

The association of initiating HPV vaccination at ages 9–10 years and up-to-date status among adolescents ages 13–17 years, 2016–2020

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ABSTRACT

Recent guidelines from the American Cancer Society stress HPV vaccination series initiation at the youngest opportunity, i.e., age 9 years. There are limited data on the association between initiating HPV vaccination at ages 9–10 years and up-to-date (UTD) status. In this study, we compare nationally representative UTD HPV vaccination rates between adolescents who initiated the series younger (ages 9–10 years) vs. older (\geq age 11 years). Five years of pooled data (2016–2020) from National Immunization Survey-Teen were used to estimate the UTD HPV vaccination prevalence among younger vs. older initiating 13–17-year-olds. Adjusted logistic regression models estimated prevalence ratios (aPRs), differences (aDs), and difference in differences (aDDs) in prevalence of being UTD to assess the overall association of age at initiation with being UTD and differences in sociodemographic predictors of being UTD among younger vs. older initiators. UTD prevalence for younger initiators was 93% compared with 72% among older initiators (aPR: 1.27, 95%CI: 1.24, 1.31). Among older initiators, UTD prevalence was significantly different by sex, insurance status, and current age; no such differences were observed among younger initiators. Results indicate that younger initiation is associated with a 27% higher UTD prevalence, highlighting the importance of promoting younger initiation, particularly among those with health-care barriers.

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Introduction

In 2020, the American Cancer Society (ACS) updated the Federal Advisory Committee on Immunization Practices (ACIP) guidelines by recommending routine HPV vaccinations between ages 9–12, rather than at ages 11–12 or starting at age 9, similar to updated recommendations made by the American Academy of Pediatrics (AAP) in their 2018–2021 *Red Book*.^{1,2} Despite substantial increases in initiation of the HPV vaccination series among 9–12 year-olds in the United States (US),³ the Healthy People 2020 goal of attaining 80% HPV vaccination coverage by 2020 was not achieved due to continued suboptimal uptake.⁴ The potential reduction in disease burden associated with optimal coverage of HPV vaccinations is well documented,⁵ and growing evidence suggests the benefits of initiating the HPV vaccination series at ages 9–10. Recent literature has found physicians' recommending HPV vaccinations to 9- and 10-year-olds may increase parental vaccine acceptance due to easier disentanglement from conversations relating to sexual activity and allowing for a fewer number of vaccinations per visit, which may be even more compelling in the age of COVID-19 vaccinations.^{1,6,7} Younger recommended initiation may also allow for more opportunities for series completion at well-child visits and potentially avert HPV vaccine hesitancy "fatigue," where physicians delay recommending the HPV vaccine at ages 11–12 due to assumptions of parental refusal.⁸ A study on a quality improvement initiative to shift the initiation of the HPV vaccination series to

age 9 showed rapid vaccine uptake prior to age 11, suggesting willingness of both physicians and parents to vaccinate at ages 9–10.⁹

Yet, evidence regarding the association of younger series initiation age with up-to-date (UTD) status is limited. A prior study based on a county-wide primary care network in Minnesota reported that HPV vaccination initiation before age 11 years is associated with increased series completion.¹⁰ These findings, however, may not be generalizable to the US population as they were not based on nationally representative data. In this brief report, we examined whether younger initiation of HPV vaccination (at ages 9–10 years) is associated with UTD status and potential sociodemographic differences associated with UTD status in those initiating younger (at ages 9–10 years) vs. older (at or after 11 years) based on nationally representative data.

