A Quantitative Examination of Policy Impact on HPV Vaccination Coverage

By

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Introduction

Human papillomavirus (HPV) is prevalent in the United States among sexually active adults and can be acquired during adolescence. In 2013-2014, national estimates suggested an HPV prevalence of 42.5% among sexually active adults.[1] Annually, 31,500 cancers are associated with HPV in the U.S,[2] including cervical, penile, anal, and oropharyngeal cancers.[3,4] Adolescents remain the most important focus of the HPV vaccination program in the U.S. However, initiation and completion of the HPV vaccine is low among U.S. adolescents. Current vaccination rates are even lower for young males as compared to young females. Low vaccination rates occur as a result of varying provider (defined as vaccine administrator) recommendations for vaccines.[5] Additional reasons for low rates can also differ by sex. For example, parental concerns about sexual activity for young females lead to mixed vaccination results, and parental belief in lack of risk for young males is associated with low vaccination.[5] Increasing HPV vaccination rates among adolescents is critical for reducing HPV-associated infections and potential subsequent cancers later in adulthood. In order to lower the prevalence of HPV infection and consequent cancers, adolescents should be targeted for vaccination efforts.

The U.S. Food and Drug Administration (FDA) approved a bivalent vaccine (Gardasil®) against HPV types 16 and 18 in 2006.[6] Vaccination reduced the HPV strain types associated with the vaccine[2,7] and has been associated with decreased cervical lesions in young females.[1] The HPV vaccine was originally marketed towards females until 2009, when the recommendation changed to include males receiving the vaccine.[2,7] The quadrivalent and nonavalent vaccines are recommended at age 11 or 12, with two doses recommended for most individuals and immunocompromised individuals requiring three doses.[8] Individuals can receive the vaccine up through age 26,[9] although the most benefit is for younger individuals not yet exposed to HPV.

Questions remain as to how to raise HPV vaccination levels to recommended levels among U.S. adolescents. National vaccination rates fall short of the Healthy People 2020 goal of 80% coverage for adolescents ages 13-15 years.[1] Vaccination coverage was 48.9% for females ages 13-15 and 47.1% for males ages 13-15 in 2018.[10] Factors associated with acceptance of HPV vaccination among adolescents include maternal education, provider recommendation, and parental information.[11,12,13] Insurance coverage is also positively associated with HPV vaccination.[14] Barriers to vaccination include lack of parental knowledge, parental concern about the HPV vaccine, and absent provider recommendation for vaccination.[5]

State-level policies related to HPV vaccination can impact vaccination coverage.[15,16] Policies of interest include permission of HPV vaccination in pharmacies, school-entry vaccination mandates, parental education mandates, Centers for Disease Control and Prevention (CDC) funding, public health governance, classroom sex education policies, and state Medicaid expansion.[15,16] School-entry vaccination mandates and sex education policies have significant impact on HPV vaccination.[16] A combination of the policies of Medicaid expansion, permission of HPV vaccination in pharmacies, school-entry requirements, and classroom sex education policies positively increased HPV vaccine uptake in adolescents ages 13-17 years.[15]

Assessing HPV vaccination coverage through Medicaid expansion is important for developing strategies to increase HPV vaccination rates. Medicaid expansion could reduce disparities in access to care for under- and uninsured families, making HPV vaccination access more equitable. This state policy has the opportunity to increase uptake through access in a way that other policies do not, as they provide information or mandates.

State Medicaid expansion as a result of the Affordable Care Act (ACA) gave states the opportunity to raise their Medicaid eligibility thresholds for adults to 138% of federal poverty

level (FPL), starting in January 2014.[17] The minimum Medicaid eligibility threshold for children under 19 was also raised to 138% of FPL, higher than prior thresholds (100% FPL) for children 6 to 18.[18] The ACA did not shift coverage eligibility much for children, but increases in children's insurance coverage have been documented. These increases are particularly notable for children whose parents became eligible for Medicaid as a result of expansions.[19]

