Practice Issues

What Is New in Human Papillomavirus–Related Lower Anogenital Tract Disease Prevention and Screening?

Best Articles From the Past Year

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This month we focus on current research in human papillomavirus–related lower anogenital tract disease prevention and screening. Dr. Boardman discusses four recent publications, which are concluded with a "bottom line" that is the take-home message. The complete reference for each can be found in Box 1 on this page, along with direct links to the abstracts.

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Box 1. Abstracts Discussed in This Commentary

1. Kreimer AR, Struyf F, Del Rosario-Raymundo MR, Hildesheim A, Skinner SR, Wacholder S, et al. Efficacy of fewer than three doses of an HPV-16/18 AS04-adjuvanted vaccine: combined analysis of data from the Costa Rica Vaccine and PATRICIA trials. Lancet Oncol 2015;16:775–86. Available at: http://dx.doi.org/10.1016/S1470-2045(15)00047-9.
2. Saraiya M, Unger ER, Thompson TD, Lynch CF, Hernandez BY, Lyu CW, et al. US assessment of HPV types in cancers: implications for current and 9-valent HPV vaccines. J Natl Cancer Inst 2015;107:djv086. Available at: http://dx.doi.org/10.1093/jnci/djv086.
3. Wright TC, Stoler MH, Behrens CM, Sharma A, Zhang G, Wright TL. Primary cervical cancer screening with human papillomavirus: end of study results from the ATHENA study using HPV as the first-line screening test. Gynecol Oncol 2015;136:189–97. Available at: http://dx.doi.org/10.1016/j.ygyno.2014.11.076.
4. Huh WK, Ault KA, Chelmow D, Davey DD, Goulart RA, Garcia FA, et al. Use of primary high-risk human papillomavirus testing for cervical cancer screening: interim clinical guidance. Obstet Gynecol 2015;125:330–37. Available at: http://dx.doi.org/10.1097/AOG.0000000000000669.

Efficacy of Fewer Than Three Doses of an HPV-16/18 AS04-Adjuvanted Vaccine: Combined Analysis of Data From the Costa Rica Vaccine and PATRICIA Trials

Using summary data from two double-blind randomized controlled trials of the bivalent human papillomavirus (HPV) 16/18 vaccine in 22,327 adolescents and young women aged 15–25 years, Kreimer et al demonstrate high vaccine efficacy against one-time detection of incident HPV 16/18 among women in the modified total vaccinated cohort regardless of the number of doses received (77.0%, 95% confidence interval [CI] 74.7–79.1 for three doses, 76.0%, 95% CI 62.0–85.3 for two doses, and 85.7%, 95% CI 70.7–93.7 for one dose). Evidence of protection for HPV 31/33/45 infection was also seen, although the magnitude was lower and differed by dose (59.7% for those receiving all three doses, 37.7% for two doses, and 36.6% for a single dose). Among adolescents and women receiving two doses of the bivalent vaccine,

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timing of the second dose mattered. Two doses given 6 months rather than 1 month apart was associated with significantly higher vaccine efficacy (68.1% compared with 10.2%) and was similar to that reported for three doses. Current U.S. estimates indicate that, although 57.3% of adolescent girls received at least one dose of HPV vaccine, only 37.6% completed the three-dose series.[1] Among 19–26 year-old women, 36.9% reported receipt of at least one dose of vaccine in 2013.[2]

Bottom Line: Four years after bivalent HPV 16/18 vaccination, protection against cervical vaccine–type infection was similar regardless of the number of doses received.

