Invited Commentary

Human Papillomavirus Vaccine and Sexual Activity
How Do We Best Address Parent and Physician Concerns?

Robert A. Bednarczyk, PhD

Compared with other routinely recommended adolescent vaccines (eg, diphtheria and tetanus toxoids and acellular pertussis [Tdap] vaccine and quadrivalent meningococcal conjugate [MCV4] vaccine), human papillomavirus (HPV) vaccine uptake has been lower, with only 57% of adolescent females and 35% of adolescent males initiating the 3-dose HPV vaccine series.[1] Often, the reasons cited for these low HPV vaccination rates pertain to the vaccine's role in preventing a sexually transmitted infection (STI). Parents commonly indicate that they have not had their children vaccinated against HPV because the vaccine is not needed or because their child is not sexually active,[2] and even some physicians express hesitancy toward strongly recommending the HPV vaccine. In a recently published series of qualitative interviews,[3] physicians expressed concerns about discussing sexual activity with 11- and 12-year-olds and indicated preferences for deferring vaccination to later ages. However, just as we do not wait until we have been in the sun for 2 hours to apply sunscreen, we should not wait until after an individual is sexually active to attempt to prevent HPV infection.

Related article page 617

The hesitancy on the part of parents and physicians to vaccinate or discuss vaccination may be attributable to worries that HPV vaccination will be seen as a tacit approval for sexual activity. Concerns about increased sexual activity and risk disinhibition have been discussed since before the initial recommendation for HPV vaccination. In this issue of *JAMA Internal Medicine*, Jena et al[4] add to the literature by presenting a novel analysis that indicates no evidence for increased sexual activity after HPV vaccination.

Jena et al evaluated STI-related insurance claims for more than 200 000 adolescent (aged 12-18 years) females insured from January 1, 2005, through December 31, 2010, in the United States. The researchers matched vaccinated and unvaccinated adolescents by age and keyed on an index quarter (quarter of the year that included vaccination date for the vaccinated adolescents) for assessment of risk of STI claims. If analyses were limited to only direct measures of postvaccination STI-related claims, results could be biased by longitudinal increases in STI rates with increasing age and potential selection bias related to prevaccination differences in STI risk among HPV vaccine recipients. To account for this bias, the researchers computed odds ratios (ORs) for the association between the vaccine and sexual activity for 1-year periods before and after the index quarter and conducted a difference-in-difference analysis by taking the ratio of the postvaccination OR relative to the prevaccination OR. Thus, the difference-in-difference OR of 1.05 (95% CI, 0.80-1.38) reported by Jena et al indicates that there was no increased risk of STI claims among HPV vaccinees relative to nonvaccinees after adjustment for preindex quarter STI risk.[4] This pattern was consistent after stratification by age and restriction to adolescent females with insurance claims for contraceptives in their vaccine index quarter. These subanalyses indicate that even among those who may have already been sexually active, sexual activity levels, as measured by incidence of STIs, did not increase after HPV vaccination.

These findings should not come as a surprise to researchers in the field of HPV vaccinology and should serve as continued reassurance that HPV vaccination does not lead to sexual disinhibition. However, this reassurance leaves us with the question, "How can we use these findings to address concerns of anxious parents of adolescents?"

Concerns about HPV vaccine are not always directly expressed in terms of potential for increasing sexual activity; parents often express concerns about the recommended age of the vaccine. According to the 2013 National Immunization Survey-Teen, among parents of 13- through 17-year-olds included in the survey who did not intend to have their children receive HPV vaccine in the next year, 15% indicated they believed the vaccine was not needed or not necessary, and 11% indicated their child was not sexually active.[2] These concerns overlook the 3 major reasons why HPV vaccine is recommended for 11- and 12-year-olds.

First, the antibody response in younger adolescents (9-15 years of age) is greater for all HPV types in the quadrivalent HPV vaccine than it is in older adolescents and young adults (16-26 years of age).[5] Second, estimates from the 2006-2010 National Survey of Family Growth indicate that, by 15 through 17 years of age, 27% of adolescents in the United States have ever had sexual intercourse; by 18 through 19 years of age, this proportion increases to 63%.[6] Third, with the Tdap and MCV4 vaccines also recommended for 11- and 12-year-olds, health care professionals can leverage the well-child visit for 11- and 12-year-olds recommended by the American Academy of Pediatrics to administer the Tdap and MCV4 vaccines and initiate the HPV vaccine series, reducing missed opportunities for vaccination.[2]

It is not just parents who need this information, however. Physicians have indicated reluctance to recommend HPV vaccine with the same emphasis used for the Tdap and MCV4 vaccines, citing concerns about discussing sexual activity or lack of perceived susceptibility of HPV infection or HPV-related diseases among 11- and 12-year-olds.[3] We often think of the Health Belief Model constructs (perceived susceptibility and perceived severity) as they relate to an individual's choice to elect a preventive vaccination. However, these constructs also need to be considered in terms of physicians' perceptions of their patients' risk of disease. From qualitative interviews with physicians, Perkins et al[3] highlighted physician concerns, including, "I don't get as scared of cervical cancer just because ... the