Methods

Publicly available, deidentified, provider-verified HPV vaccination data were pooled from the National Immunization Survey-Teen (NIS-Teen) survey years 2016–2020 for adolescents aged 13–17 years. Adolescents were classified as being UTD at their current age of being interviewed had they received three doses if the series was started after the age of 15 years; or two doses if the series was started before age 15 years and there were at least 5 months between the first

and second doses.¹¹ Information on the age of receipt of the first HPV vaccination was used to classify adolescents as younger (9–10 years) vs. older (≥ 11 years) series initiators. Descriptive statistics, including unweighted sample counts and weighted percentages representative of the US population and adjusted for non-response, were generated for younger vs. older initiators by year and sociodemographic characteristic, including sex (male, female), current age (13–17 years), race/ethnicity (non-Hispanic (NH) White, NH Black, Hispanic, and NH Other), poverty level ($\geq 100\%$ Federal Poverty Level (FPL), $< 100\%$ FPL), region (Northeast, Midwest, South, and West), insurance status (private, uninsured, Medicaid, and other), and facility type (private, public, hospital, all STD/school/teen clinic, mixed). Chi-square analyses were applied to determine statistically significant differences in sociodemographic characteristics.

The prevalence of UTD HPV vaccination for adolescents with younger vs. older series initiation was also calculated by survey year and sociodemographic characteristics. A logistic regression model was used to calculate prevalence ratios to estimate the association of age at initiation and UTD status while adjusting for survey year and sociodemographic characteristics, where UTD status was the dependent variable and initiation status (younger vs. older) was the main independent variable, adjusted for survey year and sociodemographic characteristics. To assess whether the association of initiation age and UTD status varied according to sociodemographic characteristics, logistic regression models with interaction terms between initiation status and sociodemographic variables were used to estimate adjusted differences (aDs) and difference-in-differences (aDDs) in probability of being UTD (dependent variable) by initiation status (main independent variable) according to levels of sociodemographic variables. All statistical analyses were conducted in the SAS-callable SUDAAN version 11.0.4.

Results

Of the 65,708 adolescents included in the sample, approximately 5% or 3,307, initiated the HPV vaccination series at ages 9–10 (Table 1). Sixty-two percent ($n = 2006$) of adolescents with younger initiations were female compared to 38% ($n = 1301$) who were male, whereas no female ($n = 30292$, 50%) vs. male ($n = 32109$, 50%) differences were evident among adolescents with older initiation ($p < .001$). Among adolescents with younger initiations, 33% ($n = 1397$) were NH White, 19% were NH Black ($n = 443$), and 38% ($n = 1123$) were Hispanic in comparison to 50% ($n = 37926$), 14% ($n = 5315$) and 25% ($n = 11656$) of the sample initiating older, respectively ($p < .001$). About 40% ($n = 1100$) of adolescents initiating younger people were below the federal poverty level in comparison to 22% ($n = 10939$) of adolescents who initiated older ($p < .001$). Among those who initiated younger, 32% ($n = 1278$) were privately insured, 57% ($n = 1613$) were on S-Chip/Medicaid and 4% ($n = 138$) were uninsured in comparison to 53% (36897), 37% ($n = 19264$), and 4% ($n = 1919$) of the sample initiating older, respectively ($p < .001$). Among those who initiated younger, 20% ($n = 535$) received vaccinations at all public facilities and 42% ($n = 1307$) received vaccinations at all private facilities in comparison to 13% ($n = 7557$) and 49% ($n = 29203$) for those who initiated older ($p = .001$). Sample

distributions by year and region were comparable between the two age-at-initiation groups.

