

American Cancer Society Proposed Recommendations for Cervical Cancer Screening

Frequently Asked Questions

Why are we updating our recommendations?

The American Cancer Society reviews new evidence on an ongoing basis and updates screening recommendations when new evidence suggests that a change may be needed. The Society last updated its cervical cancer prevention and early detection guidelines in 2002, with the introduction of two new screening technologies: liquid-based Pap tests and HPV DNA tests. Many new studies have been published since that time.

What other groups were involved with this proposed guideline, and why?

There are three sponsoring organizations: the American Cancer Society (ACS), the American Society for Colposcopy and Cervical Pathology (ASCCP), and the American Society for Clinical Pathology (ASCP). In addition, many other organizations were included on the Steering Committee, Data Group, and Working Groups, including the American College of Obstetricians and Gynecologists (ACOG), National Cancer Institute (NCI), Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), Society of Gynecologic Oncologists (SGO), College of American Pathologists (CAP), and American Society of Cytopathology (ASC). Approximately 25 organizations will be sending voting delegates to participate in a guideline symposium in November to consider the submitted comments, and make revisions to these proposed recommendations based on that input and available evidence. This process involved a number of experts with diverse expertise and representation serving on small working groups, and invites appointed delegates from all the major organizations with an interest in cervical cancer screening to participate.

Organizations sending voting delegates to the November symposium: Agency for Healthcare Research & Quality, American Academy of Family Physicians, American Cancer Society, American Board of Obstetrics and Gynecology, American College Health Association, American College of Obstetricians & Gynecologists, American Social Health Association, American Society for Clinical Pathology, American Society for Colposcopy & Cervical Pathology, American Society for Cytopathology, American Society for Cytotechnology, CDC - Division of Cancer Prevention & Control, CDC - Division of High-Consequence Pathogens and Pathology, CDC - Division of Laboratory Science and Standards (Epidemiology & Surveillance), Centers for Medicare & Medicaid, College of American Pathologists, Food & Drug Administration (OIVD), National Cancer Institute, National Comprehensive Cancer Network, Nurse Practitioners in Women's Health, Planned Parenthood Federation of America, Society of Canadian Colposcopists, Society of Gynecologic Oncologists, Society of Gynecologic Oncology of Canada, Society of Obstetricians & Gynecologists of Canada, Veterans Health Administration, US Preventive Services Task Force

How were these proposed recommendations created?

The proposed recommendations were created by six Working Groups convened by the American Cancer Society and its partner organizations who focused on specific key questions, reviewed the evidence, and developed the draft documents that have been posted on the ASCCP website.

Are these your final recommendations?

No. These are draft recommendations that are being reviewed by interested individuals and organizations/stakeholders who are invited to provide feedback through a web-based open comment period. The Working Groups that developed the recommendations will review the comments submitted and consider revisions to these proposed recommendations. The members of all of the Working Groups will then meet, along with delegates from 25 organizations, at a symposium in November 2011 to further discuss and finalize the recommendations.

What are the key issues addressed in the update?

In the current review process, six main areas were reviewed:

1. Screening women with cytology alone, before age 30 and ages 30+
2. Screening strategies for women ages 30+ with a focus on co-testing with cytology plus HPV testing
3. Management strategies for women with a positive Pap test result (called ASC-US) and a negative HPV test result, or with a normal Pap test result and a positive HPV test result
4. Exiting screening, based on older age or after a hysterectomy
5. Looking to the future: Screening women vaccinated against HPV
6. Looking to the future: Screening with the HPV test alone, or with triage to a second test such as the Pap

What's new in the proposed recommendations for cervical cancer?

- Current recommendations from the ACS say all women should begin cervical cancer testing (screening) 3 years after they start having sex (vaginal intercourse), or no later than age 21. The proposed recommendation says all women should start screening at age 21.
- Current: A conventional (regular Pap) test should be done every year. If a liquid-based Pap test is used instead, testing should be done every 2 years. Proposed: Pap tests (conventional or liquid-based) should be done every 3 years for women 21-29. The proposed guideline recommends *against* annual Pap testing.
- Current: Beginning at age 30, many women who have had 3 normal Pap test results in a row may be tested less often, every 2 to 3 years. Proposed: Pap tests should be done every 3 years for women aged 30 and over. The proposed guideline recommends *against* annual or more frequent Pap testing.
- Current: Either the conventional (regular) Pap test or the liquid-based Pap test can be used. Proposed: No change.
- Current: Another reasonable option for women over 30 (who have normal immune systems and no abnormal Pap results) is to get tested only every 3 years with a Pap test plus the HPV DNA test. The Pap test used can be either the regular or the liquid-based Pap test. Proposed: Pap plus HPV testing every 3-5 years is the preferred strategy for woman aged 30 and older. The proposed guideline recommends *against* screening with any test or combination of tests more often than every 3 years if both results are normal.

