### Abstract

## Screening for Cervical Cancer: U.S. Preventive Services Task Force Recommendation Statement

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**Description:** Update of the 2003 U.S. Preventive Services Task Force (USPSTF) recommendation statement on screening for cervical cancer.

**Methods:** The USPSTF reviewed new evidence on the comparativetest performance of liquid-based cytology and the benefits and harms of human papillomavirus (HPV) testing as a stand-alone test or in combination with cytology. In addition to the systematic evidence review, the USPSTF commissioned a decision analysis tohelp clarify the age at which to begin and end screening, the optimal interval for screening, and the relative benefits and harms of different strategies for screening (such as cytology and co-testing).

Recommendations: This recommendation statement applies to women who have a cervix, regardless of sexual history. This recommendation statement does not apply to women who have received a iagnosis of a high-grade precancerous cervical lesion or cervical cancer, women with in utero exposure to iethylstilbestrol, or women who are immunocompromised (such as those who areHIV positive). The USPSTF recommends screening for cervical cancer in women aged 21 to 65 years with cytology (Papanicolaou smear) every 3 ears or, for women aged 30 to 65 years who want to lengthen the screening interval, screening with a combination of cytology and HPV testing every 5 years. See the Clinical Considerations for discussion of cytology method, HPV testing, and screening interval (A recommendation).

The USPSTF recommends against screening for cervical cancer in women younger than age 21 years (D recommendation). The USPSTF recommends against screening for cervical cancer in women older than age 65 years who have had adequate prior screening and are not otherwise at high risk for cervical cancer. See the Clinical Considerations for discussion of adequacy of prior screening and risk factors (D recommendation). The USPSTF recommends against screening for cervical cancer in women who have had a hysterectomy with removal of the cervix and who do not have a history of a high-grade precancerous lesion (cervical intraepithelial neoplasia grade 2 or 3) or cervical cancer (D recommendation).

The USPSTF recommends against screening for cervical cancer with HPV testing, alone or in combination with cytology, in women younger than age 30 years (D recommendation).

World Health Organization. Prevention of cervical cancer through screening using visual inspection with acetic acid (VIA) and treatment with cryotherapy. 2012 https://apps.who.int/iris/ bitstream/handle/10665/ 75250/ 9789241503860\_ eng.pdf; jsessionid= 51BE 26A6AB 0223562 A34137A469EC7B7? sequence=1

The demonstration project, "prevention of cervical cancer through screening using visual inspection with acetic acid (VIA) and treatment with cryotherapy" began in September 2005, and involved seven sites in six African countries (Madagascar, Malawi, Nigeria, Uganda, United Republic of Tanzania and Zambia), and was completed in May 2009. Training of project coordinators took place in the Department of Obstetrics and Gynaecology, University of Zimbabwe, Harare. Training in data management was undertaken at all project sites, with consultants from the African Population and Health

Research Centre (APHRC) and the International Agency for Research on Cancer (IARC) providing technical assistance to ensure that all those involved in recruiting women into the project were familiar with the instruments for data collection. The project created awareness in communities about cervical cancer and its prevention. Women were counselled and offered screening using VIA, and patients with a positive screening test were treated using cryotherapy. Patients who were not eligible for cryotherapy were referred to a higher level of health care, for further evaluation and treatment. Continuous monitoring and evaluation of the project was carried out by IARC and APHRC, through a pre-cervical cancer information system that was developed by IARC in order to generate evidence about the

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acceptability and feasibility in a primary health-care setting, referral site or district hospital. The project targeted all women resident in the catchment area and aged between 30 and 50 years.

Between September 2005 and May 2009, a total of 19 579 clients were screened from the six countries. Overall, 10.1% of with VIA results were positive, and 1.7% of clients had lesions suspicious of cancer on inspection. A total of 87.7% of all VIA-positive cases were eligible for cryotherapy. The majority of clients (63.4%) received cryotherapy within one week of initial screening. The single-visit approach enabled 39.1% of clients to be screened and treated on the same day. However, over 39.1% of all clients eligible for cryotherapy did not receive treatment, for various reasons, including equipment not being in working order at the time of screening, and clients requiring to get consent from their spouses before cryotherapy could be done. The VIA and cryotherapy procedures were well tolerated by women, and almost all of those who underwent these procedures would recommend them to other women. This demonstration project has shown that the "screen and treat" approach can be introduced into existing reproductive health services in low-resource countries. Screening for precancerous lesions using VIA, and treatment with cryotherapy, is acceptable and feasible at low-level health facilities in six African countries.