The UTD vaccination rate for adolescents who were initiated at ages 9–10 was 93% compared to 72% for those who initiated at 11 or later (Table 2). In adjusted regression models, this translated to a 27% (aPR: 1.27, 95% CI: 1.24–1.31) higher prevalence of UTD status in adolescents initiating younger vs. older. When examining sociodemographic differences, significant interactions were observed by sex ($p = .02$), insurance status ($p = .01$) and current age ($p < .001$) for the association between initiation status and being UTD for the series (Table 3). For younger initiators, the UTD prevalence was similar for males and females, while for older initiators, the UTD prevalence among male adolescents was 5% lower than in female adolescents (aDD: -0.07 , p -value = .02). Among younger initiators, UTD prevalence was similar among uninsured vs. privately insured adolescents, while older initiating, uninsured adolescents had completion rates that were 13% lower in comparison to privately insured adolescents (aDD: -0.11 , p -value = .01). By age at being interviewed, prevalence of being UTD among 14-, 15-, 16- and 17-year-olds initiating older were 11%, 16%, 18%, and 17% higher in comparison to 13-year-olds, respectively, whereas among younger initiators, differences in UTD prevalence were not statistically significant. Significant interactions in the association between current age and series completion were observed for all ages in comparison to age 13, as increased age at being interviewed was significantly associated with higher prevalence of being UTD for older initiators, but no such association was observed for younger initiators. Among older initiators, completion rates among Hispanic adolescents were 3% higher (p -value = .03) compared to NH White adolescents and 8% lower among adolescents receiving vaccinations from public facilities vs. private facilities (p -value $< .001$), whereas, among younger initiators, these sociodemographic differences were not statistically significant. However, interactions by race or facility type for the association between initiation age and completion rate were not statistically significant.

Discussion

Our analysis of a nationally representative contemporary sample of US adolescents showed that those who initiated at ages 9–10 had a 27% higher UTD prevalence between the ages of 13–17 years while controlling for various sociodemographic factors including race/ethnicity, insurance status, and poverty status in comparison to those who initiated at age 11 or later. Significant differences in prevalence of UTD relating to facility type, insurance status, sex, and race/ethnicity seen among adolescents initiating older were generally not detected for those initiating at ages 9–10.

When examining interactions for the association between age at initiation and UTD status, age, sex, and insurance status were the only sociodemographic factors where a statistically significant interaction was observed. For those initiating at age 11 or later, older adolescents were more likely to be UTD, while this pattern did not hold for those initiating younger, meaning those initiating at ages 9–10 were largely UTD by age 13. Among older initiating adolescents, males were significantly less likely to have

Table 1. Sociodemographic characteristics* by age at initiation, adolescent ages 13–17 years, NIS-Teen 2016–2020.

	Younger Initiators (Initiated at ages 9-10)		Older Initiators (Initiated \geq 11)		p-value
	N	%	N	%	
Total	3307	—	62401	—	—
Year					
2016	553	17.2	11430	17.7	.09
2017	684	19.7	12749	19.1	
2018	656	19.5	11782	12.1	
2019	660	22.2	12437	20.9	
2020	754	21.5	14003	22.2	
Age at Initiation					
9	1150	34.68	—	—	—
10	2157	65.32	—	—	—
11	—	—	23369	38.2	—
12	—	—	17527	26.9	—
13	—	—	9869	15.3	—
14	—	—	6442	10.3	—
15	—	—	3010	5.2	—
16	—	—	1644	2.9	—
17	—	—	540	0.9	—
Current Age**					
13	757	22.3	11998	18.1	< .001
14	784	26.6	12886	19.8	—
15	653	19.1	12723	21.2	—
16	615	16.7	12964	20.8	—
17	498	15.3	11830	20.1	—
Sex					
Female	2006	61.8	30292	50.2	< .001
Male	1301	38.2	32109	49.8	—
Race^a					
NH White	1397	33.4	37926	50.2	< .001
NH Black	443	19.0	5315	14.2	—
Hispanic	1123	38.3	11656	24.8	—
NH Other	344	9.3	7506	10.8	—
Poverty Status					
<100% FPL	1100	39.8	10939	22.0	< .001
\geq 100% FPL	2207	60.2	51462	77.3	—
Region					
Northeast	544	14.5	13377	17.2	.05
Midwest	656	19.9	13656	21.4	—
South	1371	37.0	21986	36.4	—
West	736	28.6	13382	25.0	—
Facility Type					
All public facilities	535	19.2	7557	12.6	.001
All hospital facilities	399	10.6	7807	10.0	—
All private facilities	1307	42.0	29203	49.4	—
All STD/school/teen clinics	93	2.2	1350	2.3	—
Mixed	648	15.9	11286	15.7	—
Insurance					
Private only	1278	32.4	36897	53.0	< .001
Any Medicaid	1613	56.6	19264	37.2	—
Other	278	7.1	4320	6.2	—
Uninsured	138	3.9	1919	3.6	—

NH: non-Hispanic. FPL: Federal poverty level. STD: Sexually transmitted disease.