Children's insurance coverage is linked to increased HPV vaccination rates. Earlier studies focusing on females found higher likelihood of HPV vaccine initiation for insured female adolescents.[20,21] Later studies with both males and females indicate that overall insured adolescents were more likely to initiate the HPV vaccine than uninsured, with higher vaccine completion rates for insured female adolescents.[14] Insured females were also more likely to complete the vaccine series while insurance did not impact vaccine completion for males.[14]

However, the association between HPV vaccination and Medicaid coverage is mixed. Medicaid-insured teenagers had higher rates of vaccine initiation as compared to privately-insured,[14] and national data suggested higher rates of vaccine completion for Medicaid-insured teenagers as compared to commercial plans.[22] Evidence differed by teenager's sex: Medicaid-insured male teenagers had higher probability of HPV vaccine initiation[23] and lower probability of vaccine completion.[24] Yet, Medicaid-insured female adolescents had a higher probability of HPV vaccine completion.[22] None of these previous studies used a quasi-experimental, longitudinal approach which would be useful to better understand how insurance coverage, specifically Medicaid coverage, impacts HPV vaccination for each sex. The advantage of a quasi-experimental longitudinal approach such as difference-in-differences analysis is the ability to isolate only the effects of the intervention. This is done by comparing treatment and control

groups pre and post intervention of interest. In this study, the intervention of interest is state expansion of Medicaid thresholds.

The aim of this paper was to explore the impact of Medicaid expansion on HPV vaccination rates for teenagers, including whether Medicaid expansion differentially impacted vaccination rates for males and females given the initial exclusive vaccine recommendation to females. The longitudinal effects of state expansions of Medicaid thresholds on HPV vaccination rates were analyzed, improving upon the current cross-sectional literature. This analysis was conducted to guide statewide policy that could increase HPV vaccination rates in order to decrease related cancer cases in future years. We hypothesized that adolescents ages 13-17 in treatment states that expanded Medicaid eligibility on January 1, 2014 had higher rates of HPV vaccine initiation and completion than adolescents in unexpanded control states. Additionally, we hypothesized that HPV vaccination rates for male adolescents in particular would be increased in expanded states as compared to unexpanded states.

Methods

Data are from the National Immunization Survey-Teen (NIS-Teen). The NIS-Teen is a cross-sectional survey based on telephone interviews conducted with parents and guardians of teens ages 13-17. Households are sampled from both landline and cell phone numbers. The NIS-Teen contacted teenager's providers to verify reported vaccinations, if the parent consented.[25] We analyzed three years of data pre-Medicaid expansion (2011, 2012, 2013) and three years in the implementation period (2014, 2015, 2016).

HPV vaccination was based on the parental response to the question, "Has teen ever received any human papillomavirus shots?" and their report of number of shots received. Only responses verified by a teen's providers were used. Vaccine series initiation was defined as either

zero shots or at least one shot. Vaccine series completion was defined as at least three doses, based on 2011-2016 guidelines for teenagers.[25]

Medicaid expansion status was represented by treatment and control groups of states. Treatment states expanded Medicaid on January 1, 2014 and included Washington, Oregon, California, Arizona, Nevada, New Mexico, Colorado, North Dakota, Minnesota, Iowa, Illinois, Arkansas, Kentucky, Ohio, West Virginia, Maryland, Delaware, New Jersey, New York, District of Columbia, Connecticut, Rhode Island, Massachusetts, Vermont, and Hawaii. Control states did not expand at any time and included Alabama, Florida, Georgia, Kansas, Mississippi, Missouri, North Carolina, Oklahoma, South Carolina, South Dakota, Tennessee, Texas, Wisconsin, and Wyoming.[26] States that expanded Medicaid coverage in 2015 or at a later time were not included in the analysis.

