Preventive Medicine 88 (2016) 134–139

Contents lists available at ScienceDirect

Preventive Medicine

journal homepage: www.elsevier.com/locate/ypmed

Effect of number of human papillomavirus vaccine doses on guideline adherent cervical cytology screening among 19–26 year old females

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ARTICLE INFO

Article history:
Received 2 November 2015
Received in revised form 31 March 2016
Accepted 12 April 2016
Available online 13 April 2016

Keywords:
Human papillomavirus
Papillomavirus vaccines
Cervical intraepithelial neoplasia
Papanicolaou test
Papanicolaou smear
Health care providers

ABSTRACT

Purpose. Little is known about how the number of HPV vaccine doses affect adherence to screening guidelines. This study compared adherence to cervical cancer screening by the number of HPV vaccine doses received by young women and assessed whether the specialty of vaccinating providers affected behavior.

Methods. This retrospective cohort study using administrative insurance claims records included 24,964 19–26 year old women who received at least 1 injection of the HPV vaccine between January 2006 and November 2009. Vaccinated young women continuously enrolled in a nationally-representative private insurance plan for 6 months prior to and 37 months after HPV vaccine administration were included. Logistic regression was used to compare the odds of Papanicolaou (Pap) testing 3 years after vaccine initiation by number of vaccine doses and provider type.

Results. In this sample, 79.3% had a Pap test 3 years following vaccine initiation. Receiving 1 (aOR: 0.60, 95% CI 0.55–0.65) or 2 (aOR: 0.80, 95% CI 0.74–0.87) doses was associated with decreased odds of Pap testing compared to 3 doses. Many young women in our sample (16.5%) were diagnosed with cervical dysplasia prior to HPV vaccination. Patients vaccinated by non-obstetrician/gynecologists were less likely to get a Pap test following vaccination.

Conclusions. Women who received 1 or 2 doses of the HPV vaccine were less likely than those who received 3 doses to be screened for cervical cancer 3 years following vaccine initiation. Pediatricians and primary care physicians should convey the importance of initiating and continuing screening to HPV vaccinated patients.

1. Introduction

Human papillomavirus (HPV) vaccination is an important strategy to reduce HPV-related diseases and cancers in the US. The most commonly used vaccine in the US protects against 4 types of HPV that cause genital warts (types 6 and 11) and a high proportion of cervical cancers (types 16 and 18). In a randomized clinical trial, HPV vaccination among 18–25 year old women reduced abnormal Pap tests, referral for colposcopy, and treatment related to abnormal cervical cytology (Rodríguez et al., 2013). However, since the vaccine does not provide protection against all HPV types that cause cervical cancer, and does not clear infections that are present before vaccination, vaccinated women still need to get regular Papanicolaou (Pap) tests every 3 years, starting at age 21 (Saslow et al., 2012; U.S. Preventive Services Task Force, 2014; ACOG Committee on Practice Bulletins-Gynecology, 2012).

More than 98% of vaccinated women report they intend to be screened after vaccination, (Price et al., 2011) but intention does not always lead to actual participation (Armitage and Conner, 2001; Hofman et al., 2014). Recent literature has indicated that young women who initiated HPV vaccination were more likely than unvaccinated women to report having a Pap test in the previous 3 years (Sauer et al., 2015). Although the effect of vaccination on compliance with Pap testing guidelines has been examined, there is little information about how the number of vaccine doses affects subsequent cervical cancer screening behavior. Pap testing behavior among young women who received the vaccine after 16 is particularly important, as they may have already been exposed to HPV, and may still be at risk, as the vaccine is not effective at clearing established infections (Hildesheim et al., 2007). In addition, although 2 doses of the vaccine appear to produce an adequate immune response in girls <16 years of age, women ≥16 years of age have a lower immunological response to HPV vaccination compared to younger adolescents (Block et al., 2006), and it is unknown what level of immunogenicity is needed to protect against HPV infection long-term. For these reasons, young women need appropriate screening after vaccination, particularly those who received fewer than 3 doses.

The purpose of this study was to examine the association between the number of HPV vaccine doses that young women (19–26 years old

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http://dx.doi.org/10.1016/j.ypmed.2016.04.004
0091-7435/

at vaccination) received and receipt of a Pap test during the 3 year interval after vaccine initiation. We also assessed whether the specialty of the vaccinating physician and receiving the vaccine at appropriate intervals was associated with guideline-consistent screening behaviors.

2. Methods

2.1. Participants and procedure

We conducted a retrospective cohort study of health insurance claims from Clinformatics™ DataMart, a product of OptumInsight Life Sciences, Inc. (Eden Prairie, MN). Clinformatics™ DataMart consists of all claims paid for enrollees of one nationally available insurance group, including vaccinations, medical services, and prescriptions. Although they may have enrolled in different types of plans, all enrollees had the same eligibility for HPV vaccination, but reimbursement may have varied depending on a particular plan's premiums, co-insurance, and deductibles. Enrollees include over 53 million Americans, with more than 4.8 million female 19–26 year olds. Enrollees are largely representative of working adults in the U.S., with slightly higher representation in Northern states. We included females who received at least 1 HPV vaccination (either bivalent or quadrivalent) any time between January 2006 and November 2009, with 37 months of follow-up. Data were available through December 31st, 2012. Although 19–20 year olds were no longer recommended to receive screening after 2009 according to guidelines from the American College of Obstetricians & Gynecologists (ACOG) (ACOG Committee on Practice, 2003; ACOG Committee on Practice Bulletins-Gynecology, 2009, 2012), we included these women because the youngest would have reached age 21 by the third year of follow-up.