^aNH Other includes non-Hispanic Asian, non-Hispanic American Indian and Alaskan Native, and non-Hispanic individuals of multiple races.

*Sample sizes are unweighted, and percentages are weighted.

**Current age refers to age of adolescent at time of participation in the survey.

UTD in comparison to females, while this pattern did not hold among younger initiators. Older initiating adolescents who were uninsured or received vaccinations from public facilities had completion rates that were 11% and 8% lower in comparison to those who were privately insured or received vaccinations from private facilities, respectively. Among adolescents initiating younger, lower prevalence of being UTD was observed among uninsured vs. privately insured and those who received vaccination in public facilities vs. private, although these differences in prevalence did not reach statistical significance, and no significant interaction was observed for vaccination receipt from a public facility by initiation status.

Significant interactions involving age, sex, and insurance status when examining the association between age at initiation and completion of the series may exist for several reasons. Adolescents initiating younger have more years to complete the series before the age of 13, likely explaining why more younger initiators are UTD by the age of 13 in comparison to older initiators. Also, among older initiators, females were more likely to be UTD in comparison to males, whereas among younger initiators, females were no more likely to be UTD in comparison to males. Sex differences by initiation status potentially indicate increased HPV vaccination uptake in males since guidelines were expanded in 2011 to include

Table 2. UTD HPV vaccination prevalence for younger and older initiators, adolescents aged 13–17 years, NIS-Teen 2016–2020.

	Younger Initiators (Initiated at ages 9-10)	Older Initiators (Initiated \geq 11)
	Crude Prevalence (95% CI)	
Total	93.1 (90.14–95.22)	71.9 (70.99–73.38)
Year		
2016	97.21 (95.40–98.33)	69.19 (67.51–70.83)
2017	90.06 (80.61–95.17)	71.91 (70.39–73.38)
2018	93.94 (90.38–96.23)	72.67 (71.13–74.16)
2019	90.38 (78.73–95.97)	73.82 (72.10–75.47)
2020	94.96 (92.56–96.61)	76.09 (74.69–77.43)
Current Age*		
13	93.40 (90.44–95.49)	61.02 (59.35–62.66)
14	89.69 (79.89–95.01)	71.26 (69.62–72.85)
15	95.23 (91.92–97.22)	75.86 (74.36–77.30)
16	92.55 (79.41–97.56)	77.96 (76.56–79.29)
17	96.51 (93.89–98.03)	76.80 (75.15–78.37)
Sex		
Female	92.85 (88.77–95.52)	75.4 (74.43–76.35)
Male	93.5 (88.51–96.41)	70.39 (69.38–71.37)
Race^a		
NH White	92.98 (90.67–94.76)	73.09 (72.28–73.88)
NH Black	91.35 (79.06–96.73)	71.36 (69.38–73.26)
Hispanic	93.80 (87.25–97.10)	72.86 (71.08–74.57)
NH Other	93.96 (89.41–96.63)	74.14 (72.15–76.03)
Poverty Status		
<100% FPL	93.12 (87.38–96.36)	71.74 (70.11–73.33)
\geq 100% FPL	92.59 (88.36–95.36)	73.52 (72.75–74.28)
Region		
Northeast	96.98 (94.69–98.30)	77.86 (76.67–79.01)
Midwest	92.89 (90.00–94.99)	73.90 (72.81–74.95)
South	93.01 (89.84–95.25)	70.62 (69.61–71.62)
West	91.42 (80.16–96.56)	71.91 (69.87–73.87)
Facility Type		
All public facilities	89.31 (75.76–95.71)	66.04 (63.75–68.27)
All hospital facilities	94.96 (91.21–97.16)	75.08 (72.87–77.16)
All private facilities	94.48 (89.99–97.02)	74.90 (73.97–75.81)
All STD/school/teen clinics	92.79 (79.75–97.67)	68.21 (62.30–73.58)
Mixed	92.16 (85.47–95.92)	72.52 (70.85–74.12)
Insurance		
Private only	93.74 (91.40–95.47)	73.99 (73.08–74.88)
Any Medicaid	92.84 (87.46–96.01)	58.07 (54.00–62.04)
Other	94.20 (88.52–97.15)	72.96 (71.74–74.14)
Uninsured	89.82 (81.48–94.65)	72.14 (69.38–74.75)

