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Cervical Cancer Screening Guideline

Last guideline approval: May 2019

Guidelines are systematically developed statements to assist patients and providers in choosing appropriate health care for specific clinical conditions. While guidelines are useful aids to assist providers in determining appropriate practices for many patients with specific clinical problems or prevention issues, guidelines are not meant to replace the clinical judgment of the individual provider or establish a standard of care. The recommendations contained in the guidelines may not be appropriate for use in all circumstances. The inclusion of a recommendation in a guideline does not imply coverage. A decision to adopt any particular recommendation must be made by the provider in light of the circumstances presented by the individual patient.

Guideline Scope

This guideline focuses exclusively on recommendations for screening.

For the management of Pap and high-risk human papillomavirus (hrHPV) test results and follow-up colposcopy results, the recommendations of the 2012 ASCCP Updates Consensus Guidelines Conference (Massad 2013) have been adopted. A presentation of the recommendations is available on the Guidelines page of the ASCCP website: http://www.asccp.org/asccp-guidelines. See "Algorithms – PDFs for your personal use."

The ASCCP recommendations and algorithms are available in a mobile application for iPhone, iPad, and Android devices at http://www.asccp.org/store-detail2/asccp-mobile-app. As of February 2019, the cost for the app is $10.

Major Changes as of May 2019

New	Previous
Primary high-risk HPV screening for cervical cancer (i.e., hrHPV only) is now recommended as a third option for screening (where available) for women aged 30–65.	Primary hrHPV screening was not recommended for women of any age.

Prevention

Cervical cancer prevention measures include regular screening with Pap tests and reducing the risk of human papillomavirus (HPV) infection through condom use and HPV vaccination. In the presence of HPV infection, cigarette smoking is thought to be associated with a significantly increased risk of squamous cell carcinoma, and tobacco cessation is an important aspect of decreasing risk of cervical dysplasia (ACOG 2009).

- HPV vaccination is recommended for both males and females aged 9–26 years for the prevention of HPV-related diseases. See the Immunization Schedules.
- Tobacco cessation is recommended for all individuals. See the KPWA Tobacco Use Guideline.

Screening

Virtually all cervical cancers are caused by HPV infections, with just two types—16 and 18—responsible for approximately 70% of all cases. Other high-risk genotypes (such as 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) are also included in the hrHPV test.

Screening tests

The Pap test is the preferred screening option for women aged 21 through 29 and should be repeated every 3 years. The Pap test is also an alternative screening option for women aged 30 and older. For women aged 25 and older, a reflex hrHPV test is performed when Pap results are ASC-US (atypical squamous cells of undetermined significance).

Co-testing (with both Pap and hrHPV tests) is the preferred screening option for women aged 30 to 65 and should be repeated every 5 years. Co-testing is **not** recommended for women under age 30.
Note: Patients should be made aware that not all health plans cover hrHPV testing without co-insurance/deductible.

Primary hrHPV screening: Screening with hrHPV testing alone (with reflex to Pap) is a third screening option (USPSTF 2018) for women aged 30–65. Primary hrHPV screening is more effective than co-testing, detecting more cervical intraepithelial neoplasia (CIN) 3+ with fewer missed cases, resulting in a

lower likelihood of CIN 3+ at 4 years. Primary hrHPV screening is also more efficient and cost-effective than co-testing and simplifies outreach, result interpretation, and follow-up of abnormal results.

However, there are currently two significant barriers to the full adoption of primary hrHPV screening as the preferred screening method at KPWA. The first barrier is that the current HEDIS® measure for cervical cancer screening does not yet include primary hrHPV as an acceptable screening method. The second is that the lab test currently used KPWA, Hologic, is not yet FDA-approved for primary hrHPV screening.

While KPWA does not yet offer primary hrHPV screening, women who have previously had primary hrHPV screening with a negative result are considered sufficiently screened for the current round. Rescreening after a negative primary hrHPV screen in women 30–65 should follow the current screening interval of 5 years.

For women screened with primary hrHPV whose results are positive for:

- Type 16/18, follow up with colposcopy.
- Other types, follow up with cytology.

Who to screen

- All women aged 21 through 64 years should be screened regardless of whether they have ever been sexually active.
- Women who are immunized against HPV should be screened by the same regimen as non-immunized women.

Table 1. Recommendations for cervical cancer screening

Eligible population	Test(s)	Frequency
Average-risk women aged 21 through 29 years	Pap test	Every 3 years
Average-risk women aged 30 through 64 years	***Preferred*** Co-testing (Pap test plus hrHPV test)	Every 5 years
	Alternative Pap test	Every 3 years
	Alternative Primary hrHPV screening [1]	Every 5 years

[1] Primary hrHPV screening is not currently available at KPWA.