US Assessment of HPV Types in Cancer: Implications for Current and 9-Valent HPV Vaccines

In 2006, the Centers for Disease Control and Prevention partnered with seven U.S. population–based registries to obtain archival tissue for cancers diagnosed between 1993 and 2005. Using specimens from 2,670 women and men with HPV-associated carcinoma in situ (CIS) or invasive cancers, Saraiya et al found the highest attribution of HPV 16/18 in vulvar CIS (80.9%), anal cancer (79.4%), invasive cervical cancer (66.2%), and oropharyngeal cancer (60.2%). The additional types in the 9-valent vaccine (HPV 31, 33, 45, 52, 58) contributed the most for cervical CIS (21.4%), vaginal cancer (18.3%), cervical cancer (14.7%), and vulvar cancer (14.2%). An estimated 24,858 HPV-associated cancers in the United States could be prevented annually with the HPV 16/18 vaccines (63.4%), with an additional 3,944 (10.1%) preventable through the 9-valent vaccine. Under ideal circumstances, the percentage of preventable cancers based on HPV-positive cancers would exceed 80% through use of HPV 16/18 vaccines, with an additional 13% preventable with 9vHPV.

Bottom Line: Current HPV 16/18 vaccines will reduce most HPV-associated cancer. The 9-valent vaccine (recommended by the Advisory Committee on Immunization Practices in February 2015 for routine vaccination in the United States[3]) would potentially prevent an additional 4.2–18.3% of cancers.

Primary Cervical Cancer Screening With Human Papillomavirus: End of Study Results From the ATHENA Study Using HPV as the First-Line Screening Test

On March 12, 2014, the U.S. Food and Drug Administration approved modified labeling of a currently marketed high-risk HPV assay to include primary high-risk HPV screening for women aged 25 years and older. The data supporting this application came from a large, prospective trial of primary high-risk HPV screening called ATHENA (Addressing the Need for Advanced HPV Diagnostics). In 3-year end-of-study results from this trial, primary HPV testing had the highest adjusted sensitivity for cervical intraepithelial neoplasia (CIN) 3+ (76.1%, 95% CI 70.3–81.8%). In comparison, the adjusted sensitivities of cotesting or cytology were 61.7% (95% CI 56.0–67.5%) and 47.8% (95% CI 41.6–54.1%), respectively. Although primary HPV screening led to detection of more cases of high-grade disease, significantly more colposcopies were required compared with cytology or cotesting. Lastly, and relevant to the U.S. Food and Drug Administration's decision to approve an HPV test to be used in primary screening of women aged 25–29 years, data from ATHENA demonstrated that women in this age group, although only 16% of the study population, represented 34.3% of the cases of CIN 3+. More than half of the women aged 25–29 years with CIN 3+ had negative cytology.

Bottom Line: Primary HPV testing in women aged 25 years or older, although more sensitive than cytology alone or cotesting, results in significantly more colposcopies.

Use of Primary High-Risk Human Papillomavirus Testing for Cervical Cancer Screening: Interim Clinical Guidance

An interim guidance panel was convened in 2014 to address specific questions regarding the use of high-risk HPV testing for primary screening. Huh et al provide a summary of the panel's discussion of the safety and effectiveness of primary high-risk HPV screening compared with current cytology-based screening methods, followed by recommendations for the management of negative and positive test results. For those currently using cotesting, genotyping of high-risk HPV–positive test results among women with negative cytology results will be familiar. In the primary HPV screening algorithm, women who are HPV 16/18–positive will be referred to colposcopy; reflex cytology is recommended for women positive for the 12 other high-risk HPV genotypes. As acknowledged by the authors, the other major recommendation to initiate primary high-risk HPV screening at age 25 years raised multiple concerns. Balancing the improved detection of CIN 3 in 25- to 29-year-olds with the increased need for colposcopies, treatment of lesions that may regress, integration with current screening regimens, and lingering questions as to the effect of early detection of preinvasive disease on cancer prevention require ongoing investigation.

Bottom Line: Primary high-risk HPV screening has the potential to reduce the morbidity and mortality of cervical cancer. To maximize the benefit of any cervical cancer screening program in the United States, however, requires identifying and targeting unscreened and underscreened women.

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3. Petrosky E, Bocchini J, Hariri S, Chesson H, Curtis CR, Saraiya M, et al. Use of 9-valent human papillomavirus (HPV) vaccine: updated HPV vaccination recommendations of the Advisory Committee on Immunization Practices. MMWR Morb Mortal Wkly Rep 2015;64:300–4.