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

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Disclosures

Brianna Lindsay is an employee of Merck & Co., Inc.
HPV Vaccination in the United States

• Human papillomavirus (HPV) is a common sexually transmitted infection with an incidence of approximately 14 million new persons in the US annually.

• Persistent HPV infection can lead to cervical cancer, anogenital cancer, and genital warts.

• 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 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, gaining Food and Drug Administration (FDA) approval in December of 2014 and an ACIP recommendation in February of 2015.
Primary Study Objective

• To describe the transition from 4vHPV to 9vHPV in aggregate and identify determinants of the receipt of 9vHPV (vs. 4vHPV) among youth following the introduction of 9vHPV in North Carolina
Methods: Study Design

• Retrospective cohort analysis using North Carolina Immunization Registry (NCIR) data from January 2008 through October 2016

• Interrupted time series design to measure associations between ZIP Code Tabulation Area (ZCTA)-level HPV vaccination outcomes over time with the introduction of 9vHPV in North Carolina (NC) in July 2015
North Carolina Immunization Registry

• Registry’s primary users:
  – Local health departments (100% participate)
  – Private provider offices that receive vaccines from the federally funded Vaccines for Youth (VFC) program (over 90% of offices that receive VFC vaccines participate)
  – Clinics associated with the state’s medical schools
Methods: Sample

• Age-eligible youth from the NCIR starting in 2008 through October 2016
• October 2016 provides over one year of data after the introduction of 9vHPV in NC and also captures the peak summer vaccination season in 2016
• Excluded youth in the NCIR with missing values for date of the HPV vaccine, HPV vaccine type, sex or ZIP code
Methods: Vaccination Outcomes

- **Uptake**: the number of HPV doses per capita in the age-eligible population
- **Initiation**: the proportion of age-eligible youth who had received an initial dose of HPV vaccine during the relevant time period
- **Completion**: the proportion of youth who initiated the series and completed three or more doses
- **Compliance**: the proportion of youth who completed receiving their third dose within one year of their first dose
Methods: Statistical Analyses

• **De-trended monthly time series**
  – adjusted the ZCTA-level monthly time series for each dependent variable as to not conflate the introduction of 9vHPV with increases in HPV vaccination due to underlying secular trends or seasonal patterns.
  – Overall time trend through first-differences
  – Seasonally adjusted the data by differencing each month with the same month in the previous year.

• **Regression on an indicator variable for ZCTA/months post release of 9vHPV**
## Results: Primary Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Overall Proportion (SD)</th>
<th>10/2008–6/2015 Proportion (SD)</th>
<th>7/2015–10/2016 Proportion (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Female</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initiation</td>
<td>0.661 (0.009)</td>
<td>0.521 (0.008)</td>
<td>0.120 (0.002)</td>
</tr>
<tr>
<td>Completion</td>
<td>0.332 (0.005)</td>
<td>0.248 (0.004)</td>
<td>0.067 (0.001)</td>
</tr>
<tr>
<td>Compliance</td>
<td>0.168 (0.002)</td>
<td>0.142 (0.002)</td>
<td>0.026 (0.0005)</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initiation</td>
<td>0.567 (0.009)</td>
<td>0.416 (0.008)</td>
<td>0.118 (0.002)</td>
</tr>
<tr>
<td>Completion</td>
<td>0.247 (0.004)</td>
<td>0.163 (0.003)</td>
<td>0.061 (0.001)</td>
</tr>
<tr>
<td>Compliance</td>
<td>0.117 (0.002)</td>
<td>0.092 (0.002)</td>
<td>0.022 (0.0005)</td>
</tr>
</tbody>
</table>

*Population-weighted ZCTA-level HPV vaccination outcomes by time period, proportion of Census age-eligible population (N=805 ZCTAs)
Results: Doses per capita, Female

Doses per capita, raw vs. Doses per capita, detrended

9vHPV Intro
Results: Doses per capita, Male

Doses per capita

Month

Doses per capita, raw
Doses per capita, detrended

9vHPV Intro
Results: Initiation, Female

Month

Initiation

Initiation, raw

Initiation, detrended

9vHPV Intro
Results: Initiation, Male

-0.005
0.000
0.005
0.010
0.015
0.020

Month

Initiation

Initiation, raw

Initiation, detrended

9vHPV Intro
Results: Completion, Female

Completion, raw
Completion, detrended

Month

Completion

Jan-08  Jul-08  Jan-09  Jul-09  Jan-10  Jul-10  Jan-11  Jul-11  Jan-12  Jul-12  Jan-13  Jul-13  Jan-14  Jul-14  Jan-15  Jul-15  Jan-16  Jul-16

