



The American College of
Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS



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Joya Chowdhury, MPH
Senior Coordinator, USPSTF
Department of Health and Human Services
Agency for Healthcare Research and Quality
Center for Evidence and Practice Improvement
Room 06E65A
5600 Fishers Lane
Rockville, MD 20857

Dear Ms. Chowdhury:

The [American College of Obstetricians and Gynecologists](#) (ACOG), the [American Society for Colposcopy and Cervical Pathology](#) (ASCCP), and the [Society of Gynecologic Oncology](#) (SGO) thank the U.S. Preventive Services Task Force (USPSTF) for the opportunity to review its new draft recommendation statement, "Screening for Cervical Cancer." As three major stakeholder organizations in the shared mission of well-woman care and cervical cancer prevention, screening, and management, ACOG, ASCCP, and SGO applaud the USPSTF's attention to this critical area and its exhaustive literature review and commissioned modeling study. We are reassured by the large areas in which the USPSTF draft recommendations and our organizations' joint guidelines^{1,2} remain fully aligned and supported by the evidence that has accumulated since their last revision.

However, we urge the USPSTF to retain 5-year co-testing as a screening option for women aged 30–65 years and to strongly consider a shorter interval for primary hrHPV screening. Although our organizations agree with the USPSTF's enthusiasm for the promise of primary

¹ Saslow D, Solomon D, Lawson HW, Killackey M, Kulasingam SL, Cain J, et al. American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology screening guidelines for the prevention and early detection of cervical cancer. ACS-ASCCP-ASCP Cervical Cancer Guideline Committee. CA Cancer J Clin 2012;62:147–72.

² Cervical cancer screening and prevention. Practice Bulletin No. 168. American College of Obstetricians and Gynecologists. Obstet Gynecol 2016;128:e111–30.

hrHPV screening and have previously provided interim guidance for its use,³ we are very concerned about the removal of cotesting from the USPSTF draft recommendations and about the proposed 5-year interval for hrHPV primary screening.

Concerns About Removal of Cotesting as a Screening Option

- **Denial of Insurance Coverage.** Although the USPSTF has not explicitly recommended against cotesting, it also has not given it an A or B rating. While we understand that cost consideration is not part of USPSTF's purview, this change has very important implications. In particular, we are deeply concerned that payers may consequently deny coverage for cotesting, which remains the preferred method in our guidelines and is supported by Level 1 evidence demonstrating its efficacy for cervical cancer prevention.
- **Availability of FDA-Approved hrHPV Test for Primary Screening.** The USPSTF's draft recommendation statement does not comment on acceptable hrHPV tests for primary screening. As noted in our organizations' interim guidance³, different HPV tests have different test characteristics, and use for primary screening should be restricted to tests that have been validated through rigorous clinical trials for this use. Currently, there is only one test that has been validated in the U.S. and is FDA approved for primary hrHPV screening (Roche Cobas® 4800), and it is available only in a limited number of laboratories and institutions. While we do not have data on how many labs have implemented this test, it is only a minority of institutions and laboratories, which limit its use and access. BD has applied to the FDA for approval of a new primary hrHPV screening test, but this application remains pending. Compliance with USPSTF draft guidance using FDA approved testing would require many institutions either to purchase the equipment for a new test, which may be cost prohibitive, or to use 3-year cytology, which has decreased sensitivity that makes it inferior to primary hrHPV screening or co-testing.
- **Increased Confusion and Decreased Compliance.** Health care provider compliance with new clinical guidelines lags well behind their dissemination. This is an ongoing problem, particularly in the case of cervical cancer screening. Cervical cancer screening guidelines have changed several times in the last decade. However, many women's health care providers continue to perform routine annual cervical cancer screening with cytology or cotesting, screen women younger than age 21 years, and screen women after hysterectomy—long after recommendations were made to end these practices. Logistically, our organizations think that a strategy of preserving cotesting as an option

³Huh 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;125:330–7.

(possibly an alternative option) and adding primary hrHPV screening will be less confusing to health care providers and patients. Removal of a cotesting recommendation risks taking a step backward and further contributing to problems with cervical cancer screening guideline compliance.

- **Decreased detection compared with cotesting.** Although hrHPV testing provides most of the sensitivity in cotesting, there is added detection through the addition of cervical cytology. In a National Cancer Institute analysis of U.S. data from Kaiser Permanente Northern California⁴, the difference in cumulative risk of cervical intraepithelial neoplasia (CIN) grade 3 and cancer between primary hrHPV screening and cotesting was much smaller compared with cytology alone. The risk of CIN grade 3 and cancer appeared roughly equivalent between 4-year primary hrHPV screening and 5-year cotesting (**Fig. 1**).