- Current: Women 70 years of age or older who have had 3 or more normal Pap tests in a row and no abnormal Pap test results in the last 10 years may choose to stop having cervical cancer testing. Women with a history of cervical cancer, DES exposure before birth, HIV infection, or a weakened immune system should continue to have testing as long as they are in good health. Proposed: Screening is *not* recommended for women 65 years of age or older who have had 3 or more normal Pap tests in a row and no abnormal Pap test results in the last 10 years, or 2 or more negative HPV tests in the last 10 years.
- Current: Women who have had a total hysterectomy (removal of the uterus and cervix) may also choose to stop having cervical cancer testing, unless the hysterectomy was done as a treatment for cervical cancer or pre-cancer. Women who have had a hysterectomy without removal of the cervix (called a supra-cervical hysterectomy) need to continue cervical cancer screening according to the guidelines above. Proposed: Screening is *not* recommended for women who have had a total hysterectomy for benign reasons, or who have had a hysterectomy for cancer more than 20 years ago.

New Proposed recommendations:

- For women who have a normal Pap result and a positive HPV test result, we recommend genotyping for HPV types 16 and 18 *or* repeating both the Pap and HPV tests in one year. We recommend *against* immediate colposcopy.
- Women having an ASC-US Pap result and a negative HPV test result should be followed by either HPV testing plus Pap or HPV testing alone at a minimum of 3 years.
- At this time there is insufficient evidence to recommend for or against a comprehensive program for primary screening with HPV testing alone (with defined follow-up testing) in the US.
- At this time we suggest that the age to start cervical cancer screening among women receiving a series of the HPV vaccine according to routine recommendations should not be any different for an individual or a group than an unvaccinated individual or group.

Why are you recommending starting screening later?

The question of when to begin screening was addressed during a symposium on cervical cancer screening and management in adolescents and young women in June, 2009. There was consensus that screening should begin at age 21 (regardless of previous sexual history). The conclusion of this symposium was that screening women under age 21 is potentially harmful, because it can lead to unnecessary evaluation and treatment, while offering little or no benefit.

Why are you recommending less frequent screening with the Pap test? Why are you recommending *against* annual Pap tests?

With our better understanding of the natural history of HPV infections and development of cervical cancer, we recognize now that screening more frequently leads to unnecessary procedures, and to potentially harmful treatment of lesions (cervical changes detected by Paps) destined to clear without intervention. This is most pronounced with annual screening. Annual screening results in almost 4

times the number of colposcopies (compared to screening every 5 years) with a reduction in lifetime risk of cervical cancer of 50%-60%. Screening every 2 or 3 years is associated with further gains in terms of a reduced risk of cancer (up to almost 90%) with an increase of 1.5 to 1.8 times the number of colposcopies predicted compared to screening every 5 years. For co-testing with the HPV test, a negative HPV test has a high ability to predict the absence of CIN3+ and cancer in the subsequent 6 years, with less risk of invasive cancer than does cytology alone. This provides reassurance that women screened at intervals substantially in excess of 3 years after negative co-testing retain significant protection against cancer.

Why are you recommending Pap plus HPV testing as the preferred strategy?

Studies show that HPV testing detects more cancers, more advanced precancers earlier, detects a second type of cervical cancer (called adenocarcinoma) that Pap tests usually miss, and provides added reassurance to women who test negative—safely allowing a much longer screening interval.

Why are you recommending that women exit screening at age 65 rather than age 70?

Modeling studies show that continuing screening beyond age 65 leads to many additional false positive results and unnecessary procedures and only rarely finds cancer. For example, screening until age 90 would prevent 1 cervical cancer death for every 2000 women compared to screening until age 65 while adding 250 colposcopy procedures. The age of 65 is also recommended by the USPSTF; agreement between organizations will be less confusing for providers and patients.

How do these guidelines relate to the ones also released today by the United States Preventive Services Task Force (USPSTF)?

The ACS-ASCCP-ASCP and USPSTF worked independently to develop guidelines. The ACS-ASCCP-ASCP conducted its own systematic evidence review but, where key issues overlapped with the USPSTF, we supplemented our effort with the USPSTF evidence review.