Who not to screen

Women younger than 21 years: Screening is not recommended for women younger than 21 years regardless of age of onset of sexual activity, as it may lead to unnecessary and harmful evaluation and treatment in women at very low risk of cervical cancer. Findings from observational studies suggest that high-risk HPV infections and cytologic abnormalities are common and transient in women younger than 21. In addition, CIN 3+ is much less common in the younger cohort. Sexually active women younger than 21 should be counseled regarding safe sex and contraception and tested for sexually transmitted infections.

Women aged 65 and older: Screening is generally not recommended for women aged 65 and older. There is adequate evidence that screening with Pap tests in women aged 65 and older who have had adequate prior screening and are not otherwise at high risk provides little to no benefit. The 2012 ACS-ASCCP-ASCP guideline (Saslow 2012) defines adequate prior screening as three or more documented, consecutive, and technically satisfactory normal/negative Pap tests, or two consecutive negative co-tests, with the most recent test occurring within the past 5 years and no abnormal/positive Pap tests within the last 10 years. The one exception is women who have been treated for CIN 2, CIN 3, or adenocarcinoma in situ, who should continue to be screened for at least 20 years, even if the screening extends past age 65.

Women who have had a hysterectomy: Screening for cervical cancer is not recommended in women who have had a hysterectomy that included removal of the cervix and no prior history of CIN.

Evidence Summary

The Cervical Cancer Screening Guideline was developed with an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis.

As part of our improvement process, the Kaiser Permanente Washington guideline team is working towards developing new clinical guidelines and updating the current guidelines every 2–3 years. To achieve this goal, we are adapting evidence-based recommendations from high-quality national and international external guidelines, if available and appropriate. The external guidelines should meet several quality standards to be considered for adaptation. They must: be developed by a multidisciplinary team with no or minimal conflicts of interest; be evidence-based; address a population that is reasonably similar to our population; and be transparent about the frequency of updates and the date the current version was completed.

In addition to identifying the recently published guidelines that meet the above standards, a literature search was conducted to identify studies relevant to the key questions that are not addressed by the external guidelines.

External guidelines meeting KPWA criteria for adaptation/adoption

ACOG Committee on Practice Bulletins—Gynecology. ACOG Practice Bulletin no. 109: Cervical cytology screening. *Obstet Gynecol.* 2009 Dec;114(6):1409-1420.

Huh WK, Ault KA, Chelmow D, et al. Use of Primary High-Risk Human Papillomavirus Testing for Cervical Cancer Screening: Interim Clinical Guidance. *Obstet Gyn.* 2015 Feb;125(2):330-337.

Massad MS, Einstein MH, Huh WK, et al; 2012 ASCCP Consensus Guidelines Conference. 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. *J Low Genit Tract Dis.* 2013 Apr;17(5 Suppl 1):S1-S27.

Melnikow J, Henderson JT, Burda BU, Senger CA, Durbin S, Weyrich MS. Screening for Cervical Cancer with High-Risk Human Papillomavirus Testing: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. *JAMA.* 2018 Aug 21;320(7):687-705.

Saslow D, Solomon D, Lawson HW, et al; ACS-ASCCP-ASCP Cervical Cancer Guideline Committee. 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. *CA Cancer J Clin.* 2012 May-Jun;62(3):147-172.

US Preventive Services Task Force, Curry SJ, Krist AH, et al. Screening for Cervical Cancer: US Preventive Services Task Force Recommendation Statement. *JAMA.* 2018 Aug 21;320(7):674-686.

Effectiveness of hrHPV testing as a primary screening strategy in reducing the incidence of cervical cancer, compared to the currently recommended screening strategies in women aged 21–65 years

There are no published trials to date that directly compare primary hrHPV versus hrHPV co-testing. All comparisons were made versus cytology screening, and none of the trials reported on mortality.

A systematic evidence review prepared for the AHRQ (Melnikow 2018) on screening for cervical cancer with hrHPV testing reported on the results of seven large randomized controlled trials (RCTs), three of hrHPV and four of hrHPV co-testing as part of cervical cancer screening with cytology alone for detection of cervical intraepithelial neoplasia (CIN) grade 3 or higher. All trials were conducted as organized screening programs and used HPV tests approved for co-testing (not for primary HPV testing).

The quality of most of the included studies was rated as fair and no trial had sufficient power to assess the effect of screening on the incidence of cervical cancer or mortality. There were differences among the trials in the type of cytology (smear or liquid-based), hrHPV test used (PCR, HC2), screening interval (201505 years), follow-up protocols for abnormal results, number of screening rounds, and protocols for screening beyond the first round of screening.

