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Determinants of the receipt of the 9-valent human papillomavirus vaccine in the first year after introduction in North Carolina

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ABSTRACT

Objectives: The objective of this study was to describe the transition from bi- and quadrivalent HPV vaccines to 9vHPV in aggregate and identify determinants of the receipt of 9vHPV among youth following the introduction of 9vHPV in North Carolina.
Methods: The study used a retrospective cohort design with data from the North Carolina Immunization Registry (NCIR). Our sample included all doses of HPV vaccine administered between July 2015 and October 2016 to age-eligible youth (ages 9–17). We used a logistic regression model to associate individual child-level and ZIP Code Tabulation Area (ZCTA)-level characteristics with an indicator variable for receiving 9vHPV (vs. other HPV vaccines).
Results: Youth receiving the HPV vaccine were *more* likely to receive 9vHPV if they lived in a ZCTA with a larger age-eligible (i.e., 9–17) population, a health professional shortage area, or a higher number of annual outpatient visits per capita. They were *less* likely to receive 9vHPV 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.
Conclusions: While the transition from other HPV vaccines to 9vHPV was relatively quick, there were disparities in the diffusion of 9vHPV across North Carolina.

1. Introduction

Human papillomavirus (HPV) is the most common sexually transmitted infection in the United States (US) with an incidence of approximately 14 million new cases in the US annually [1]. While there are over 100 types of HPV that humans can contract, about 40 types infect the anogenital tract. Oncogenic HPV types cause nearly all cervical and anal cancers and many vulvar, vaginal, penile, and oropharyngeal cancers [2]. Approximately 26,200 cancers annually in the US are attributable to HPV (17,400 among females and 8800 among males) [2].

The bivalent HPV vaccine (2vHPV), licensed and indicated for females only, prevents infection with oncogenic HPV types 16 and 18. The quadrivalent HPV vaccine (4vHPV) protects against HPV nononcogenic types 6 and 11 and oncogenic types 16 and 18; it is licensed for use among both females and males. These HPV vaccines have been shown to be cost-effective and have high efficacy in protecting against HPV and related cancers [3–7].

In December 2014, the Food and Drug Administration approved a 9-valent HPV vaccine (9vHPV; Gardasil 9, Merck and Co., Inc.) that adds protection against HPV oncogenic types 31, 33, 45, 52 and 58 to the 4vHPV vaccine. 9vHPV demonstrated an efficacy of 97% against these additional HPV types [8]. The 9vHPV vaccine was added to the US Advisory Committee on Immunization Practices (ACIP) recommendation in February 2015 [9]. By the end of 2016, only the 9vHPV vaccine was commercially available in the US.

While many providers were transitioning stock from other HPV vaccines to the new 9vHPV, little is known about how the transition was rolled out to different populations. The literature suggests that several factors affect the likelihood of HPV vaccination with either type of vaccine (e.g., insurance coverage [10,11], provider recommendation [2], religious affiliation [2], access to the health care system [12], area-level poverty [11,13], and urbanicity [12]). However, there is scant evidence about the determinants of the type of vaccine received (e.g., 9vHPV vs. 4vHPV). The objective of

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this study was to describe the transition from other HPV vaccines to 9vHPV in aggregate and identify determinants of the receipt of 9vHPV (vs. other HPV vaccines) among adolescents following the introduction of 9vHPV. However, it is recognized that since the utilization of the bivalent HPV vaccine was so low in the US, less than 2%, we recognize that this analysis will primarily reflect a transition from 4vHPV to 9vHPV.

2. Methods

2.1. Design

We used a retrospective cohort design to analyze HPV vaccine administration with data from the North Carolina Immunization Registry (NCIR) information system. We used a logistic regression model to associate potential determinants of vaccine type received with an indicator variable for receiving 9vHPV (vs. other HPV vaccines). The key explanatory variables were child and area-level demographic characteristics and other area-level market characteristics. The sample was restricted to those age-eligible adolescents aged 9–17 who received the HPV vaccine after July 1st, 2015, the date on which the 9vHPV vaccine was first distributed within the state by the NC Department of Health and Human Services.