Why do the proposed recommendations from the ACS and the USPSTF differ?

For the most part, the recommendations of both groups are very similar. Both groups recommend screening women ages 21-65 (who have not had a hysterectomy) every 3 years with either liquid-based or conventional Pap tests. The ACS included several additional key questions in their review. The major difference between the two sets of draft recommendations is that the ACS recommends that starting at age 30, the preferred screening strategy is screening with the HPV test in addition to the Pap test (our recommendation in 2002 called this approach “an option”). The USPSTF concludes that there is insufficient evidence to recommend for or against use of HPV testing in primary screening.

All medical interventions represent a trade-off between potential benefits and harms to both the patient and society. The potential benefits and harms that specifically apply to cervical cancer screening were provided to each Work Group. The weights assigned to these potential benefits and harms will vary depending on the specific screening recommendation being considered. Each Work Group was instructed to base their recommendations on the trade-offs between potential benefits and harms expected for specific cervical cancer screening strategies.

The ACS and USPSTF evaluated the same set of studies. These studies show that HPV testing detects more cancers, more advanced precancers earlier, detects a second type of cervical cancer (called adenocarcinoma) that Pap tests usually miss, and provides added reassurance to women who test

negative—safely allowing a much longer screening interval. The USPSTF concluded that while the studies show the HPV testing detects more cancers including adenocarcinomas, more and longer-term data are needed on the potential harms of this screening strategy, including the number of unnecessary follow-up procedures.

What do other organizations recommend?

	ACS 2002	ACS-ASCCP-ASCP DRAFT 2011	ACOG 2009	USPSTF DRAFT 2011
Age to start	Approximately 3 years after initiation of intercourse or by age 21	Age 21	Age 21	Age 21
Interval 21-29	Annual with conventional Pap; 2 years with liquid Pap	Every 3 years (liquid or conventional); Recommend AGAINST annual Pap	Every 2 years (liquid or conventional)	Every 3 years (liquid or conventional)
Interval 30+ (with Pap alone)	Every 2-3 years	Every 3 years	Every 3 years	Every 3 years
Age to stop	Age 70 after 3 negative tests in last 10 years	65 after 3 negative tests in last 10 years or 2 negative HPV tests in last 10 years	Age 65-70 after 3 negative tests in last 10 years	65 after adequate screening
Hysterectomy	Discontinue if for benign reason	Discontinue if for benign reason	Discontinue if for benign reason	Discontinue if for benign reason
Screening test Type of Pap test HPV test	Conventional or liquid Paps; option of HPV co-testing starting at age 30 repeated no sooner than every 3 years	Conventional or liquid Paps; HPV co-testing every 3-5 years is the preferred strategy for women ages 30 and older Recommend AGAINST more frequent screening, especially annual Insufficient evidence for or against HPV alone/with triage to cytology [still in discussion]	Conventional or liquid Paps; option of HPV co-testing starting at age 30 repeated no sooner than every 3 years	Conventional or liquid Paps; insufficient evidence for or against HPV co-testing or HPV testing alone/with triage to cytology
Screening after HPV vaccination	Same as for unvaccinated (2007 ACS guideline on HPV vaccination)	Same as for unvaccinated—insufficient evidence to change	Same as for unvaccinated	Not addressed
Pap normal/HPV +	Repeat both the Pap and HPV tests in 6-12	Genotyping for HPV types 16 and 18 <i>or</i>	Not addressed	Not addressed

	months; Recommend <i>against</i> immediate colposcopy (ASCCP-ACS-NCI interim guidance 2004)	repeat both the Pap and HPV tests in one year Recommend <i>against</i> immediate colposcopy		
ASC-US/HPV – (equivocal Pap result, HPV negative)	Not addressed	Repeat HPV testing plus Pap or HPV testing alone at a minimum of 3 years	Not addressed	Not addressed

How is this effort different from past efforts and why?

The previous guideline review was based on a review of the literature. While we are confident that our past efforts produced high quality, credible, evidence-based recommendations, the current process used a much more rigorous and systematic evidence review. Both processes used similar criteria to include or exclude articles. The current process followed the GRADE approach, discussed below. Many organizations that develop guidelines today use this approach to be as transparent and comprehensive as possible. The use of a systematic approach to grade the quality (level) of evidence and the strength of recommendations and then make judgments about evidence can help to prevent errors, facilitate critical appraisal of these judgments, and help to improve communication of this information.

What is the purpose of the public comment period?