Covariates were defined based on the categories provided by the NIS-Teen and reported by the parent or guardian (see Table 1). The coding of teens' insurance differed in 2016 as compared to previous years. Prior to 2016, seven separate questions were asked to determine teens' health insurance. The variable was recoded to match the coding of health insurance in 2016 as a four category variable: private insurance, Medicaid, other, and uninsured with Children's Health Insurance Program (CHIP) included as "other."[25]

Chi-square analysis was used to examine demographic differences and HPV vaccination status between teenagers living in Medicaid-expanded treatment states and those living in non-expanded control states. The difference-in-differences design was used to assess the difference in HPV vaccination rates between expanded and non-expanded states before and after state Medicaid expansion. Difference-in-differences linear regression models for HPV vaccine initiation and vaccine completion controlled for state and year fixed effects and clustered

standard errors by state, and adjusted models also included time-varying covariates. The covariates in adjusted models were teen's sex, teen's age, maternal education, maternal age group, maternal marital status, and number of teen's providers. Teen's sex was considered time-varying given changing trends in vaccination status for young males. We tested for the parallel trends assumption, which was met strongly for vaccine completion and moderately for initiation based on non-significant p-values for the interaction between a Medicaid expansion indicator and data year.

While the gender gap in HPV vaccination rates is closing between males and females, vaccination rates of males still lag those of females. Therefore, a subgroup analysis explored whether a teen's sex had an impact on the difference in HPV vaccination rates between expanded and non-expanded states before and after Medicaid expansion, controlling for state and year fixed effects and time-varying covariates. Data were weighted and analyzed to account for the complex sampling design. STATA (Version 15) was used to conduct all analyses.

Results

The final dataset resulted in a total sample of 233,160 household interviews. Respondents in the analytic sample had provider-verified data, non-missing data on HPV vaccination status, and lived in a treatment (Medicaid-expanded) or control (non-expanded) state. The final analytic sample of provider-verified interviews used for the difference-in-differences analysis was n=95,987 (see Figure 1). The weighted analytic sample was 51% male and 49% female, with age evenly distributed (approximately 20% each for years 13-17). The majority of the weighted analytic sample was non-Hispanic white (52%), with 25% identifying as Hispanic, 14% non-Hispanic black, and 9% non-Hispanic other.

Demographic characteristics differed significantly by state expansion status for both teenagers (race/ethnicity, insurance status, and number of medical providers) and mothers (maternal age, education, and marital status) (see Table 1). The outcome of HPV vaccination status for both vaccine initiation and completion also differed significantly by state Medicaid expansion status.

HPV vaccine initiation rates for 13-17-year-old teenagers increased in expansion states after the 2014 state Medicaid expansion. Rates of HPV vaccine initiation increased by 3.9 percentage points (95% CI -0.4-8.1, p=0.072) after the policy change, controlling for state and year fixed effects and clustering standard errors by state. Similarly, rates of HPV vaccine initiation additionally adjusted for time-varying covariates increased by 3.8 percentage points (95% CI -0.5-8.1, p=0.079) in expansion states as compared to non-expansion states after the policy change.

HPV vaccine completion rates for 13-17-year-old teenagers significantly increased in expansion states post-expansion. Rates of HPV vaccine completion significantly increased by 4.9 percentage points (95% CI 2.6-7.2, p<0.0001), controlling for state and year fixed effects and clustering standard errors. Result adjusted for additional time-varying covariates were unattenuated. Rates of HPV vaccine completion adjusted for time-varying covariates significantly increased 4.9 percentage points (95% CI 2.6-7.3, p<0.0001) in expansion states as compared to non-expansion states after the policy change. The adjusted model for vaccine completion included the same time-varying covariates as the vaccine initiation model (Table 2).

Figures 2 and 3 display the comparison of unadjusted weighted trends of HPV vaccination rates between expanded and non-expanded states before and after 2014. Rates

diverge in each graph by state expansion status after 2014. The difference in vaccination rates indicates the importance of Medicaid expansion, particularly for vaccine completion.

Subgroup analyses by adolescent's sex revealed significant increases in vaccination rates for males. HPV vaccine initiation rates for males adjusted for covariates increased 6.4 percentage points (95% CI 1.4-11.4, $p<0.014$). HPV vaccine completion rates for males adjusted for covariates increased 6.6 percentage points (95% CI 3.7-9.6, $p<0.0001$).

However, change in vaccine initiation rates for females was not significant (1.1 percentage point increase, $p=0.6$). Only vaccine completion rates for females adjusted for covariates increased significantly by 3.0 percentage points (95% CI 0.3-5.7, $p<0.03$).

