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Original article

Epidemiology of Any and Vaccine-Type Anogenital Human Papillomavirus Among 13–26-Year-Old Young Men After HPV Vaccine Introduction

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A B S T R A C T

Purpose: The aims of this study were to determine prevalence of and factors associated with any human papillomavirus (HPV) and vaccine-type HPV among young men after vaccine introduction, stratified by vaccination status.
Methods: Young men were recruited from clinical sites from 2013 to 2015, completed a survey, and were tested for 36 anogenital HPV types. We determined factors associated with ≥1 HPV type among all participants, and vaccine-type HPV (HPV6, 11, 16, and/or 18) among all, vaccinated and unvaccinated participants, using multivariable regression.
Results: Mean age was 21.5 years and 26% had received at least one HPV vaccine dose. HPV prevalence was lower in vaccinated versus unvaccinated young men (50.5% vs. 62.6%, $p = .03$). HPV positivity was discordant by anogenital site. At both sites, 59.4% were positive for ≥1 HPV type and 26.0% for ≥1 4-valent vaccine type. In multivariable logistic regression, factors associated with ≥1 HPV type among all participants were frequency of oral sex (odds ratio [OR] = 1.80, 95% confidence interval [CI] = 1.00–3.24), recent smoking (OR = 1.84, CI = 1.17–2.90), and sexually transmitted infection history (OR = 1.56, CI = 1.02–2.38). Factors associated with vaccine-type HPV among all participants were white versus black race (OR = 1.91, CI = 1.10–3.34) and gonorrhea history (OR = 2.52, CI = 1.45–4.38); among vaccinated participants were private versus Medicaid insurance (OR = 5.6, CI = 1.46–20.4) and private versus no insurance (OR = 15.9, CI = 3.06–83.3); and among unvaccinated participants was gonorrhea history (OR = 1.83, CI = 1.03–3.24).

IMPLICATIONS AND CONTRIBUTION

Few studies have examined the prevalence and risk factors for HPV and concordance between genital sites in adolescent males after vaccine introduction. This study demonstrates that HPV prevalence was high and vaccination rates low among young men 2–4 years after vaccine introduction, underscoring the importance of vaccination according to national guidelines.

Conflicts of Interest: Dr. Brown has received honoraria and grant support from Merck. Dr. Franco has served as occasional advisor to companies involved with HPV vaccination (Merck, GSK) and HPV and cervical cancer diagnostics (Roche, BD, Qiagen). Dr. Franco's institution has received unconditional funding from Merck for investigator-initiated studies carried out in his unit. Dr. Kahn has co-chaired two NIH-funded HPV vaccine clinical trials in HIV-infected individuals, for which Merck & Co., Inc., provided vaccine and immunogenicity titers. The other authors have indicated no potential conflicts of interest to disclose.
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Conclusions: Anogenital HPV prevalence was high and vaccination rates low among young men 2–4 years after vaccine introduction, underscoring the urgency of increasing vaccination rates and vaccinating according to national guidelines.

Human papillomavirus (HPV) infects nearly 14 million people each year in the United States; almost half of infections occur in 15–24 year-olds [1]. Infection may cause anogenital warts, anogenital cancers such as cervical cancer, and oropharyngeal cancers. The Centers for Disease Control and Prevention estimates that approximately 30,700 new cancers each year are attributable to HPV, including 11,600 cancers in men [2].

Male HPV vaccination is effective, and could greatly decrease the burden of anogenital warts and cancers caused by HPV in men as well as decrease the disease burden in young women through herd immunity [3,4]. In 2011, the Advisory Committee on Immunization Practices recommended routine vaccination of young men aged 11–21 years old and vaccination of young men aged 22–26 years old at high risk for HPV [3]. However, HPV vaccine coverage in young men is low. In 2015, only 49.8% of 13–17-year-old men in the United States had received at least one dose of the vaccine and 28.1% had completed the series [5].

