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Impact of gender-specific human papillomavirus vaccine recommendations on uptake of other adolescent vaccines: Analysis of the NIS-Teen (2008–2012)

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Abstract

In the United States, human papillomavirus (HPV) vaccination was routinely recommended for adolescent females in 2006 and provisionally recommended for adolescent males in 2009. We evaluated the hypothesis that gender-specific HPV vaccination recommendations would impact gender-specific uptake of other vaccines using National Immunization Survey-Teen public use datasets (2008–2012). Female adolescents had higher coverage than males of at least one other adolescent vaccine in 2008 (3.0% higher) and 2009 (4.3% higher). Gender differences abated in 2010, 2011, and 2012 (0.2%, 0.9%, 0.4%, respectively). To evaluate unintended consequences of gender-based recommendations, countries with female-only HPV vaccination recommendations should evaluate gender-specific uptake of other adolescent vaccines.

Keywords

adolescent; vaccine; vaccination; gender; human papillomavirus; HPV

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Introduction

The United States Advisory Committee on Immunization Practices (ACIP) first recommended human papillomavirus (HPV) vaccination for adolescent females aged 11–12 years in June 2006, with the recommendation formally published in the Morbidity and Mortality Weekly Report (MMWR) in March 2007.[1] HPV vaccination was first recommended for males three years later, in October 2009 (MMWR publication in May 2010).[2] This 2009 update to the recommendations was a “permissive” recommendation, indicating that quadrivalent HPV vaccine “may be given” to prevent genital warts in males. In October 2011, HPV vaccination recommendations were updated to reflect a recommendation for routine provision of HPV vaccine of males (MMWR publication in December 2011).[3]

The evolution of HPV vaccine recommendations contrasts with the implementation of recommendations for other adolescent vaccines for 11–12 year olds. The tetanus and diphtheria toxoids and acellular pertussis vaccine [Tdap] was recommended for routine use in adolescents in June 2005 (MMWR publication in March 2006)[4] and quadrivalent meningococcal conjugate vaccine (MCV4) was recommended for routine use in adolescents in February 2005 (MMWR publication in May 2005).[5] The Tdap and MCV4 recommendations were made for the same target population (11–12 year olds) with no gender preference for vaccination.

Historically, risk-based (e.g., hepatitis B and influenza vaccines in the US)[6] and gender-based (e.g., female-specific rubella vaccine in Japan, the United Kingdom, and Chile)[7, 8] recommendations have been implemented, often replaced later by universal, non-targeted recommendations.[8, 9] Little is known about the impact of targeted vaccination recommendations on the uptake of other vaccines routinely recommended for related target populations. We sought to determine if the gender-specific HPV vaccine recommendation was associated with additional preventive care seeking or vaccination with other routinely recommended vaccines among female, relative to male, adolescents, and if these differences persisted following the gender-neutral HPV vaccine recommendation.

Methods

Analyses were conducted using data from the 2008 through 2012 National Immunization Survey-Teen (NIS-Teen).[10] The NIS-Teen is a national survey using random digit dialing to identify households with 13–17 year old adolescents, for whom routine vaccine coverage is measured and verified with the adolescent’s healthcare provider.[10]

The primary outcome of interest was gender-specific non-HPV adolescent vaccine coverage. We evaluated uptake of: (a) at least one dose of Tdap compared to zero doses of Tdap, (b) at least one dose of MCV4 compared to zero doses of MCV4, and (c) at least one dose of Tdap and/or one dose of MCV4. Annual national-level estimates of non-HPV adolescent vaccine coverage were computed for 2008 through 2012, inclusive. The secondary outcome was preventive care seeking, defined as having had a routine check-up examination at 11 or 12 years of age. This outcome was included to evaluate underlying levels of healthcare seeking

among adolescent females and males, to provide context to differences in receipt of preventive immunizations.

Analyses were conducted in SAS v9.3 (The SAS Institute, Cary NC), using SAS procedures specific to analysis of complex survey designs, including PROC SURVEYMEANS (for vaccine and preventive care uptake) and PROC SURVEYREG (to obtain female minus male coverage differences, with 95% confidence intervals (CI)). All estimates utilized appropriate survey weights as provided in the NIS-Teen data files, as specified in the appropriate NIS-Teen User's Guide for Public Use Data File (available for 2008–2012 data files at http://www.cdc.gov/nchs/nis/data_files_teen.htm). For 2012, when a wireless sample was included with the landline sample, we utilize the dual-frame (landline and wireless) survey weights to utilize this larger dataset. Analyses were conducted only for adolescents for whom adequate provider-verified vaccinations were recorded in the dataset, and for whom complete data were available for socio-demographic characteristics used in multivariate linear regression. General NIS-Teen sample size and response rate data, and the proportion of respondents analyzed in this report are presented in Supplemental Digital Content (Text-Supplemental Digital Content 1). Multivariate linear regression analyses were evaluated for unadjusted results, as well as adjustment for socio-demographic characteristics (age at interview, poverty status, history of routine check-up at 11–12 years of age, and race and ethnicity). Gender- and year-stratification were computed using domain analyses in the survey procedures.

This analysis used existing, previously collected, and freely available public data with no protected health information identifiers, and thus was considered non-human subjects research not requiring Institutional Review Board approval.

Results

In 2008 and 2009, female adolescents had higher uptake of Tdap, MCV4, and Tdap and/or MCV4 than male adolescents (Table-Supplemental Digital Content 2). During the period 2010 through 2012, these female minus male differences in vaccine coverage declined to near null differences, and in some cases, male coverage began to exceed that of female coverage. Female minus male coverage differences for these vaccines ranged from 1.8% to 4.3% (absolute percentage coverage differences) during the period 2008 through 2009. During the period 2010 through 2012, female minus male coverage differences ranged from -1.4% to 1.4% (Figure and Table-Supplemental Digital Content 2).