Pap test is another screening method. So the other things just feel more dramatic to me … and it's not like HPV is going to kill the boys," and "It probably is more likely that they would die from meningococcal meningitis then die from cervical cancer."[3(p e670)] Diseases such as meningococcal meningitis or pertussis will typically be addressed by pediatricians with greater frequency than anogenital cancers. However, just because physicians may not proximally see the effects of a vaccine-preventable disease does not mean they should not routinely recommend preventive strategies for that disease. We know that a strong, unequivocal physician recommendation is associated with increased childhood vaccination uptake among vaccine-hesitant parents[7]; it is unclear whether this finding translates to adolescent vaccines. With 13% of parents who did not intend to get their adolescent vaccinated against HPV indicating that the vaccine was not recommended to them,[2] a strong physician recommendation is a logical starting point for increasing HPV vaccine coverage.

To date, much research has been conducted to identify HPV vaccination barriers, but less research has been conducted to identify the preferred content and mode of delivery of information to mitigate these barriers. Addressing this knowledge gap through the development and delivery of information relative to all key partners (adolescents, their parents, and their health care professionals) will be critical in removing the stigma of HPV vaccine in our efforts to fully use this vaccine. The materials should also address other fears that parents might have, including the safety of the vaccine, especially because many parents worry about their children receiving multiple vaccines at the same time. In the meantime, physicians should recommend the HPV vaccine as part of the adolescent vaccination platform, as is done for the Tdap and MCV4 vaccines, and highlight the reasons that support early vaccination: better immune response, importance of vaccinating before sexual activity, and consistent evidence that HPV vaccination does not lead to increased sexual activity.

ARTICLE INFORMATION

Author Affiliations: Hubert Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, Georgia; Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, Georgia; Emory Vaccine Center, Atlanta, Georgia; Winship Cancer Institute, Cancer Prevention and Control Program, Emory University, Atlanta, Georgia.

Corresponding Author: Robert A. Bednarczyk, PhD, Hubert Department of Global Health, Rollins School of Public Health, Emory University, 1518 Clifton Rd NE, Claudia Nance Rollins Bldg 7019, Mailstop 1518-002-7BB, Atlanta, GA 30322 (rbednar@emory.edu).

Published Online: February 9, 2015. doi:10.1001/jamainternmed.2014.7894.

Conflict of Interest Disclosures: Dr Bednarczyk has received research funding from the National Institutes of Health. He has also received honoraria and travel support from the US Embassy University Research Program in Tbilisi, Georgia, to conduct training workshops in Georgia and travel support from the Open Society Foundations to conduct training workshops in Istanbul, Turkey. No other disclosures were reported.

Funding/Support: This Invited Commentary was supported in part by grant 1K01AI106961-A1 from the National Institutes of Health (Dr Bednarczyk).

Role of the Funder/Sponsor: The funding source had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and the decision to submit the manuscript for publication.

Additional Contributions: Saad B. Omer, MBBS, MPH, PhD, Hubert Department of Global Health and Department of Epidemiology, Rollins School of Public Health, Emory University; Department of Pediatrics, School of Medicine, Emory University; and Emory Vaccine Center, and Walter Orenstein, MD, Department of Infectious Disease, School of Medicine, Emory University; and Emory Vaccine Center, provided thoughtful review and comments to improve the manuscript. Drs Omer and Orenstein were not compensated for their contributions.

REFERENCES

1. Elam-Evans LD, Yankey D, Jeyarajah J, et al; Immunization Services Division, National Center for Immunization and Respiratory Diseases; Centers for Disease Control and Prevention (CDC). National, regional, state, and selected local area vaccination coverage among adolescents aged 13-17 years—United States, 2013. *MMWR Morb Mortal Wkly Rep*. 2014;63(29):625-633.

2. Stokley S, Jeyarajah J, Yankey D, et al; Immunization Services Division, National Center for Immunization and Respiratory Diseases, CDC; Centers for Disease Control and Prevention (CDC). Human papillomavirus vaccination coverage among adolescents, 2007-2013, and postlicensure vaccine safety monitoring, 2006-2014—United States. *MMWR Morb Mortal Wkly Rep*. 2014;63(29):620-624.

3. Perkins RB, Clark JA, Apte G, et al. Missed opportunities for HPV vaccination in adolescent girls: a qualitative study. *Pediatrics*. 2014;134(3):e666-e674.

4. Jena AB, Goldman DP, Seabury SA. Incidence of sexually transmitted infections after human papillomavirus vaccination among adolescent females [published online February 9, 2015]. *JAMA Intern Med*. doi:10.1001/jamainternmed.2014.7886.

5. Markowitz LE, Dunne EF, Saraiya M, et al; Centers for Disease Control and Prevention (CDC). Human papillomavirus vaccination: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2014;63(RR-05):1-30.

6. Abma JC, Martinez GM, Copen CE. Teenagers in the United States: sexual activity, contraceptive use, and childbearing, national survey of family growth 2006-2008. *Vital Health Stat 23*. 2010;(30):1-47.

7. Opel DJ, Heritage J, Taylor JA, et al. The architecture of provider-parent vaccine discussions at health supervision visits. *Pediatrics*. 2013;132(6):1037-1046.