Concerns About 5-Year Interval for Primary HPV Testing

- **Lack of U.S. Validation Studies.** In the USPSTF evidence review, no primary hrHPV screening trials included a second round of testing at the 5-year interval, and only a single non-U.S. based cotesting trial (POBSCAM, Netherlands) used this interval. That trial was conducted in western Europe, which has a formal screening program, unlike the U.S., which depends on opportunistic screening. The recommendation of the 5-year screening interval in the current draft USPSTF guidelines was driven strictly by a 2017 modeling study with assumptions. The modeling study, although elegant and comprehensive, does not have prospective U.S.-based validation. Both USPSTF and our own organizations used modeling studies to choose screening intervals in the last round of major revisions to the cervical cancer screening guidelines; however, at that time, there was a study with a 5-year follow-up interval to validate the model.

Our organizations' interim guidance specifies rescreening after a negative primary hrHPV screening result should occur no sooner than every 3 years. We appreciate that having similar intervals for primary hrHPV screening and cervical cytology alone may not make sense and that primary hrHPV screening intervals should be longer than cytology alone to balance benefits and harms. However, without prospective U.S.-based validation, available data are insufficient to justify extending the interval for primary hrHPV screening to 5 years.

⁴ Gage J, Katki HA, Schiffman M, Castle PE, Fetterman B, Poitras NE, et al. Reassurance against future risk of precancer and cancer conferred by a negative human papillomavirus test. *J Natl Cancer Inst* 2014;106:1–4.

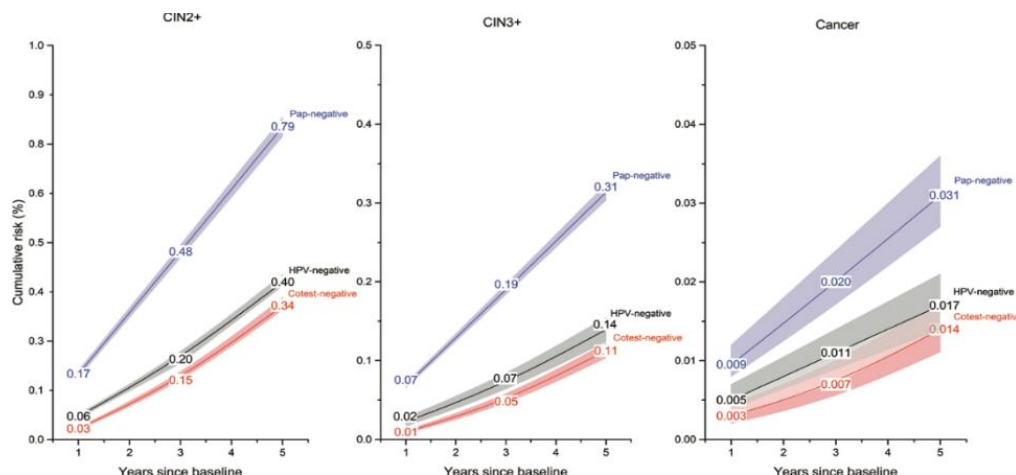


Figure 1. Cumulative risks of cervical intraepithelial neoplasia grade 2 or more severe (left panel), grade 3 or more severe (center panel) and cancer (right panel) among women aged 30 to 64 years at Kaiser Permanente Northern California by enrollment Pap and human papillomavirus (HPV) test result, 2003 to 2012.⁴

- Safety.** Although our organizations understand that a shorter interval for primary hrHPV screening would come with an increased number of colposcopies, we are concerned that the USPSTF may place greater emphasis on this as a harm than individual patients. In addition, because the model estimates at 5 years have not been validated, they may potentially not be as extreme as modeled. It is difficult to weigh the balance of the cumulative risk of an increase in colposcopies with the potential for missing cervical cancer. Most of us who treat patients with cervical cancer have our own bias that we would rather do more colposcopies than see women suffer from a preventable cancer that affects women in the prime of their reproductive lives.

ACOG, ASCCP, and SGO are deeply appreciative to the USPSTF for its work in advancing cervical cancer screening and prevention. We are very impressed by the enormous amount of work that went into the updated evidence review and modeling study. Although our organizations are very supportive of USPSTF's proposal to incorporate primary HPV testing into its guidelines, **we urge the USPSTF to retain 5-year co-testing as a screening option for women aged 30–65 years and to strongly consider a shorter interval for primary HPV screening.**

Sincerely,

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