Controlling for race/ethnicity, poverty status, history of a routine check-up at 11–12 years of age, or adolescents' age at interview (individually and in combination) did not alter any female minus male difference point estimates by more than an absolute level of 0.3%, and did not alter the observed patterns (data not shown).

Annual prevalence of reported history of routine check-ups at 11–12 years of age was similar for both genders over the evaluation period. In 2008, 84.3% of female adolescents and 83.7% of male adolescents reported an 11–12 year old checkup, increasing to 90.2% (female) and 90.7% (male) in 2012. There were no significant gender-specific differences in

routine health care seeking behavior, with the female minus male difference in checkup prevalence ranging from -0.6% to 0.6% (Table-Supplemental Digital Content 2).

Discussion

This is the first analysis we are aware of to address differences in gender-specific coverage of individual non-HPV vaccines, during the period of HPV vaccine gender-specific and gender-neutral recommendations. When HPV vaccine was recommended for female adolescents only (2008–2009) receipt of other adolescent vaccines (Tdap and/or MCV4) was higher for female adolescents compared to male adolescents. This difference diminished in 2010 and later, when HPV vaccine was recommended for male adolescents. Most strikingly, these vaccine coverage differences occurred when both male and female adolescents had very high, and very similar, rates of routine checkups at 11–12 years of age, indicating that this difference may be independent of general health care seeking behaviors.

The consistency of this pattern, particularly with a sustained lower female minus male difference after the introduction of a permissive HPV vaccine recommendation for males in the US, leads us to believe that this is not a statistical artifact. Without detailed behavioral data regarding adolescent vaccination practices, it is difficult to know why these differences may have arisen. It is possible that the recommendation of an additional vaccine for female adolescents, with the corresponding advertising and promotion of this vaccine, may have increased parental perceptions of the need to immunize female adolescents to a greater extent than male adolescents.

There is little available data for gender-specific adolescent vaccine coverage prior to 2008. One published report evaluated gender-specific up-to-date status (receipt of both a tetanus-containing vaccine and meningococcal conjugate vaccine) for the years 2006 through 2009, noting no differences in up-to-date status by gender.[11] However, our study found slightly different patterns for specific vaccines and receipt of at least one adolescent vaccine. With a between Tdap and MCV4 receipt persisting over the years, we believe that addressing these differences on an individual vaccine level provides additional important information to help understand adolescent vaccination coverage.

With a diminished female-to-male non-HPV vaccination coverage difference in recent years and increasing male HPV vaccination coverage, this difference is not likely to reappear in the United States. However, other countries currently have gender-specific HPV vaccine recommendations, potentially making these findings applicable in other settings. HPV vaccine coverage is high in the United Kingdom (80% of 12–13 year old girls have received 3 doses of HPV vaccine as of June 2014[12]) and Australia (71% of girls turning 15 in 2012 received 3 doses of HPV vaccine as of October 2013).[13] In the UK, meningococcal C conjugate (MenC) booster vaccine is recommended for all adolescents[14] and in Australia, Tdap is recommended for all adolescents.[15] As HPV vaccine is recommended only for female adolescents in these countries, the UK and Australian Departments of Health should evaluate gender-specific coverage of MenC and Tdap vaccines, respectively, to evaluate if there are similar to those reported here. However, the UK and Australia extensively utilize

school-located vaccination programs, therefore these comparisons for non-HPV vaccines may be difficult to conduct.

There are other vaccines in development that could have targeted recommendations, such as the group B streptococcus vaccine (pregnant women). Additionally, there are still other gender-related differences in HPV vaccine recommendations, from different recommendations by vaccine type (bivalent/quadrivalent/9-valent HPV vaccine)[16] and different age ranges for male and female catch-up HPV vaccination. Policy makers should consider the potential impact of targeted vaccine recommendations on uptake of other vaccines when making vaccine recommendations.

This study has some limitations. First, it was a secondary analysis of pre-existing data, so we were unable to evaluate specific behavioral decision making processes regarding why one vaccine may have been received while another was not in the context of HPV vaccination recommendations. Second, the analysis was an ecologic analysis using national-level data which does not provide the means to assess causality between gender-specific HPV vaccine recommendations and differential uptake of other vaccines. However, the consistency of the pattern relative to the timing of the first male HPV vaccine recommendation, even after adjustment for potential confounders makes this unlikely to be just a statistical artifact. Finally, with only two years of NIS-Teen data available for the period prior to the initial male HPV vaccine recommendation, and five years of data total, we could not evaluate longer-term patterns. As additional NIS-Teen data become available, continued monitoring of these gender-specific differences in Tdap and/or MCV4 should occur.

Our finding that differential adolescent vaccine uptake by gender was mostly eliminated after extending the HPV vaccine recommendation to males highlights the need for a more comprehensive evaluation of vaccine uptake. Countries that currently have gender-specific HPV vaccine recommendations should evaluate uptake of other adolescent vaccines by gender, to determine if there are unintended consequences of a female-only HPV vaccine recommendation. National level policy makers should consider these findings when evaluating future targeted immunization recommendations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

National Immunization Survey-Teen datasets from 2008–2012 are available from the United States Centers for Disease Control and Prevention (http://www.cdc.gov/nchs/nis/data_files_teen.htm). All analyses, interpretations, or conclusions reached are attributed to the authors and not to the National Center for Health Statistics, which is responsible only for the initial data.

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Figure 1. Female minus male differences in coverage of Tdap, MCV4, and Tdap and/or MCV4, among 13–17 year olds, United States, 2008–2012, as evaluated through the National Immunization Survey-Teen.