NH: non-Hispanic. FPL: Federal poverty level. STD: Sexually transmitted disease.

^aNH Other includes non-Hispanic Asian, non-Hispanic American Indian and Alaskan Native, and non-Hispanic individuals of multiple races.

*Current age refers to age of adolescent at time of participation in the survey.

adolescent boys and young men.^{3,12} Regarding significant interactions involving insurance status, results indicate lower UTD rates among uninsured vs. privately insured adolescents initiating older but not among adolescents initiating younger. This is further emphasized by significant differences in UTD prevalence among older initiators vaccinating at public vs. private facilities, but not among younger initiators, although no significant interaction was observed. Additional research is needed to determine if younger initiations may indeed be associated with improved vaccine access, as this finding may have significant implications for initiatives addressing disparities in HPV vaccination uptake, potentially leading to stronger emphasis on the importance of initiating the series at ages 9–10.

Our results are consistent with previous studies examining the prevalence of being UTD with age at initiation.^{10,13} In a cohort study conducted in Minnesota, for example, it was found that 97.5% of the adolescents who initiated the series between ages 9 and 10 were UTD by 13.5 years old, in comparison to 78% of adolescents who initiated the series between

ages 11 and 12.¹⁰ It is a possibility, however that age at initiation is a marker for other factors related to increased likelihood of series completions, such as vaccination access, having additional years to complete the series during the recommended 9–12 age range for routine vaccinations, and more frequent use of health care^{10,14,15} Younger series initiations may also signal positive parental attitudes toward HPV vaccinations and their intent to vaccinate their children, which have been shown to be associated with HPV series initiation and completion.¹⁶ Additionally, younger initiation may relate to provider beliefs regarding parental vaccine acceptance and access to and utilization of health care as both factors are associated with series initiation.^{7,8,17} More research is needed to better understand socioeconomic, cultural, political and health system factors that influence HPV vaccination initiation at a younger age as it relates to being UTD for the series.

The strengths of this study include the use of nationally representative, provider-verified HPV vaccination data to provide results that are generalizable to adolescents in the US. This study, however, does have limitations. First, the NIS-Teen

Table 3. Adjusted differences (aDs) and adjusted differences in differences (aDDs) in UTD HPV vaccination prevalence for younger and older initiators, adolescents aged 13–17 years, NIS-Teen 2016–2020.

