

Impact of 9-Valent Human Papillomavirus Vaccine on HPV Vaccination Coverage of Youths, Ages 9-17, in North Carolina

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Background and Research Objectives

Human Papillomavirus (HPV) Vaccination

- Most common sexually-transmitted infection in the United States
- Causes genital warts, and is associated with cervical, vaginal, vulvar, anal, penile, and throat cancers
- Routine vaccination at age 11 or 12 years has been recommended by the Advisory Committee on Immunization Practices (ACIP) since 2006 for females and since 2011 for males

HPV Vaccination Rates

- In 2015, completion of the three-dose series among adolescents ages 13 to 17 was:
 - 42% for girls
 - 28% for boys
- HPV vaccination coverage also lags far behind childhood and other adolescent vaccines.

HPV Vaccine Types

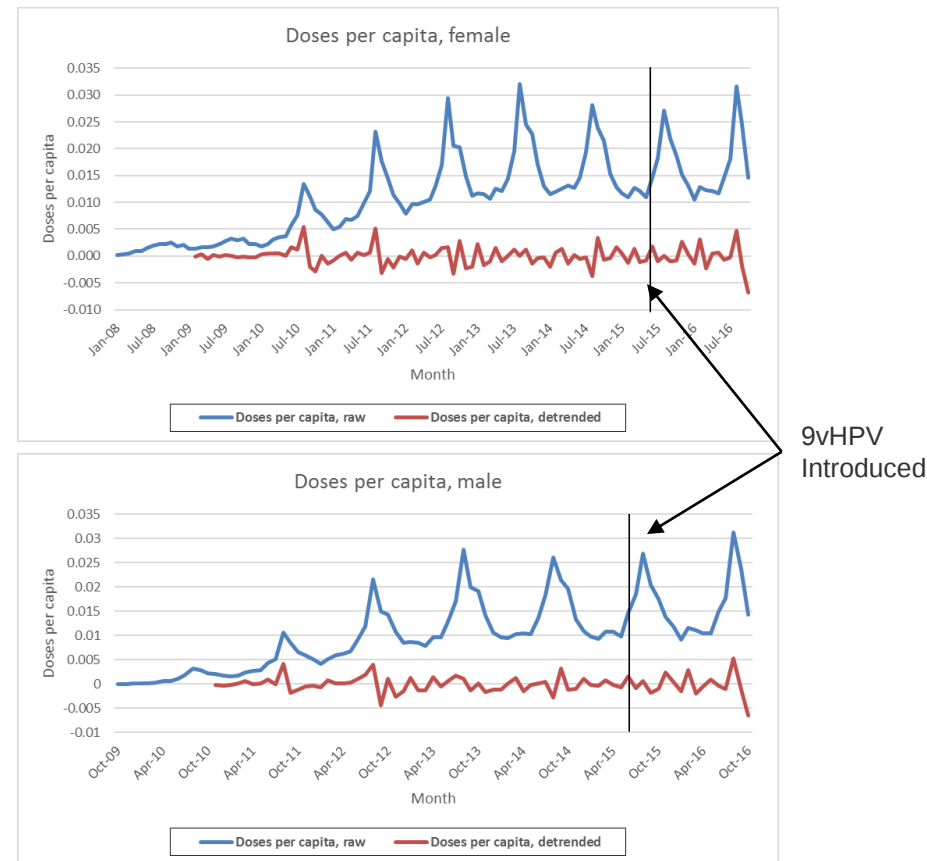
- Quadrivalent HPV vaccine (4vHPV) and 9-valent HPV vaccine (9vHPV) are currently licensed and indicated for use among both females and males in the US to protect against several of the most common HPV types associated with cancer.
- Bivalent HPV vaccine (2vHPV) is indicated for females only
- 9vHPV is the most recent HPV vaccine to enter the market
 - Food and Drug Administration approval in December 2014
 - ACIP recommendation in February 2015

Objectives:

- The primary objective was to evaluate the impact of introduction of 9vHPV vaccine on
 - HPV vaccination uptake (# doses)
 - Initiation (≥ 1 dose)
 - Completion (≥ 3 doses)
 - Compliance (≥ 3 doses within 1 year)
- The secondary objective was to describe timing of administration and characteristics of children who received 9vHPV compared to those who received another HPV vaccine (2vHPV or 4vHPV) beginning in July 2015.