Discussion

The findings suggest that Medicaid expansion is an important correlate of HPV vaccine initiation and completion. The difference-in-differences analysis using national and state data found that Medicaid expansion had a significant impact overall on HPV vaccine completion, but not on HPV vaccine initiation. This study strengthens findings in past cross-sectional research that found associations between the policy of state Medicaid expansion and HPV vaccination in U.S. adolescents.[15] To our knowledge, this is the first study using difference-in-differences analysis to answer how Medicaid expansion impacted adolescent HPV vaccination rates. Study findings contribute to the literature on using difference-in-differences methods to evaluate the effects of Medicaid expansion on health outcomes, from preconception health insurance coverage[27] to improved cervical cancer screenings and hypertension control.[28]

The increased rates of HPV vaccine completions may be due to increased coverage for adolescents with raised Medicaid eligibility thresholds for parents, referred to as "spillover" or "welcome mat" effects.[19, 29] Increases in parental eligibility for Medicaid through the expansions

resulted in increased probability of children receiving preventive medical care, such as a well-child visit.[29] Increased insurance coverage may have led to improved vaccine access: the HPV vaccine is covered by health insurance plans, including Medicaid and the Vaccines for Children program for children up through age 18.[30] Most private insurance plans are required to include the preventive measure of the HPV vaccine without cost-sharing if given according to national guidelines.[30,31] Additionally, any adolescents who gained Medicaid eligibility through expansion were then eligible for the Vaccines for Children program—further improving access to the HPV vaccine.

It is possible that state-related conditions in expansion versus non-expansion states could act as confounders since Medicaid expansion was a state-wide policy. Such conditions could include political climate and religiosity.[16] Furthermore, Rhode Island and D.C. have the highest HPV vaccination rates which could be due to factors beyond Medicaid expansion, such as their vaccine mandate for school entry.[16] However, the parallel trends assumption was met for the difference-in-differences analysis, meaning that expansion and non-expansion states had similar vaccination trends prior to Medicaid expansion.

While the difference-in-difference approach provides strong evidence, this study does have limitations. The use of the NIS-Teen does not permit a full explanation of the mechanism behind the significant result for HPV vaccine completion. The NIS-Teen does not include parental insurance information to be able to test for parental spillover effects from Medicaid expansion, and the teenager's insurance variable is less reliable when combined over six years. As previously discussed, teenagers covered by CHIP were coded differently in 2016 versus previous years, which could lead to missing some observations covered by Medicaid. When

insurance data is further examined, there is not a large increase in Medicaid coverage for teenagers living in expansion states post-policy.

Other limitations stem from working with several years of data. The HPV vaccination guidelines for adolescents changed from three shots to two in 2016; this study used three shots to signify vaccination completion given the majority of the study period was from 2011-2016. Additionally, the surveys pre and post 2014 are not directly comparable according to NIS-Teen Data User's Guides due to differences in provider verification of records. We followed guidelines for appending data, and weighted it to the best of our ability for provider verification.

Finally, the parallel trends assumption was not met for all subgroup analyses by teenager's sex. These exploratory tests require further research to understand how Medicaid expansion impacted HPV vaccine initiation and completion for males and females separately.

Conclusion

Difference-in-difference analysis reveals a significant impact of Medicaid expansion on HPV vaccine completion. Furthermore, there is a significant impact of Medicaid expansion on vaccine initiation and completion for teenage males, with a significant impact on completion for teenage females.

Future research should examine the mechanism behind these difference-in-differences results. More reliable insurance coverage information could reveal if teenagers had increased Medicaid coverage after Medicaid expansion. Estimates from the American Community Survey can be used in further analyses.

Policy implications of these results are that expanding Medicaid eligibility thresholds is a way to improve HPV vaccination rates. Raising eligibility thresholds seems particularly beneficial for teenage males, which is promising given their lower HPV vaccination rates.

Policymakers should look to expanding Medicaid thresholds in non-expanded states to raise HPV vaccination rates for both males and females.

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Table 1. Characteristics of study sample by state Medicaid expansion status.

