07 (0.23, 5.06)	
Other	0.59 (0.26, 1.33)		0.57 (0.24, 1.39)	
Insurance status[b]		0.84		0.89
No/unknown	Reference		Reference	
Commercial	1.43 (0.66, 3.11)		1.21 (0.54, 2.71)	
Government	1.40 (0.48, 4.07)		0.87 (0.27, 2.80)	
Other	1.40 (0.17, 11.36)		0.95 (0.11, 8.17)	
Number of clinic visits > upper 25th percentile[c]	2.78 (1.18, 6.55)	0.02	3.74 (1.55, 9.02)	0.003

Characteristic	Unadjusted		Adjusted[a]	
Completion of the vaccine by age 13.5	**OR (95% CI)**	**P**	**OR (95% CI)**	**P**
Year of first vaccination	1.70 (1.41, 2.06)	<0.001	1.87 (1.50, 2.33)	<0.001

[a] Adjusted for all variables in the table.

[b] Insurance status closest to August 2, 2006.

[c] Upper quartile of the number of visits based on clinic visits from August 2, 2006 through December 31, 2012 for patients who initiated the HPV vaccine at 9–10 or 11–12 years of age.