9vHPV Intro
Results: Completion, Male

Completion

Month

Completion, raw  Completion, detrended

9vHPV Intro
Results: Compliance, Female

-0.001
0.000
0.001
0.002
0.003
0.004

Compliance

Month

9vHPV Intro

Compliance, raw
Compliance, detrended
Results: Compliance, Male

9vHPV Intro
Results: Primary Outcomes

• 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: Doses Distributed
## Results: Regression Outcome 9vHPV Receipt, Female

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio</th>
<th>95% confidence interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age*</td>
<td>0.98</td>
<td>(0.97, 0.99)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>White race</td>
<td>1.00</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>African American race</td>
<td>0.98</td>
<td>(0.93, 1.05)</td>
<td>0.61</td>
</tr>
<tr>
<td>Other race*</td>
<td>1.21</td>
<td>(1.07, 1.37)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Publicly funded dose*</td>
<td>0.64</td>
<td>(0.60, 0.69)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Age-eligible ZCTA population (units of 10,000)*</td>
<td>2.14</td>
<td>(1.64, 2.81)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Percent of ZCTA population that is female</td>
<td>0.20</td>
<td>(0.01, 6.24)</td>
<td>0.36</td>
</tr>
<tr>
<td>Percent of ZCTA population that is non-White</td>
<td>1.02</td>
<td>(0.67, 1.57)</td>
<td>0.92</td>
</tr>
<tr>
<td>Percent of ZCTA population with less than HS education*</td>
<td>0.15</td>
<td>(0.03, 0.63)</td>
<td>0.01</td>
</tr>
<tr>
<td>Percent of ZCTA population with a college degree</td>
<td>0.49</td>
<td>(0.22, 1.10)</td>
<td>0.08</td>
</tr>
<tr>
<td>Percent of ZCTA population in poverty</td>
<td>0.89</td>
<td>(0.66, 1.21)</td>
<td>0.47</td>
</tr>
<tr>
<td>Indicator for health professional shortage area*</td>
<td>1.18</td>
<td>(1.00, 1.39)</td>
<td>0.04</td>
</tr>
<tr>
<td>Number of annual outpatient visits per capita in ZCTA*</td>
<td>1.05</td>
<td>(1.02, 1.08)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Number of religious organizations in ZCTA (units of 100)*</td>
<td>1.00</td>
<td>(1.00, 1.00)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

*P<0.05
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<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>0.97</td>
<td>(0.96, 0.98)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>White race</td>
<td>1.00</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>African American race</td>
<td>0.97</td>
<td>(0.92, 1.03)</td>
<td>0.31</td>
</tr>
<tr>
<td>Other race*</td>
<td>1.13</td>
<td>(1.02, 1.26)</td>
<td>0.02</td>
</tr>
<tr>
<td>Publicly funded dose*</td>
<td>0.63</td>
<td>(0.58, 0.68)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Age-eligible ZCTA population (units of 10,000)*</td>
<td>2.12</td>
<td>(1.59, 2.83)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Percent of ZCTA population that is female</td>
<td>0.52</td>
<td>(0.02, 12.77)</td>
<td>0.69</td>
</tr>
<tr>
<td>Percent of ZCTA population that is non-White</td>
<td>0.91</td>
<td>(0.60, 1.39)</td>
<td>0.67</td>
</tr>
<tr>
<td>Percent of ZCTA population with less than HS education*</td>
<td>0.10</td>
<td>(0.02, 0.44)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Percent of ZCTA population with a college degree*</td>
<td>0.42</td>
<td>(0.19, 0.93)</td>
<td>0.03</td>
</tr>
<tr>
<td>Percent of ZCTA population in poverty</td>
<td>0.80</td>
<td>(0.63, 1.02)</td>
<td>0.07</td>
</tr>
<tr>
<td>Indicator for health professional shortage area</td>
<td>1.19</td>
<td>(1.01, 1.40)</td>
<td>0.04</td>
</tr>
<tr>
<td>Number of annual outpatient visits per capita in ZCTA*</td>
<td>1.05</td>
<td>(1.02, 1.09)</td>
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<td>Number of religious organizations in ZCTA (units of 100)*</td>
<td>1.00</td>
<td>(1.00, 1.00)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

*P<0.05
Results: Secondary

• Transition from 4vHPV to 9vHPV was relatively quick in North Carolina

• There were disparities in the diffusion of 9vHPV across areas of NC. Findings suggest that 9vHPV was slower to reach rural areas and areas with lower levels of education.
Discussion

• 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
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