The ACS-ASCCP-ASCP draft recommendations and public comment surveys will be posted on the ASCCP website at www.asccp.org/practice-management/molecular-screening-symposium beginning Wednesday, October 19 and continuing through Wednesday, November 9. This is an opportunity for interested individuals and organizations/stakeholders to review and provide feedback on the proposed recommendations. The USPSTF is also posting draft recommendations for cervical cancer screening for public comment beginning October 19.

What is currently covered by health insurance?

Most health insurers cover Pap tests and most cover HPV testing. The Patient Protection and Affordable Care Act (ACA) includes a provision that patients will no longer be required to provide copayments for certain preventive services. For cervical cancer screening:

- New private health plans are required to cover liquid or conventional Pap tests at least every three years for women aged 21-65.
- Starting August 2012, new health plans will be required to cover HPV DNA testing for women aged 30-65 every 3 years.
- Medicare covers these screening tests once every 24 months, or once every 12 months for women at high risk, and for women of child-bearing age who have had an exam that indicated

cancer or other abnormalities in the past 3 years. ACA eliminates cost sharing for pap tests for Medicare beneficiaries.

Medicaid is a state administered program and each state sets its own guidelines regarding eligibility and services. Medicaid programs are required to cover cervical cancer screening in their state if they receive funding for the National Breast and Cervical Early Detection Program. There is also an incentive in the ACA for Medicaid to cover all "A" or "B" preventive services recommended by the USPSTF.

How was the evidence review done?

For this review process, six main areas were identified and an independent Working Group was assigned to each area. The systematic evidence review was designed to be as thorough as feasible. The initial literature search resulted in 10,151 abstracts of which about 600 were deemed relevant for this review. The relevant abstracts were provided to the Work Groups, who used the evidence to answer key question criteria identified by the Steering Committee and Working Group co-chairs. Working Group co-chairs randomly assigned each abstract to Working Group members for review. The Working Groups then evaluated those articles that 2 members agreed should be included. To assure a comprehensive and systematic review, the Working Groups also reviewed the systematic evidence reviews conducted for the Agency for Health Research and Quality (AHRQ) in support of the USPSTF guideline update.

We used the *Grading of Recommendations Assessment, Development and Evaluation (GRADE)* System to guide the review and evaluation of evidence. The GRADE Working Group developed a standardized approach to grading quality of evidence and strength of recommendations. Many US and international organizations use this approach now to make clinically-based recommendations.

Did the group look at economic outcomes?

We chose not to consider the financial cost or other economic factors related to screening and follow-up. Economic outcomes may be considered if we decide to recommend two screening strategies that are equivalent in terms of benefits and harms, and one strategy is significantly more costly than the other. Given concerns raised by the public about basing health care decisions on cost, we felt that our recommendations should stand on their own scientific and medical merit rather than on financial considerations.

What comes next?

After the public comment period, all the Working groups, the Steering Committee, Data Group, and delegates from organizations will meet to hear presentations from each Working Group, discuss issues that cut across two or more Working Groups, resolve any inconsistencies between Working Groups, and come to consensus on the final recommendations. Immediately following that meeting, the ACS will meet to decide how to incorporate the recommendations into updated ACS guidelines. We anticipate the release of the final guideline in mid-2012.

How did you address potential conflicts of interest?

In planning this workshop, the Steering Committee (SC) critically examined some of the issues involved in defining conflict-of-interest (COI). Often, COI rules emphasize disclosure of an individual's association with commercial entities and remuneration or other financial interests in a company. However, the SC

recognizes other financial conflicts of interest may arise in conjunction with shifts in recommendations for standard practice. For example, on an individual level, a clinician's practice and income may be impacted by changes to the recommended frequency of patient visits. At another level, an entire professional specialty might be adversely impacted, or advantaged, by such changes. The SC recognizes that all such financial interests – whether an affiliation with a company, the success of one's clinical practice, the prominence of a professional specialty – represent potential conflicts.

Therefore, for this workshop, all participating individuals were required to disclose all real or potential conflicts of interest including but not limited to: association with relevant commercial interests, involvement with professional societies in an executive or policymaking role, and the nature of their primary employment. Commercial interests are defined as any proprietary entity producing health care goods or services consumed by or used on patients. These may include pharmaceutical companies, device manufacturers or distributors, service companies or other for-profit entities.

We recognize that under this broader definition of COI, virtually everyone has potential conflicts. In forming committees and working groups, the SC sought expertise and balance in the composition of group members so that a broad a range of interests were represented.