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Correlates of human papillomavirus (HPV) vaccine coverage: A state-level analysis

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Abstract

Background—We tested the hypothesis that states with higher rates of cancers associated with human papillomavirus (HPV) would have lower HPV vaccine coverage.

Methods—We gathered state-level data on HPV-related cancer rates and HPV vaccine initiation coverage for girls and boys, separately, and HPV vaccine follow-through (i.e., receipt of 3 doses among those initiating the series) for girls only. In addition, we gathered state-level data on demographic composition and contact with the healthcare system. We calculated Pearson correlations for these ecological relationships.

Results—HPV vaccine initiation among girls was lower in states with higher levels of cervical cancer incidence and mortality (r=−.29 and −.46, respectively). In addition, vaccine follow-through among girls was lower in states with higher levels of cervical cancer mortality (r=−.30). Other cancer rates were associated with HPV vaccine initiation and follow-through among girls, but not among boys. HPV vaccine initiation among girls was lower in states with higher proportions of non-Hispanic black residents and lower proportions of higher income residents. HPV vaccine follow-through was higher in states with greater levels of adolescents' contact with the healthcare system.

Conclusions—HPV vaccine coverage for girls was lower in states with higher HPV-related cancer rates. Public health efforts should concentrate on geographic areas with higher cancer rates. Strengthening adolescent preventive healthcare use may be particularly important to increase vaccine follow-through. Cost-effectiveness analyses may overestimate the benefits of current vaccination coverage and underestimate the benefits of increasing coverage.

Keywords

human papillomavirus (HPV) vaccine; demographics; healthcare access; cancer; states

National guidelines recommend that 11- and 12-year-old adolescents receive three doses of human papillomavirus (HPV) vaccine.[1] However, HPV vaccine uptake remains low, with coverage levels falling far short of public health goals and uptake of other recommended

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adolescent vaccines.[2,3] In addition, considerable variation in HPV vaccination levels between states exists: receipt of all three doses of HPV vaccine ranges from 12.1% of adolescent girls in Mississippi to 57.7% of adolescent girls in Rhode Island.[3]

Preliminary studies demonstrate the effect of HPV vaccination on reducing population levels of HPV infection and genital warts,[4–6] but the potential impact on cancer outcomes remains to be seen. However, examining the relationship between current vaccination patterns and cancer rates could foreshadow the future benefits of widespread vaccination. Bach[7] investigated two state characteristics that correlated with levels of HPV vaccine initiation among girls (using 2008 vaccination data), highlighting the negative relationship with cervical cancer mortality and the positive relationship with median household income. The author found that HPV vaccine initiation was more common in states in which girls were at lower risk of cervical cancer mortality.

To update and extend these findings and to better understand the ecological pattern of HPV vaccination in states across the U.S., we analyzed the relationships between states' HPV vaccine coverage and (a) the incidence and mortality rates of HPV-related cancers, (b) demographic characteristics, and (c) measures of contact with the healthcare system. We hypothesized that states with higher HPV-related cancer rates, including cervical cancer, would have lower HPV vaccine coverage.

Materials and Methods

Data sources

We examined data for 50 states and Washington D.C. For the sake of simplicity, we refer to all 51 jurisdictions as states hereafter.

Vaccination—Vaccination data came from the 2012 National Immunization Survey-Teen (NIS-Teen) (the most recent year of available data at the time of analyses).[3] We examined HPV vaccine initiation (i.e., received ≥ 1 dose) among adolescents ages 13-17, stratified by sex. We examined HPV vaccine follow-through (i.e., received all 3 recommended doses, among those who initiated HPV vaccination) only among girls ages 13-17. Follow-through differs from three dose completion in that it examines completion only among vaccine initiators rather than the entire population; NIS-Teen reports these outcomes separately and has noted the different pattern of sociodemographic correlates for initiation and completion of three doses versus for follow-through.[3] We also gathered data on coverage with tetanus, diphtheria, and pertussis booster (Tdap) and meningococcal conjugate vaccine (receipt of first dose) for adolescents ages 13-17.

Rates of HPV-related cancer—We obtained incidence and mortality rates per 100,000 population from the 2001–2010 United States Cancer Statistics database[8] for cancers that HPV vaccine is currently approved to prevent[9,10]: anal cancer (both genders) and cervical, vaginal, and vulvar cancers (females only). We created a measure of cancer deaths attributable to HPV types protected against by the bivalent and quadrivalent HPV vaccines (i.e., types 16 and 18).[11] Thus, we discounted the annual death rate per 100,000 population by the attributable fraction (87% of anal, 76% of cervical, 56% of vaginal, and 44% of

vulvar cancer), and then we summed the discounted attributions. Any state with missing data on at least one cancer mortality rate (because of fewer than 16 observations during the study period) was coded to missing on the summary measure.