	aD ^a	aDD ^a	p-value	aD ^a	aDD ^a	p-value	aD ^a	aDD ^a	p-value	aD ^a	aDD ^a	p-value
Sex	Male vs. Female											
Younger initiators	0.01	-0.07	.02	—	—	—	—	—	—	—	—	—
Older Initiators	-0.05	—	—	—	—	—	—	—	—	—	—	—
Race^b	Hispanic vs. NH White			NH Black vs. NH White			Other vs. NH White					
Younger initiators	0.01	0.02	.50	-0.02	0.01	.75	0.01	0.01	.79	—	—	—
Older Initiators	0.03	—	—	0	—	—	0.02	—	—	—	—	—
Insurance	Uninsured vs. Private			Medicaid vs. Private			Other vs. Private					
Younger initiators	-0.02	-0.11	.01	-0.01	0.02	.34	0.01	-0.01	.69	—	—	—
Older Initiators	-0.13	—	—	0.02	—	—	0	—	—	—	—	—
Poverty Status	<100% FPL vs. ≥ 100% FPL											
Younger initiators	0	-0.01	.70	—	—	—	—	—	—	—	—	—
Older Initiators	-0.01	—	—	—	—	—	—	—	—	—	—	—
Region	Northeast vs. Midwest			Northeast vs. South			Northeast vs. West					
Younger initiators	-0.04	0.01	.57	-0.04	-0.03	.15	-0.06	0.01	.85	—	—	—
Older Initiators	-0.03	—	—	-0.07	—	—	-0.05	—	—	—	—	—
Facility Type	Public vs. Private			Hospital vs. Private			All STD/School/Teen clinic vs. Private			Mixed vs. Private		
Younger initiators	-0.05	-0.02	.65	0	0	.89	-0.01	-0.04	.47	-0.02	0.01	.76
Older Initiators	-0.08	—	—	0	—	—	-0.05	—	—	-0.01	—	—
Current Age*	14 vs. 13			15 vs. 13			16 vs. 13			17 vs. 13		
Younger initiators	-0.04	0.15	<.001	0.01	0.15	<.001	-0.01	0.19	<.001	0.03	0.14	<.001
Older Initiators	0.11	—	—	0.16	—	—	0.18	—	—	0.17	—	—
Year	2017 vs. 2016			2018 vs. 2016			2019 vs. 2016			2020 vs. 2016		
Younger initiators	-0.08	0.1	.01	-0.03	0.07	<.001	-0.08	0.13	.01	-0.02	0.09	<.001
Older Initiators	0.03	—	—	0.04	—	—	0.05	—	—	0.07	—	—

NH: non-Hispanic. FPL: Federal poverty level. STD: Sexually transmitted disease. aD: Differences in adjusted predicted marginals. aDD: Difference-in-differences of adjusted predicted marginals.

^aaDs and aDDs are adjusted by all variables in table. Bold estimates are statistically significant.

^bNH Other includes non-Hispanic Asian, non-Hispanic American Indian and Alaskan Native, and non-Hispanic individuals of multiple races.

*Current age refers to age of adolescent at time of participation in the survey.

dataset is cross-sectional, meaning that longitudinal analysis is not possible, and individuals cannot be followed over time to assess their UTD status. Second, NIS-Teen does not include several variables that have been established as significant to the receipt of HPV vaccinations, such as living in a rural vs. urban areas. Third, due to the small number of adolescents initiating the series at ages 9–10, the sample size may not provide adequate statistical power to detect statistically significant sociodemographic differences in prevalence of being UTD. Finally, due to the study including NIS-Teen data from years 2016–2020, the impact of stronger recommendations for younger age initiation on subsequent UTD status may not be fully captured in this analysis.

In conclusion, using nationally representative data, we show that initiation of HPV vaccination at ages 9–10 is associated with a higher prevalence of being UTD for adolescents ages 13–17 years. The findings underscore the need for novel nationwide strategies to encourage younger HPV vaccine initiation, particularly among those with known healthcare access barriers, such as being uninsured, publicly insured, having a lower socioeconomic status, and living in rural geographic areas. Additional research is needed to better understand how healthcare access and continuity of care influence age at HPV series initiation and ultimately being UTD.

Author contributions

Adair K. Minihan had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Disclosure statement

A.K. Minihan, P. Bandi, J.R. Star, M. Fisher-Borne, D. Saslow, and A. Jemal were employed by the American Cancer Society while this work was conducted. The American Cancer Society receives grants from private and corporate foundations, including foundations associated with companies in the health-care sector, for research outside of the submitted work.

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Acquisition of data

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Drafting of the manuscript

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Interpretation of data and critical revision of the manuscript for important intellectual content

All authors.

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interpretation of the data; preparation, review, or approval of the manuscript; and decision to submitting the manuscript for publication.

Statistical analysis

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Study concept and design

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Study supervision

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