In conclusion, as a result of a demonstration project, VIA and cryotherapy have been incorporated into the cervical cancer-prevention services in existing reproductive health services in six countries. VIA is an attractive alternative to cytology-based screening in low-resource settings. Similarly, cryotherapy has been selected as the treatment option for the eligible test-positive cases. The alternative simple and safe cervical cancer-prevention techniques simplify the process and render it feasible and acceptable to women and providers in low-resource settings.

At the final meeting of the project, country teams presented plans on how best to scale-up cervical cancer-prevention services using the "see and treat" approach. The country teams noted that funding shortages and limited human resources are some of the factors that may detract the Ministries of Health in the six countries from sustaining and scaling-up the programme. To optimize the use of VIA and cryotherapy for cervical cancer-prevention programmes, training of adequate number of providers will be needed, along with sustainable supervision and supply and maintenance of equipment and consumables.

Scaling-up programmes will facilitate extension of cervical cancer-prevention services to the target population in both urban and rural areas through development of referral linkages with high-level health facilities. Recommendations provided in this report can help facilitate phased and coordinated scalingup of services in the six countries.

#### Use of primary high-risk human papillomavirus testing for cervical cancer screening Huh WK, et al

Interim clinical guidance, Gynecol Oncol (2015), http://dx.doi.org/10.1016/j.ygyno.2014.12.022.

In 2011, the American Cancer Society, the American Society for Colposcopy and Cervical Pathology, and the American Society for Clinical Pathology updated screening guidelines for the early detection of cervical cancer and its precursors. Recommended screening strategies were cytology and cotesting (cytology in combination with hrHPV testing). These guidelines also addressed the use of hrHPV testing alone as a primary screening approach, which was not recommended for use at that time. There is now a growing body of evidence for screening with primary hrHPV testing, including a prospective US-based registration study. Thirteen experts including representatives from the Society of Gynecologic Oncology, American Society for Colposcopy and Cervical Pathology, American College of Obstetricians and Gynecologists, American Cancer Society, American Society of Cytopathology, College of American Pathologists, and the American Society for Clinical Pathology, convened to provide interim guidance for primary hrHPV screening. This guidance panel was specifically triggered by an application to the FDA for a currently marketed HPV test to be labeled for the additional indication of primary cervical cancer screening. Guidance was based on literature review and review of data from the FDA registration study, supplemented by expert opinion. This document aims to provide information for healthcare providers who are interested in primary hrHPV testing and an overview of the potential advantages and disadvantages of this strategy for screening as well as to highlight areas in need of further investigation. Primary hrHPV screening is an important scientific and clinical advance in cervical cancer screening

since it offers better reassurance of low cancer risk compared to cytology-only screening conducted at the same interval. Primary hrHPV screening can be considered as an alternative to current US cytologybased cervical cancer screening approaches including cytology alone and cotesting. The use of HPV 16/18 genotyping and reflex cytology for women positive for the 12 other hrHPV genotypes achieves a reasonable balance of disease detection with the number of screening tests and colposcopies required to achieve that detection. It is expected that more data on triage options will be available soon that could lead to updated triage recommendations. Primary hrHPV screening at 25-29 years of age may lead to increased CIN3 detection, but the impact of increased number of colposcopies, integration with screening prior to age 25, and actual impact on cancer prevention need further investigation. While there continue to be numerous practical and research questions, primary hrHPV testing has the potential to further reduce morbidity and mortality of cervical cancer in the US. However, to achieve the maximum benefit of screening, we need to continue to identify women who are either unscreened or underscreened.

Interim guidance panel recommendations and discussion-

 Is hrHPV testing for primary screening as safe and effective as cytologybased screening?

A negative hrHPV test provides greater reassurance of low CIN3+ risk than a negative cytology result.

 Can primary hrHPV screening be considered as an alternative to current US cervical cancer screening methods? Because of equivalent or superior effectiveness, primary hrHPV screening can be considered as an alternative to current US cytology-based cervical cancer screening methods. Cytology alone and cotesting remain the screening options specifically recommended in major guidelines.

- How should one manage a positive hrHPV result? Based on limited data, triage of hrHPV-positive women using a combination of genotyping for HPV 16 and 18 and reflex cytology for women positive for the 12 other hrHPV genotypes appears to be a reasonable approach to managing hrHPVpositive women.
- What is the optimal interval for primary hrHPV screening?

Re-screening after a negative primary hrHPV screen should occur no sooner than every 3 years.

At what age should one initiate primary hrHPV screening?

# Human papillomavirus in 2019: An update on cervical cancer prevention and screening guidelines.

#### Zhang S1, Batur P.

Cleve Clin J Med. 2019 Mar;86(3):173-178. doi: 10.3949/ccjm.86a.18018.

The human papillomavirus (HPV) causes most cases of cervical cancer. Healthcare providers can help prevent this cancer by recommending HPV vaccination when appropriate, regularly screening women for cervical cancer, and following up on abnormal test results.