Principal Findings

Figure 1. Population-weighted ZCTA-level HPV vaccination doses per capita by month



9vHPV
Introduced

Table 1. Individual-level logistic regression model for receiving 9vHPV vaccine type after July 2015

	Female		Male	
	N=146,405 doses		N=145,893 doses	
	Odds ratio	95% CI	Odds ratio	95% CI
Age	0.98	(0.97, 0.99)	0.97	(0.96, 0.98)
White race	1.00	—	1.00	—
African American race	1.00	(0.94, 1.05)	0.98	(0.93, 1.03)
Other race	1.19	(1.06, 1.33)	1.13	(1.02, 1.25)
Publicly funded dose	0.59	(0.54, 0.64)	0.58	(0.54, 0.63)
Age-eligible ZCTA population (in units of 10,000)	2.10	(1.62, 2.73)	2.03	(1.54, 2.67)
Percent of ZCTA population that is female	0.52	(0.02, 15.0)	1.46	(0.06, 33.56)
Percent of ZCTA population that is non-White	1.05	(0.69, 1.60)	0.94	(0.62, 1.42)
Percent of ZCTA population with less than high school education	0.20	(0.04, 0.82)	0.12	(0.03, 0.54)
Percent of ZCTA population with a college degree	0.73	(0.32, 1.66)	0.55	(0.25, 1.25)
Percent of ZCTA population in persistent poverty	0.89	(0.66, 1.20)	0.79	(0.63, 1.00)
Indicator for health professional shortage area	1.19	(1.02, 1.38)	1.17	(1.01, 1.36)
Number of annual outpatient visits per capita in ZCTA	1.05	(1.02, 1.08)	1.05	(1.01, 1.08)
Number of religious organizations per capita in ZCTA	0.86	(0.77, 0.98)	0.85	(0.76, 0.94)

Bold indicates significance at the 95% confidence level.

Quarter fixed effects and intercept not shown. Standard errors clustered by ZCTA.

Methodology

PRIMARY OBJECTIVE

Design: Area-level interrupted time series

Outcomes: Area-level uptake (doses), initiation, completion, and compliance rates

Key explanatory variable: Indicator for the introduction of 9vHPV in NC in July 2015

Analysis

- De-trended monthly time series to remove time trend and seasonality
- Regression on an indicator variable for ZCTA/months post release of 9vHPV

SECONDARY OBJECTIVE

Design: Individual-level retrospective cohort

Outcome: Indicator variable for receiving 9vHPV (relative to other HPV vaccine type)

Key explanatory variables: Youth and area-level demographic characteristics and other area-level market characteristics

Analysis

- Logistic regression
- Separate regressions by sex

Data

North Carolina Immunization Registry (NCIR)

- January 2008 through October 2016
- Youth between the ages of 9 and 17 years in 2016
 - Complete vaccination history for this cohort of youth
- Excluded youth in the NCIR with missing values for date of the HPV vaccine, HPV vaccine type, sex or ZIP code
- *Primary objective:* aggregated data to ZIP Code Tabulation Areas (ZCTAs)
- *Secondary objective:* restricted sample to doses of HPV vaccine administered during or after July 2015 (introduction of 9vHPV in NC)

Discussion

Primary objective

- Introduction of 9vHPV was not associated with changes in HPV vaccination rates in NC as measured by doses per capita or initiation, completion or compliance rates
- Results did not change when we also included ZCTA-level characteristics and allowed for autoregression in the error terms.

Secondary objective

- Following the introduction of 9vHPV, youth receiving the HPV vaccine were *more* likely to receive 9vHPV than other HPV vaccine types if they lived in a ZCTA with
 - a larger age-eligible (i.e., 9 to 17) population,
 - a health professional shortage area, or
 - a higher number of annual outpatient visits per capita.
- Following the introduction of 9vHPV, youth receiving the HPV vaccine were *less* likely to receive 9vHPV than other HPV vaccine types if
 - they were older,
 - received a publicly-funded dose, or
 - lived in a ZCTA with a higher percentage of the population with less than a high-school education or
 - a higher number of religious organizations.

Limitations

- NCIR does not include complete coverage of privately funded vaccines, vaccines given by pharmacies or to youths who may have moved out of state
- Not representative of U.S. or areas of country with different demographics and regional patterns of care
- Bias could remain from changes in unobserved confounders concurrent with the introduction of 9vHPV (e.g., changes in outreach policies in the state)

Summary

- Introduction of 9vHPV was not associated with changes in HPV vaccination rates in NC
- Transition from 4vHPV to 9vHPV was quick
- Disparities in the diffusion of 9vHPV across areas of NC