Records for 24,964 subjects were obtained that 1) contained a Current Procedural Terminology (CPT) code for HPV quadrivalent (90,649) or bivalent (90,650) vaccine, 2) were enrolled continuously 6 months before and 37 months after vaccine series initiation, and 3) were between 19 and 26 years at first vaccination (Fig. 1). We included the enrollment criteria to ensure that we had the most accurate information on the women in our study. We chose 6 months of enrollment before vaccination to avoid missing observations among those with shorter enrollment, while optimizing sample size. The final 37 months of enrollment allowed us to assess the first Pap test that occurred at least 30 days after vaccine series initiation (not during vaccine initiation), and then within 3 years following the first 30 days after initiation.

Analyses were based on current guidelines to ensure our findings were relevant across the study period and to reduce sample bias. We excluded vaccine initiators ≥27+ years of age because they received the vaccine off-label, and screening recommendations would have changed during follow-up when they reached 30 years of age. Informed consent was not required as this was an analysis of de-identified secondary data.

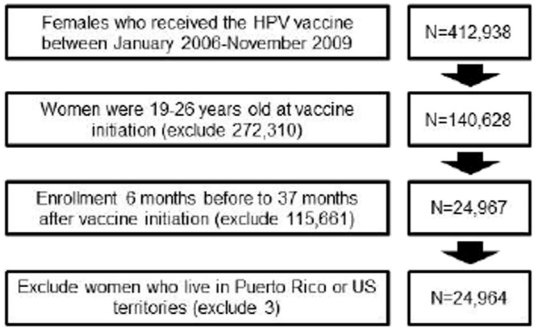

Fig. 1. Cohort selection of vaccinated 19–26 year old females from administrative health insurance records.

This study was exempted from review by the institutional review board of the University of Texas Medical Branch, Galveston, TX.

2.2. Measures

The number of HPV vaccinations received by an individual separated by at least 10 days that occurred during the study period (37 months after earliest recorded HPV vaccine) was examined. A 10-day period was used to ensure that vaccines were not repeat entries or given too soon after an initial dose to be effective. A 6-month look-back period was included to ensure that the earliest record was the first HPV vaccine received. The sequence of the dose for each vaccine given was not recorded. Therefore, we used a 6-month time period before vaccination to make sure that the first vaccine recorded in the dataset was the first actual vaccine received by the enrollee, as those enrolled for a shorter period of time prior to the first vaccine dose may have received other doses that were not recorded in this dataset. HPV vaccination was categorized into those who had received 1, 2, or 3+ doses anytime during the period of time examined for each enrollee. Young women who received 4+ doses were rare (n = 167). Therefore, we combined those who received 4+ doses with those who received 3 doses. Excessive immunization (receipt of more doses of a vaccine than recommended) has been found to be common among young children in the U.S., (Feikema et al., 2000) although the problem has not been studied among young adults. It is likely that excessive immunization also occurs in this group, especially since immunization registries in the U.S. were mostly developed for children, and may not be as reliable for ascertaining vaccination history for young adults. Further, providers may not have been aware of the flexibility of the vaccination schedule for the HPV vaccine series soon after the vaccine was introduced, and may have given extra doses to those who were not vaccinated at the recommended time intervals.

Interval appropriateness was also measured. Intervals between 6 and 8 months for the 1st and 3rd doses were considered appropriate, similar to the recommended interval (Advisory Committee on Immunization Practices (ACIP), 2010). We used this measure, rather than the standard 1-year measure because we wanted to determine whether young women who followed 1 guideline more appropriately were likely to follow the other guideline. One-year completion for women in this dataset is reported elsewhere (Hirth et al., 2012). Those with shorter or longer intervals were considered inappropriate, and we included those who did not complete in a separate category. Enrollees were not included in the data set more than once.

Pap testing was included as a dichotomized variable. We counted the first Pap test using CPT codes, Healthcare Common Procedure Coding System (HCPCS), and International Classification of Diseases, 9th Edition (ICD-9) codes established by the Healthcare Effectiveness Data and Information Sets (HEDIS) (HEDIS, 2012, 2013) which occurred between 30 days and 37 months after the initial vaccine dose.

Enrollees were categorized into two groups based on their age at first vaccination: 19–21 years and 22–26 years. The 22–26 year olds were already eligible to receive Pap testing, whereas 19–21 year olds were either not yet eligible, or newly eligible according to cancer screening guidelines (ACOG Committee on Practice Bulletins-Gynecology, 2012; U.S. Preventive Services Task Force, 2014; Saslow et al., 2012). Since cervical cancer screening guidelines changed during the study, it was determined that these age cutoffs would be best. ACOG guidelines first recommended annual Pap testing according to sexual debut among women less than 21 years of age (ACOG Committee on Practice, 2003). In 2009, these guidelines were changed, with a recommendation for Pap testing every 3 years starting at 21 years of age regardless of sexual activity, until 30 years of age (ACOG Committee on Practice Bulletins-Gynecology, 2009). Due to the way age was calculated (birth year subtracted from year of vaccine initiation), it was determined that including 21 year olds in the younger age category would be most appropriate.