



ASC POSITION STATEMENT CERVICAL CANCER SCREENING AND PREVENTION

The American Society of Cytopathology (ASC) and its membership are committed to supporting women's health and working collaboratively with other pathology and clinical professionals to effectively prevent cervical cancer in the United States. The ASC supports innovations in technology and changes in testing and management based on scientific and clinically-validated advancements.

Cervical Cancer Screening and Prevention

I. Papanicolaou Test:

- A. The Papanicolaou (Pap) test and the dedication of professionals including cytotechnologists and pathologists have significantly benefited women's health by reducing the incidence of, and mortality from, cervical cancer. It is the most successful cancer screening tool in medical history.
- B. Analogous to other medical tests, the Pap test has an inherent false negative rate associated with sample collection and laboratory interpretation.
- C. Multiple advances have occurred within the test itself and its role in cervical cancer screening, which include: pre-analytic (collection, slide preparation, staining techniques); analytic (automation and computer-assisted screening); HPV testing (triage, co-testing and primary screening), reporting terminology and clinical management guidelines.
 - i. Cervical cytology reporting
 - a. The Bethesda System for Reporting Cervical Cytology has gained essentially universal acceptance in the US and around most of the world.
 - b. The Bethesda System is currently on its 3rd Edition, formulated in 2014.⁽¹⁾
 - ii. Liquid-based technology
 - a. Currently ThinPrep® (Hologic, Inc) and SurePath® (Becton, Dickinson and Co) are the predominant liquid-based Pap test types used in the US.
 - b. Liquid-based Pap tests allow for the performance of ancillary studies directly from the same vial, such as HPV and sexually transmitted infection (Chlamydia, Gonorrhea and Trichomonads) tests.
 - c. The standardized presentation of liquid -based Pap tests allows the incorporation of computer imaging technology.

- iii. Computer imaging technology
 - a. Two devices are widely used in the US to assist in cervical cytology screening: the Hologic ThinPrep® Imaging System (Hologic, Inc) and the BD FocalPoint™ GS Imaging System (Becton, Dickinson & Co).
 - b. Both imaging systems use automated screening performed by proprietary algorithms to select fields of view (FOV) on the slide with cells of interest.
 - c. FOVs are reviewed by cytotechnologists; if any potentially significant abnormality is identified, the slide undergoes full manual review, otherwise a negative result can be issued without further screening.

II. HPV Testing

A. Background

- i. Human papillomavirus (HPV) has been established as a necessary cause for almost all cervical cancers.
- ii. Cervical cancer is caused by high-risk-HPV types, with approximately 70% of cervical cancers due to infection by HPV 16 and 18.
- iii. The majority of low-grade HPV related cervical lesions spontaneously regress without treatment.
- iv. Persistent infection with high risk HPV types is essential in progression to cervical cancer.
- v. The non-carcinogenic or low risk-HPV (LR-HPV) subtypes, such as 6 and 11, are associated with genital warts but have no role in cervical cancer screening.

B. HPV Detection Methods

- i. In the US, there are currently 5 FDA-approved HPV assays, specifically Digene Hybrid Capture® 2 High-Risk HPV DNA Test™ (Qiagen Group); Cervista™ HPV HR and Cervista™ HPV 16/18 (Hologic, Inc); Aptima® HPV Assay and Aptima® HPV 16-18/45 Genotype Assay (Hologic, Inc); cobas® HPV Test (Roche Molecular Systems, Inc); and BD Onclarity™ HPV Assay (Becton, Dickinson & Co).⁽²⁾
- ii. ASC endorses that all HPV testing should be performed using methods that are appropriately validated.⁽³⁾
- iii. The testing laboratory should be CLIA-approved and participate in regular proficiency testing, perform all required verification and continually monitor quality assurance.⁽⁴⁾
- iv. As with any laboratory test, the sensitivity of HPV testing is not 100%. A subset of carcinomas, both squamous and glandular, and other tumor types may not be detected by HPV testing.^(5, 6, 7)
- v. False positives have also been reported due to cross-reactivity, carry over, and other issues.^(8, 9, 10)



- C. Current clinical applications of high-risk HPV testing, endorsed by professional organizations include: ^(11, 12)
 - i. Co-testing with cytology in women between 30 and 65 years of age.
 - ii. Primary HPV screening
 - iii. Reflex testing on equivocal or low-grade cytological abnormalities (ASC-US in patients 21 and over, and LSIL in postmenopausal patients).
 - iv. Genotyping for HPV 16/18 (and 45 in some tests).
 - v. Follow-up of women with abnormal cytological and/or HPV screening results, negative after colposcopically-guided biopsies.
 - vi. Post-treatment follow-up of cervical intraepithelial neoplasia (CIN).