Demographics—We used data from the U.S. Census[12,13] to examine the racial/ethnic composition (2012 data) and median household income (2011–2012 data) of each state. We calculated physicians per 100,000 population for three specialties (pediatrics, family practice, and obstetrics/gynecology) using data from the Bureau of Labor Statistics[14] and standardized with population estimates from the U.S. Census.[12]

Contact with healthcare system—We captured adolescent healthcare adequacy, as reported by parents, using two constructs derived from the National Survey of Children's Health[15]: the proportion of adolescents in each state (a) with a medical home and (b) who had a healthcare provider whom their parents considered their “personal” doctor or nurse. Since around 6% of U.S. schools have health centers that may provide vaccines,[16] we used data from the School-based Health Alliance[17] and the U.S. Census[12] to measure the number of school-based health centers per 100,000 population in each state.

We calculated the proportion of adult females in each state (ages 18 and older) who had received a Pap test in the previous three years using data from the Behavioral Risk Factor Surveillance System (BRFSS).[18] To account for errors in self-report of Pap testing,[19–21] we adjusted state-level BRFSS estimates based on the methodology described by Rauscher and colleagues.[22]

Statistical analysis

We examined the relationships between HPV vaccination outcomes and other variables using Pearson product-moment correlations yielding *r* statistics. All statistical tests were 2-tailed, and we describe in-text all correlations with a *p* value of < .10 given the ecological sample size of *k*=51 states. We graphed scatterplots for notable relationships. We analyzed data using Stata version 13 (College Station, TX).

Results

According to the 2012 NIS-Teen results,[3] 53.8% of female adolescents had initiated HPV vaccine, and 66.7% of those initiators had followed through with receipt of 3 doses of HPV vaccine. Among adolescent males, 20.8% had initiated HPV vaccine.

HPV vaccine initiation (girls)

Girls' initiation was lower in states with higher levels of incidence and mortality rates of HPV-related cancers: cervical cancer incidence (*r*=−.29), cervical cancer mortality (*r*=−.46; Figure 1, Panel A), and the summary measure of mortality rates for cancers related to HPV 16/18 (*r*=−.58) (Table 1). HPV vaccine initiation among girls was higher in states with higher median household incomes (*r*=.32), lower proportions of non-Hispanic black residents (*r*=−.28), higher proportions of residents of “other” races/ethnicities (*r*=.24), and greater concentrations of pediatricians (*r*=.47; Figure 1, Panel B) and OB/GYNs (*r*=.37). Initiation among girls was also higher in states with higher levels of other vaccination

outcomes: boys' HPV vaccine initiation (r=.43; Figure 1, Panel C), Tdap vaccination (r=.43), and meningococcal vaccination (r=.48).

HPV vaccine follow-through (girls)

Follow-through was lower in states with higher rates of vaginal cancer incidence (r=−.25), cervical cancer mortality (r=−.30), and the summary measure of mortality rates for cancers related to HPV 16/18 (r=−.29) (Table 1). Interestingly, follow-through was higher in states with higher rates of vulvar cancer incidence (r=.30). In addition, follow-through was higher in states with higher levels of other measures of healthcare access: other vaccination outcomes (r=.27 to .51), adolescent healthcare adequacy (r=.26 to .37), concentration of school health centers (r=.25), and proportion of adult women with a recent Pap test (r=.36; Figure 2).

HPV vaccine initiation (boys)

HPV vaccine initiation among boys was higher in states with lower proportions of residents that were non-Hispanic white (r=−.31) and higher proportions of residents of “other” races/ethnicities (r=.32) (Table 1). Boys' initiation was also higher in states with higher levels of meningococcal conjugate vaccination (r=.39) and proportions of adolescents with a “personal” doctor or nurse (r=.26).

Discussion

In line with our hypothesis, states with higher rates of HPV-related cancers, including cervical cancer, had lower HPV vaccine coverage (both initiation and follow-through) among girls. Girls' initiation was also associated with demographic composition. However, girls' follow-through demonstrated more consistent associations with measures related to contact with the healthcare system. For boys, initiation showed some associations with demographic composition and contact with the healthcare system, but not HPV-related cancer rates. As initiation among boys and girls was highly correlated, it is possible that the pattern seen among girls could develop as vaccination among boys becomes more widely accepted and coverage increases.

