Comparison of cervical cancer screening strategies incorporating different combinations of cytology, HPV testing, and genotyping for HPV 16/18: results from the ATHENA HPV study

J. Thomas Cox, MD; Phillip E. Castle, PhD, MPH; Catherine M. Behrens, MD, PhD; Abha Sharma, PhD; Thomas C. Wright Jr, MD; Jack Cuzick, PhD; and the Athena HPV Study Group

OBJECTIVE: The objective of the study was to compare 9 cervical cancer screening strategies to the current screening standard (cytology with human papillomavirus [HPV] triage of atypical squamous cells of undetermined significance) for the detection of high-grade cervical disease.

STUDY DESIGN: Women (n = 34,254) aged 30 years or older from the Addressing the Need for Advanced HPV Diagnostics (ATHENA) study underwent screening with cytology and HPV testing with simultaneous HPV16/18 genotyping; those with atypical squamous cells of undetermined significance cytology or greater or HPV-positive status were referred for colposcopy.

RESULTS: In general, screening strategies that offered greater sensitivity also required more referral to colposcopy. HPV testing was more sensitive than cytology for detection of cervical intraepithelial neoplasia grade 2 or greater, but strategies that depended on cytology for triage of HPV-positive women decreased this sensitivity. Various strategies of cotesting with cytology increased sensitivity but did so by increasing testing. Strategies that included integrated HPV16/18 testing provided more efficient referral to colposcopy.

CONCLUSION: Strategies that maximize detection of women at greatest risk of cervical intraepithelial neoplasia grade 3 or greater by immediate referral to colposcopy, with follow-up testing of women at intermediate risk, maximize the benefits of cervical cancer screening while decreasing the potential harm. Incorporating screening with HPV and triage of HPV-positive women by a combination of genotyping for HPV16/18 and cytology provided a good balance between maximizing sensitivity (benefit) and specificity by limiting the number of colposcopies (potential harm).

Key words: Addressing the Need for Advanced HPV Diagnostics, atypical squamous cells of undetermined significance, cotesting, human papillomavirus, human papillomavirus 16/18, low-grade squamous intraepithelial lesion


In March 2012, new primary cervical screening guidelines were jointly issued by the US Preventative Services Task Force (USPSTF) and a consortium of the American Cancer Society (ACS), the American Society for Colposcopy and Cervical Pathology (ASCCP), and the American Society of Clinical Pathologists (ASCP). Based on the evidence...