Previous studies have demonstrated that the prevalence of any HPV among men ranges widely (1.3%–72.9%) but is typically greater than 20% [6]. Surveillance studies have demonstrated a decrease in HPV in women and adult men after vaccine introduction [7,8]. However, there are limited data available regarding the prevalence of HPV in adolescent men after vaccine introduction. Most studies have been conducted in adult men (i.e., men at least 18 years of age) or in young men who have sex with men (MSM) [9,10]. Furthermore, there are limited data regarding which factors are associated with HPV infection, and previous studies were conducted primarily in adults. These have demonstrated that factors associated with HPV infection include lifetime and recent number of sexual partners [9–15], lack of circumcision [11–14], inconsistent condom use [12,13,15–17], smoking [12,15], and younger age [11]. Finally, little is known about concordance between anogenital sites in young men [18].

Information regarding the epidemiology and risk factors for HPV infection in adolescent and young adult men after vaccine licensing is essential for policy decisions, public health messaging, and prevention efforts. For example, HPV epidemiology is likely to change after HPV vaccine introduction, and current data regarding HPV prevalence in vaccinated and unvaccinated young men are important for guiding policies regarding immunization, decisions about vaccine financing, and the design of public health messages for clinicians and parents. In addition, risk factors for HPV may differ after vaccine introduction because vaccinated and unvaccinated men may differ in terms of demographic characteristics, behaviors, or other factors that are associated with their risk for HPV. Information about changing risk factors is important for public health messaging and designing interventions to prevent HPV postvaccination. Therefore, the aims of this study were to [1] determine the prevalence of anogenital HPV, and concordance between genital sites, in a diverse sample of 13–26-year-old sexually active adolescent and young adult men, and [2] determine factors associated with: (1) any anogenital HPV (≥1 type) among all young men; and (2) vaccine-type HPV among all, vaccinated, and unvaccinated young men. We hypothesized that prevalence of HPV would be high in this study sample, that having received at least one HPV vaccine dose would be associated with lower prevalence of vaccine-type HPV, and that factors associated with vaccine-type HPV would differ among vaccinated and unvaccinated men.

Methods

Young men 13–26 years old (N = 400) were recruited between 2013 and 2015 from a hospital-based teen health center (THC) and a health department sexually transmitted disease (STD) clinic in Cincinnati, OH. Both sites serve a racially diverse, urban, and predominantly low income population. Men who had sexual contact (genital-oral or genital-genital with male or female partners) were eligible to participate. All vaccinated men had received the 4-valent vaccine. Men were recruited using a sequential sampling strategy (all eligible men were invited to participate): 91% of those approached agreed to participate. The study was approved by the Institutional Review Boards of the hospital and the health department, and written informed consent was obtained from participants. Participants completed a survey instrument in English or Spanish assessing sociodemographic characteristics, HPV and HPV vaccine knowledge, vaccination history, substance use history, and sexual behaviors. The survey was developed and validated in similar populations; details are described in previous manuscripts [19–21].

Three separate genital swabs (penile, including coronal sulcus, glans penis, and shaft of the penis, as well as scrotal) and one perianal/anal swab were collected from each male participant for HPV DNA testing using previously described procedures [22]. Swabs were premoistened with sterile saline, placed immediately into tubes containing 1 mL of Digene Specimen Transport Medium (STM, Qiagen, Germantown, MD), and stored at –80°C. The three penile/scrotal samples were combined to produce one genital DNA extract per participant, and the perianal/anal sample was analyzed separately. This method has been shown to optimize HPV detection among men and to result in reproducible detection of genital HPV in men, while achieving cost savings [22,23]. Samples were analyzed for HPV genotypes using the Roche Linear Array Assay, a polymerase chain reaction amplification technique that uses an L1 consensus primer system and reverse-line blot detection strip to identify 36 different HPV genotypes (Roche Molecular Systems, Alameda, CA) [24]. The Roche Linear Array tests for 37 high-risk and low-risk genotypes (6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 54, 55, 56, 58, 59, 61, 62, 64, 66, 67, 68, 69, 70, 71, 72, 73, 81, 82, 83, 84, IS39, and CP6108): IS39 has been reclassified as a subtype of HPV82, so the test detects 36 distinct genotypes. The HPV test results from genital (penile and scrotal) and perianal/anal sites were analyzed separately for descriptive analyses, but were combined for univariable and multivariable analyses due to insufficient power to analyze type-specific HPV prevalence by site in the multivariable analyses.

The primary outcome variables for this study were any HPV (≥1 type) and 4-valent vaccine-type HPV (HPV6, 11, 16, and/or 18). Independent variables included vaccination status, number of vaccine doses, demographic factors (age, race, ethnicity, in-