2.2. Data

The NCIR is a secure, web-based clinical tool to provide official immunization information to the state [14]. The registry's primary users are local health departments (100% participate), private provider offices that receive vaccines from the federally funded Vaccines for Children (VFC) program (over 90% of offices that receive VFC vaccines participate), and clinics associated with the state's medical schools. The VFC program provides vaccines at no cost to adolescents who otherwise might not be vaccinated because of their parents' inability to pay. Health care providers who receive VFC vaccines are required to document administration of those vaccines in the NCIR (approximately 95% of participating practices) or via an alternative hard copy form (approximately 5% that are not captured in the NCIR). The NCIR provided information on receipt of HPV vaccinations, including date of receipt, type of HPV vaccine administered, age, sex, race, ethnicity, source of funding for dose, and ZIP code.

We mapped ZIP codes to ZCTAs using a crosswalk created by a Health Resources and Services Administration-funded project directed by the Robert Graham Center [15]. ZCTAs are generalized area representations of ZIP code service areas developed by the U.S. Census Bureau to overcome the difficulties in precisely defining the land area covered by each ZIP code. The crosswalk lists all ZIP codes included in each ZCTA. We collected geographic boundary and demographic characteristics for North Carolina (NC) ZCTAs from the U.S. Census Bureau: 2013 TIGER shape files, 2010 U.S. Census, and 2010–2014 (5-year) American Community Survey (ACS). We also collected county-level characteristics from the 2014–2015 Area Resource File (ARF) and 2008–2014 County Business Patterns (CBP), using TIGER shape files to crosswalk from county to ZCTA.

2.3. Sample

The sample included all HPV vaccine doses given between July 1, 2015 and October 31, 2016 to adolescents between the ages of nine, the youngest age at which the HPV vaccination should be given, and 17 years in 2016. The NCIR contains complete vaccination history for adolescents that were nine and older in 2008; the oldest were 17 years in 2016. The analysis period captures over one year of data following the introduction of 9vHPV in NC including the peak summer vaccination season. We excluded adolescents in the NCIR with missing values for date of the HPV vaccine, HPV vaccine type, sex or ZIP code (Table 1).

2.4. Variables

The dependent variable was an indicator for the type of HPV vaccine received for doses administered in July 2015 and later that equals 1 if the dose was 9vHPV and equals 0 if the dose was 4vHPV or 2vHPV. Independent variables included the following individual-level characteristics from the NCIR: age, race (white [reference], African American, or other race) and an indicator for a publicly funded dose. Area-level covariates included the following: the population of age-eligible adolescents ages 9–17 in units of 10,000 (ACS); percent of the total population that is female (ACS), Hispanic, black Non-Hispanic, or other or multi-race/ethnicity (white non-Hispanic reference) (ACS); and the percent of the total population with less than high school diploma and with at least some college (high school diploma reference) (ACS). We adjusted for indicators of USDA-defined persistent poverty (ARF) and Health Professional Shortage Area (HPSA) defined by Health Resources and Services Administration (ARF). A ZCTA was designated as having a shortage of primary medical care professionals by the Health Resources and Services Administration if the following three criteria were met. (1) The area is a rational area for the delivery of primary medical services. (2) One of the following conditions prevails within the area: (a) the area has a population to full-time-equivalent primary care physician ratio of at least 3500:1 or (b) the area has a population to full-time-equivalent primary care physician ratio of less than 3500:1 but greater than 3000:1 and has unusually high needs for primary care services or insufficient capacity of existing primary care providers. (3) Primary medical care professionals in contiguous areas are over utilized, excessively distant or inaccessible to the population of the area under consideration. We also adjusted for outpatient visits per capita (ARF) and the number of religious organizations (North American Industry Classification System code 8131) per capita (CBP). The sources for ZCTA-level covariates were centered on 2010 values, but the data sources did not include all years. We used linear interpolation to fill in values for missing years.

2.5. Statistical analysis

The unit of analysis was the vaccine dose. We used logistic regression to estimate the odds of receiving 9vHPV (vs. 4vHPV or 2vHPV) with separate models by sex. Because coverage in the NCIR

Table 1
Inclusion and exclusion criteria.

	Dropped		Remaining
	N	%	
Original person and person-dose observations			3,813,416
Excluded those with missing gender	150,965	4.0%	3,662,451
Excluded those with missing ZIP code	858,490	23.4%	2,803,961
Excluded those whose birthdate is out of range	1,206,154	43.0%	1,597,807
Excluded those whose age at immunization is <9	547	0.03%	1,597,260
Excluded person-only records [no HPV vaccination given]	748,543	46.9%	848,717
Excluded doses prior to July 2015	543,545	64.0%	305,172
Excluded those whose ZIP code does not map to a North Carolina ZCTA	3270	1.1%	301,902
Excluded doses with missing vaccine type after HPV9 introduction	4738	1.6%	**297,164**