



COLLEGE of AMERICAN PATHOLOGISTS

October 15, 2020

Deana Baptiste, MPH, PhD
Director, Guideline Development Process
American Cancer Society, Inc.
250 Williams Street
Atlanta, GA 30303

Dear Dr. Baptiste,

As the world's largest organization of board-certified pathologists and leading provider of laboratory accreditation and proficiency testing programs, the College of American Pathologists (CAP) serves patients, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide. The CAP supports human papillomavirus (HPV) vaccination and has endorsed age-appropriate cervical cancer screening as recommended by and in concurrence with guidelines set forth by professional organizations such as the American Cancer Society (ACS), the American Society for Colposcopy and Cervical Pathology (ASCCP), The American College of Obstetricians and Gynecologists (ACOG), and the American Society for Clinical Pathology (ASCP).

We note with interest the updated ACS cervical cancer screening guidelines, released on July 30, 2020, as they underscore the importance of using the available HPV platforms in accordance with their FDA approval (1,2) and refer providers to the 2019 ASCCP appropriate management guidelines for women with abnormal cervical cancer screening tests, (3,4) which we support. However, the ACS guidelines elicit significant concern with the endorsement of primary HPV testing as the preferred screening test for individuals with a cervix between the ages of 25 and 65 years.

ACS RECOMMENDATION

- The preferred screening strategy is primary HPV testing every 5 years, with cotesting and cytology alone acceptable where access to US Food and Drug Administration- (FDA) approved primary HPV testing is not yet available.
- The recommended age to start screening is 25 years rather than 21 years.
- Primary HPV testing, as well as cotesting or cytology alone when primary testing is not available, is recommended starting at age 25 years rather than age 30 years.
- The guideline is transitional, ie, options for screening with cotesting or cytology alone are provided but should be phased out once full access to primary HPV testing for cervical cancer screening is available without barriers. (1)



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Cervical cancer screening in the US is not performed through an organized national system. Many women are under-screened (or unscreened) with US HPV vaccination rates still lower than other developed countries. Thus, women in the US have less primary and secondary prevention of cervical cancer than countries with organized preventive services who have adopted primary HPV screening.

Studies from the Centers for Disease Control and Prevention (CDC) (5) show women of lower socioeconomic status are at higher risk of not being screened, along with several minority groups. If cervical cytology is no longer covered by insurers, the existing disparities in preventive services for women in the US are likely to increase.

There is significant risk to patients and liability in transitioning to primary HPV screening as the existence of HPV negative HSIL, AIS, and invasive cancers by current testing methodologies is not addressed in these guidelines. (6-11) It has been established that a considerable number of invasive cancers (9-10%) test negative for HPV and that 8.3-14% of HSIL may also yield negative hrHPV results with the currently available HPV tests. These cases may be identified by a Pap test cytologic examination rather than delayed, with a cancer diagnosis and higher stage tumors made after a 5-year screening interval as a result of negative HPV results. (6,11) Endocervical adenocarcinoma and adenocarcinoma in situ (AIS) are other neoplastic processes that will be overlooked by instating primary HPV testing only. About 10-20% of these tumors are negative for HPV and are diagnosed and worked up as a result of a routine screening Pap test cytologic examination. The transition to primary HPV testing in the guidelines is mostly centered on the advantages of primary HPV testing over cytology alone and inadequately comment on the role of cotesting in comparison to primary HPV testing. (12,14) We recognize that a Pap test alone is less sensitive but more specific than primary hrHPV testing and if the screening goal is to improve sensitivity, co-testing is most sensitive, as women diagnosed with cervical cancer may be more likely detected by liquid-based cytology than an HPV test alone. This becomes especially significant in older patients, patients with uncertain or no screening history, and patients with no clinical symptoms. The microsimulation model which was instrumental in shaping these guidelines also acknowledges that “issues regarding HPV-negative cancers and the implications for the relative effectiveness of hrHPV testing alone versus cytology alone or cotesting were not fully addressed”. (1,15)

When recommending primary HPV testing with further triage by genotyping as the preferred modality in patients 25-65 years, consideration must be given to the availability of the test and barriers to implementing this test in all laboratories. (16) Currently less than half of the laboratories in the US perform primary HPV testing with the only two FDA-approved tests available (Cobas® and Onclarity™). Such barriers may include technical as well as financial challenges in medical centers that are currently performing Pap test cytologic examination. System limitations also exist, supported by the CDC data that shows that 83% of women reported being current with cervical cancer screening, which is considerably below the Healthy People 2020 target of 93%. (5) When primary HPV tests are sent to commercial/centralized laboratories, that may decrease patient access to their results in under-screened populations including patients of lower socioeconomic groups and minority groups with inability for follow up with their physician).(17),This may lead to a wider gap in screening in these groups:



The transition to primary HPV testing in screening for cervical cancer is associated with an inherent bias when a reflex Pap test for cytologic examination is performed. (18,19) Bias will be unavoidable in the absence of co-testing as reflex cytology will only be performed for HPV positive cases. Studies have shown that once the HPV status in a patient is known, it is more likely to report an abnormal result in HPV positive patients when the HPV results are known than if they are unknown to the individual interpreting the Pap test. In turn, with more Pap tests classified as abnormal, an increase in the number of colposcopies performed will follow, together with increased patient harm and psychological distress.

RECOMMENDATION

In summary, the CAP supports efforts for primary cervical cancer prevention by vaccination and by improving access and affordability of cancer screening for all individuals with a cervix. Until there is more longitudinal data applicable to US screening populations, the CAP recommends that cytology and HPV co-testing be included as a screening strategy for women ages 25-65 as it provides the sensitivity and specificity that is needed for all patients.

Sincerely,

Patrick E. Godbey, MD, FCAP
President

Sent via email



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