	Living in state that did not expand Medicaid (40.4%, n=38,088)	**Living in Medicaid expanded state (59.6%, n=57,899)**
HPV vaccine initiated*		
Did not initiate (0 shots)	57.2 (22,005)	50.2 (29,718)
Did initiate (at least 1 shot)	42.8 (16,083)	49.8 (28,181)
HPV vaccine completed*		
Did not completed (2 or fewer shots)	75.7 (28,635)	70.1 (40,231)
Did complete (at least 3 shots)	24.3 (9,453)	29.9 (17,668)
Sex of teenager		
Male	51.1 (19,852)	51.1 (30,313)
Female	48.9 (18,236)	48.9 (27,586)
Age of teenager		
13	19.8 (7,837)	19.7 (11,816)
14	20.4 (8,042)	19.9 (11,891)
15	20.3 (7,656)	21.1 (11,753)
16	20.6 (7,685)	20.5 (11,717)
17	19.0 (6,868)	18.8 (10,722)
Race/ethnicity of teenager*		
Hispanic	22.3 (8,234)	26.3 (9,167)
Non-Hispanic White	50.8 (22,321)	52.6 (37,094)
Non-Hispanic Black	19.3 (4,560)	10.3 (5,060)
Non-Hispanic other	7.6 (2,973)	10.7 (6,578)
Insurance status of teenager*		
Private insurance	52.4 (20,894)	56.5 (36,025)
Any Medicaid	38.2 (11,193)	35.9 (15,351)
Other insurance	8.2 (3,047)	7.0 (3,786)
Uninsured	1.2 (364)	0.6 (297)
Age of mother*		
<= 34 years	11.4 (3,622)	8.4 (4,127)
35 to 44 years	47.8 (17,021)	42.6 (22,302)
>= 45 years	40.8 (17,445)	48.9 (31,470)
Education level of mother*		
Less than high school	14.1 (5,260)	14.9 (5,950)
High school graduate	24.3 (7,071)	22.9 (9,747)
Some college	27.1 (10,450)	24.8 (15,046)
College graduate	34.6 (15,307)	37.4 (27,156)
Marital status of mother*		
Married	61.7 (26,898)	66.2 (42,172)
Single	38.3 (11,190)	33.8 (15,727)
Number of vaccination providers identified by parent*		
0	<0.01 (66)	<0.01 (81)
1	49.7 (18,035)	55.9 (31,825)
2	30.1 (11,787)	27.2 (16,362)
3+	20.1 (8,200)	16.8 (9,631)

Table 2. Difference-in-difference estimates of adolescent HPV vaccination rates.

	Difference-in-difference estimate controlling for state & year fixed effects and clustered standard errors by state (95% CI)	**p-value**	**Difference-in-difference estimate adjusted for time-varying covariates and controlling for fixed effects/clustered standard errors (95% CI)**	**p-value**
HPV vaccine initiation	3.9 (-0.4-8.1)	0.072	3.8 (-0.5-8.1)	0.079
HPV vaccine completion	4.9 (2.6-7.2)	<0.0001	4.9 (2.6-7.3)	<0.0001

Figure 1. Analytic sample flowchart.