Lower rates of HPV vaccination in areas with higher cancer rates could exacerbate current disparities in cancer incidence and mortality across states. One potential mechanism is that HPV is sexually transmitted,[23] and infections spread through sexual networks that are largely geographically bounded.[24–26] In addition, HPV vaccine initiation among girls was lower in states with a higher proportion of non-Hispanic black residents, an especially worrisome finding as black women have among the highest risk for cervical cancer.[27] Girls' follow-through was associated with lower incidence rates for vaginal cancer and higher incidence rates for vulvar cancer, although the reasons for the different directions of these relationships is unclear. Promotional efforts should concentrate on increasing HPV vaccination, including follow-through, for both boys and girls in areas with high rates of HPV-related cancer incidence and mortality. Our findings also suggest that cost-effectiveness analyses may overestimate the benefits of current vaccination coverage and underestimate the benefits of increasing coverage, as girls living in areas with the highest

rates of HPV-related cancers were the least likely to initiate the HPV vaccine series. Cost-effectiveness models should consider the impact of disproportionate vaccination by cancer risk on the benefits of vaccine promotional efforts.[28–31]

Ecological measures of contact with the healthcare system demonstrated consistent, positive associations with HPV vaccine follow-through among girls. That is, girls were more likely to follow-through with vaccination if they lived in states with greater use of other preventive healthcare services. This pattern is not surprising, but it does underscore the need for healthcare systems and services that meet the needs of adolescents, who have contact with primary care less often than younger children.[32] It will be important to test these associations with follow-through among boys, as well, but follow-through estimates were only available for 11 states in the 2012 NIS-Teen data.[3]

Some differences emerged between our ecological state-level findings and the individual-level findings in the report of the 2012 NIS-Teen results.[3] HPV vaccine initiation among non-Hispanic black girls did not differ from non-Hispanic whites in analyses of individual-level data, but initiation among girls was higher in states with lower proportions of non-Hispanic black residents in our ecological analyses. Follow-through was lower among black and Hispanic girls than non-Hispanic whites in the individual-level analyses, but no relationship between rates of follow-through and demographic composition emerged in our ecological analyses. However, for both the individual and ecological analyses, follow-through was positively associated with white race. Initiation was lower among non-Hispanic white boys than other racial/ethnic groups in individual-level analyses, a finding that held true in our ecological analyses. Finally, in individual analyses, all vaccination outcomes were more common among adolescents living below the federal poverty level than those living at or above the poverty level, but we found that median household income was positively associated with girls' initiation and no relationship for boys' initiation or girls' follow-through. This pattern could reflect multilevel influences on vaccination that vary across people and states, including health insurance status and personal beliefs versus public health funding and social norms. To the extent that HPV-related cancer rates vary systematically by individual race as well as state racial composition, additional research should examine the potential causes of these differences in relationships and interventions to address them, with an ultimate goal of reducing disparities in vaccination and cancer.

Our analyses have several limitations, including that the findings from the ecological analyses we report may not generalize to variability among individuals. The small number of observations (n=51) limits the options for statistical analysis of these ecological phenomena. Notably, the correlations reported here may vary when controlling for additional factors, but adding variables to the models may lead to unstable results. To examine the potential impact of controlling for sociodemographic characteristics on the relationship between HPV vaccination and cervical cancer mortality, we ran exploratory linear regression models that controlled for two state-level variables: median household income and demographic composition (percent of residents who are non-Hispanic white, non-Hispanic black, and Hispanic). The coefficients of the associations between mortality and HPV vaccine initiation and follow-through remained statistically-significant in these analyses (p=.04 and p=.02, respectively), increasing our confidence in the findings.

In addition, we gathered data that were generally cross-sectional. Such data limit our ability to make conclusions about causal mechanisms driving vaccine coverage, but they instead permitted us to characterize the context in which vaccination took place. Additional studies are needed to investigate these causal relationships. Strengths include our use of data from high-quality sources, including provider-verified NIS-Teen vaccination data, to get a more complete picture of ecological correlations with vaccination than any one data source could provide. Our analyses are also among the first to address geographic differences in HPV vaccination, an understudied and important topic.

In summary, HPV vaccine coverage in 2012 continued to be correlated with HPV-related cancer rates and several other state characteristics. For girls, initiation was associated with state-level demographics and cancer rates, while follow-through was related to healthcare access. For boys, initiation was associated with state-level demographics and healthcare access. Interventions to increase HPV vaccine coverage in areas with high HPV-related cancer incidence and mortality rates could result in meaningful public health benefits.