III. Laboratory regulations

- A. The ASC supports and endorses compliance with CLIA and laboratory accreditation quality assurance requirements for gynecologic cytology screening.⁽⁴⁾
- B. The ASC advocates for reasonable cytotechnologist workload limits to ensure the quality of screening.⁽¹³⁾

IV. Cervical cancer prevention by vaccination

- A. The ASC supports universal HPV vaccination of adolescents and catch-up vaccination to prevent cervical cancer; vaccination has the potential to dramatically reduce cervical cancer rates.
- B. Gardasil® 9 (Merck & Co), a nine-valent vaccine (types 6, 11, 16, 18, 31, 33, 45, 52, 58), is the only HPV vaccine available in the US; bivalent (types 16 and 18) and quadrivalent (types 6, 11, 16, and 18) vaccines were previously widely used and are still in use in other countries.
- C. Women fully or partially vaccinated should continue to be screened following the same cervical cancer screening guidelines as those for the general population.⁽¹⁴⁾

V. US screening and management guidelines

- A. The ASC supports current cervical cancer screening guidelines promulgated through professional societies and national organizations.^(15, 16)
- B. Management guidelines published by the American Society for Colposcopy and Cervical Pathology (ASCCP) are widely accepted in the US and are available online and through the ASCCP Mobile App in algorithmic flowcharts.⁽¹⁶⁾



VI. Current cervical cancer screening options in the US

- A. The US Preventive Services Task Force (USPTF) and the American Cancer Society (ACS) currently have similar but not identical screening guidelines.^(15, 16) The most important elements of the guidelines are listed below.
- i. For women age 21-29 both recommend cervical cytology alone every 3 years.
 - ii. For women age 30-65, the USPTF endorses three different options: cervical cytology alone every 3 years, HPV testing alone every 5 years, or combined HPV and cervical cytology co-testing every 5 years; ACS recommends co-testing every 5 years and considers cytology alone every 3 years acceptable.
 - iii. No screening is recommended for women below 21 years of age; screening is also not recommended for women with no significant history of cervical cancer or high-grade precursors who are over age 65 with adequate prior screening or have had a hysterectomy with removal of the cervix.
- B. Screening with HPV testing alone has been approved by the FDA for cobas® HPV Test on specimens prepared with ThinPrep® or SurePath™ and for BD Onclarity™ HPV Assay for SurePath™ for women age 25 and older.
- i. There is currently limited data in the US for primary HPV testing as a standalone screening modality.⁽¹⁷⁾
 - ii. There is ongoing debate about the preferability of primary HPV screening versus HPV and cytology co-testing.⁽¹⁸⁾
 - iii. If primary HPV screening is undertaken, HPV subtyping and cervical cytology should be used to triage for colposcopy; testing should be performed no more frequently than every 3 years; and screening should not start below age 25.⁽¹²⁾

Summary Statement

The ASC endorses worldwide screening as well as HPV vaccination for all women to prevent, detect and reduce cervical cancer incidence and mortality.

The ASC does not endorse any specific Pap or HPV testing modality or any specific vendor(s).

At the current time, the ASC upholds the use of routine cytology with HPV co-testing as the screening strategy most likely to diminish the adverse effects of either false negative cytology or false negative HPV screening test results. However, the choice of cervical screening method may vary for a variety of reasons. Patient and provider preference, geographic, demographic, and socio-economic considerations may all affect the choice of screening modality in a specific country, area, or practice setting.



The ASC recognizes that cervical cancer screening in the United States remains opportunistic, (not organized with a recall system), with far from uniform test accessibility and patient compliance. As participation in screening and prevention is the key to reduction in cervical cancer morbidity and mortality, the ASC advocates for screening and vaccination access for all women with consideration of all acceptable screening modalities, patient compliance, test accessibility and overall cost.

The overriding goal of the ASC and its pathologist and cytotechnologist members is to provide the highest level of quality care to the patients we serve, reiterating that no screening test is perfect.

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