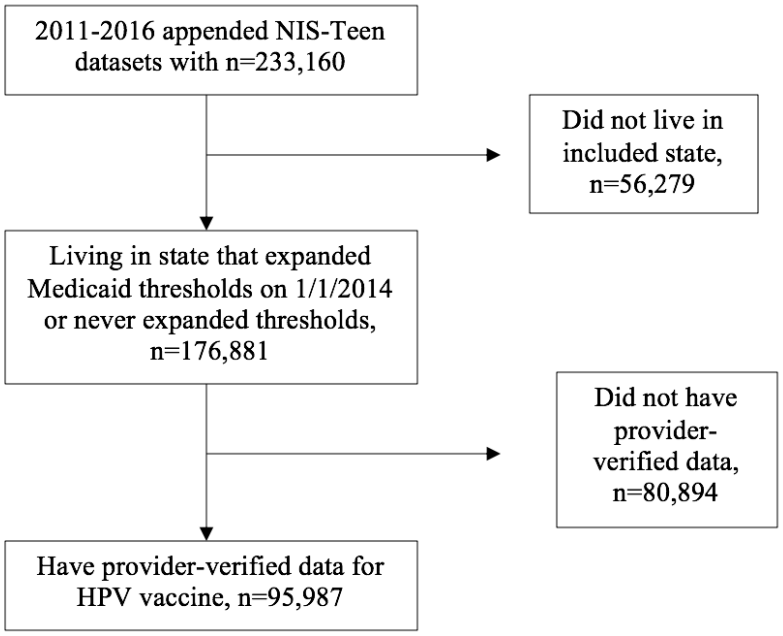

Figure 2. HPV vaccine initiation rates by state Medicaid expansion status, 2011-2016.

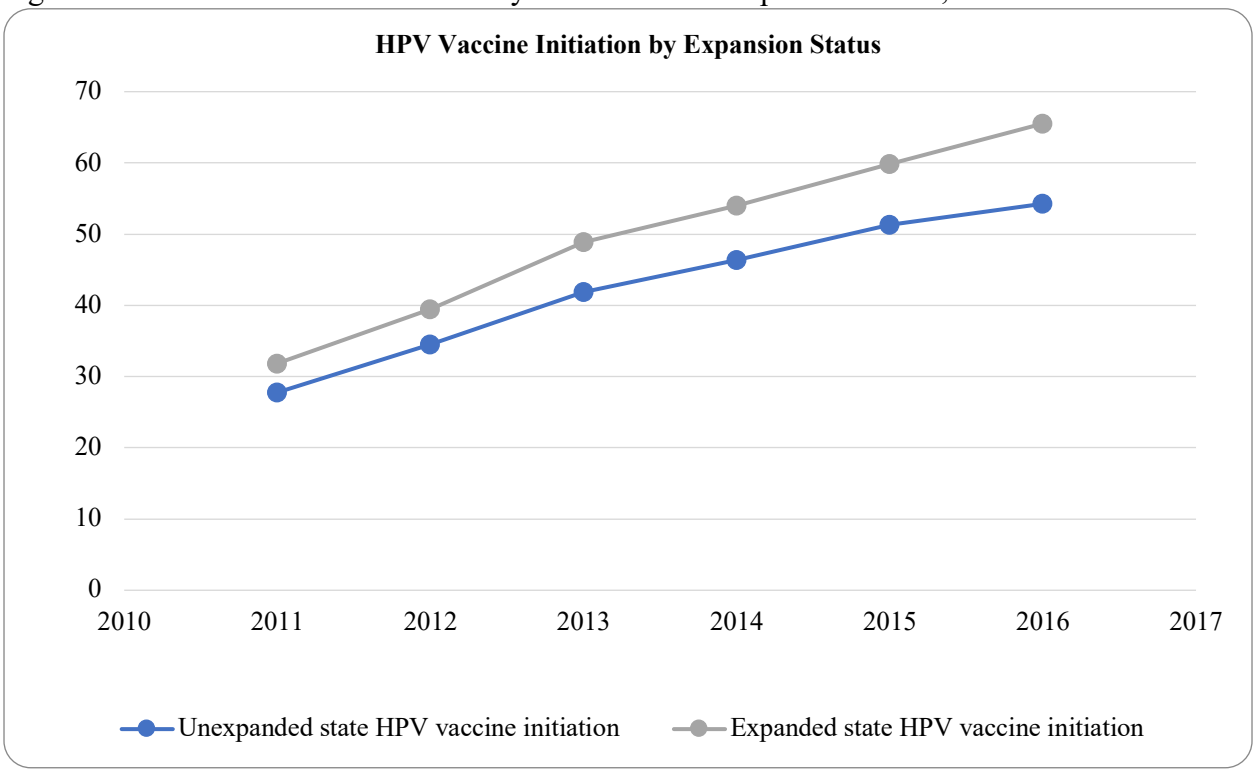

Figure 3. HPV vaccine completion rates by state Medicaid expansion status, 2011-2016.