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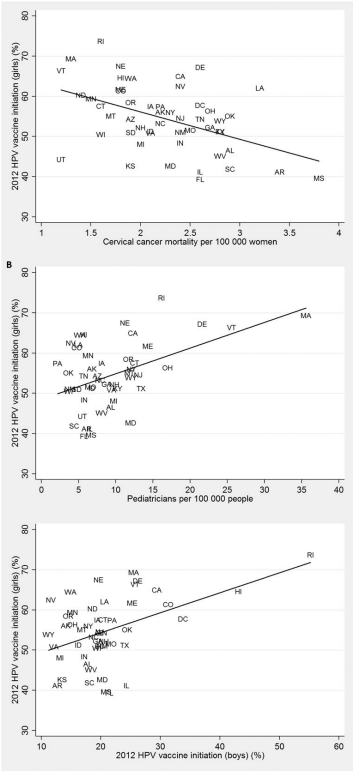

Figure 1.

Association of human papillomavirus (HPV) vaccine initiation rates for girls ages 13-17 and (A) cervical cancer mortality per 100,000 women, (B) pediatricians per 100,000 people, and (C) HPV vaccine initiation rates for boys ages 13-17.

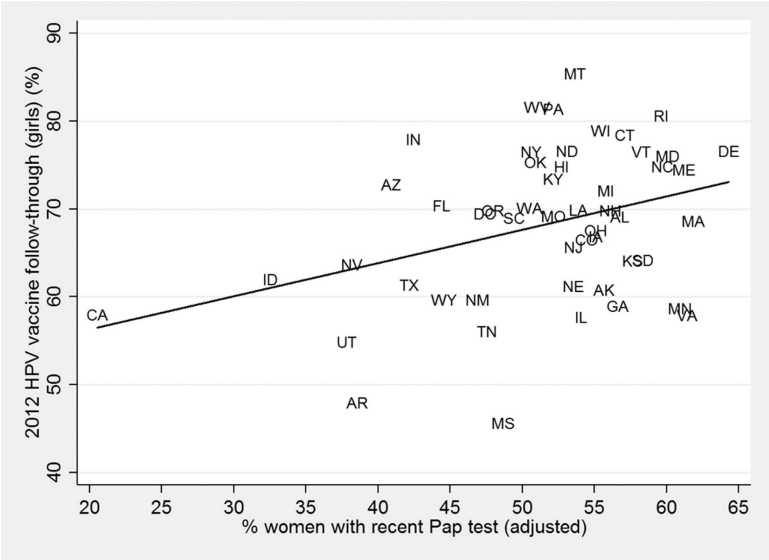

Figure 2.

Association of human papillomavirus (HPV) vaccine follow-through rates for girls ages 13-17 and recent Pap testing rates for women ages 18 and older, adjusted for differential over-reporting by race.

Table 1

Correlations of states' demographics, contact with healthcare system, and burden of human papillomavirus (HPV)-related cancer with HPV vaccine coverage.

	GIRLS		BOYS
	Initiation	Follow-through	Initiation
	r	*r*	*r*
Burden of HPV-related cancers, 2001–10			
Anal cancer incidence (*k*=50)	−0.04	−0.07	0.04
Cervical cancer incidence (*k*=50)	−0.29*	−0.19	0.06
Vaginal cancer incidence (*k*=50)	−0.22	−0.25†	−0.04
Vulvar cancer incidence (*k*=50)	0.09	0.30*	0.11
Cervical cancer mortality	−0.46*	−0.30*	−0.11
Sum of HPV 16/18-related cancer mortality rates *(k=39)*	−0.58*	−0.29†	−0.07
Demographics			
Median household income, 2011–12	0.32*	0.07	0.16
Percent population non-Hispanic white	0.01	0.22	−0.31*
Percent population non-Hispanic black	−0.28*	−0.15	0.05
Percent population Hispanic	0.06	−0.23	0.14
Percent population other race/ethnicity	0.24†	0.04	0.32*
Pediatricians per 100,000 population, 2013	0.47*	0.19	0.23
Family practitioners per 100,000 population, 2013	0.08	0.06	0.15
Obstetricians/gynecologists per 100,000 population, 2013	0.37*	0.08	0.15
Contact with healthcare system			
HPV vaccine initiation, among boys	0.47*	0.27†	--
Tdap vaccination, boys and girls	0.43*	0.41*	0.13
Meningococcal conjugate vaccination, boys and girls	0.48*	0.51*	0.39*
Adolescents with medical home, 2011–12	0.13	0.26†	0.06
Adolescents with “personal” doctor or nurse, 2011–12	0.19	0.37*	0.26†
School health centers per 100,000 population, 2010–11	0.07	0.25†	0.18
Recent Pap test, adjusted	0.18	0.36*	0.10

Note. Data from 2012 unless otherwise noted. Analyses based on *k*=51 for girls and *k=49* for boys, unless otherwise noted.

*p <.05;

†p <.10;