The results of the studies on primary hrHPV testing were (despite their heterogeneity) consistent in demonstrating that the primary hrHPV testing increased the detection of CIN3+ by two- to three-fold in the initial round of screening. In the NTTC phase II trial (Ronco 2010), all women with a positive hrHPV test were referred to colposcopy, and in the second round all women received cytology testing. CIN3+ detection was 3 times higher with the hrHPV test and the cumulative detection was 1.8 times higher after the second round of screening.

The results of the co-testing trials were mixed. In two of the four trials, round 1 CIN3+ detection was 1.2 to 1.3 times greater for co-testing. By the second round of screening 3–5 years later, the CIN3+ detection was higher in the cytology-only arm, leading to an overall similar cumulative CIN3+ detection.

In the primary HPV screening trials women aged 25–60 were eligible for screening; the results indicate that those under age 35 years had higher rates of positive hrHPV and CIN3+ compared to the women aged 35 and over.

Outcomes of different rescreening intervals could not be assessed due to the lack of direct comparison of interval.

The HPV FOCAL trial (Ogilvie 2018) randomized 19,009 women to a) an intervention group (n = 9,552) that received HPV testing (participants with negative results returned at 48 months), or b) a control group (n = 9,457) who received liquid-based cytology (LBC) testing (participants with negative results returned at 24 months for LBC). Women in the control group who were negative at 24 months returned at 48 months. At 48-month exit, both groups received HPV and LBC co-testing.

The primary outcome of the trial was the cumulative incidence of CIN3+ at 48 months following randomization. The secondary outcome was the cumulative incidence of CIN2+.

The 48-month results showed a significantly lower incidence (overall and across age groups) of CIN3+ and CIN2+ in the intervention versus the control group. The CIN3+ incidence rates were 2.3/1,000 (95% CI, 1.5–3.5) and 5.5/1,000 (95% CI, 4.2–7.2) respectively, with an absolute risk difference of 3.2/1,000 and number needed to treat (NNT) of 312.

Among women with an HPV- or LBC-negative test at baseline, the cumulative incidence of CIN3+ at 48 months was significantly lower in the intervention versus the control group in all age groups (risk difference 4.03/1,000).

It should be noted that HPV was tested using Digene Hybrid Capture 2 (HC2) assay ,which tests for the presence of DNA from 13 hrHPV types. The HC2 High-Risk HPV DNA Test is not intended for use as a

screening device for Pap-normal women under age 30 and is not intended as a substitute for regular Pap screening.

Primary HPV testing in women aged ≤ 33 years previously offered HPV vaccination

Canfell and colleagues (2017) used data from the large Compass trial that compared 5-yearly HPV screening versus 2-2 yearly LBC screening among 5,006 women aged 25–64 to assess colposcopy referral and CIN2+ detection rates for HPV-screened versus cytology-screened women in Australia's HPV-vaccinated population. (Since 2007, Australia has routinely offered HPV vaccination to 12- to 13-year-old girls. By 2014, resident women ≤ 33 years had been age-eligible for HPV vaccination, with the 3-dose uptake across age cohorts about 50–77%.)

Participants were randomized in a 1:2:2 ratio to a) image-read LBC screening with HPV triage of low-grade cytology (LBC screening), b) HPV screening with those HPV16/18-positive referred to colposcopy and with LBC triage for other oncogenic types (HPV + LBC triage), or c) HPV screening with those HPV16/18-positive referred to colposcopy and with dual-stained cytology triage for other oncogenic types (HPV + DS triage).

The main outcomes of the trial were colposcopy referral and detected CIN2+ rates at baseline screening, assessed on an intention-to-treat basis after follow-up of the subgroup of triage-negative women in each arm referred to 12 months of surveillance, and after a further 6 months of follow-up for histological outcomes.

Analysis was adjusted for whether women had been age-eligible for HPV vaccination or not.

The results of the study showed that primary HPV screening was associated with significantly increased detection of high-grade precancerous cervical lesions compared to cytology in a population where high vaccine uptake was reported in women aged 33 years or younger who were offered vaccination.

Harms of hrHPV testing as a primary screening strategy to reduce the incidence of cervical cancer, compared to the currently recommended screening strategies in women

The AHRQ review (Melnikow 2018) included seven published RCTs as well as three observational cohort studies that assessed the harms and adverse events associated with hrHPV testing**.** The reviewers could only assess the harms from the initial testing as changes were made in the protocol along the course of several studies. The overall results indicate that primary hrHPV or co-testing detects more CIN3+ in a single screening round compared to cytology, and that a similar rate of CIN3+ is detected by co-testing over two screening rounds. The majority of trials that reported on this outcome showed that the rates of positive test results and referral to colposcopy were higher in the groups receiving hrHPV testing versus cytology.

In the NTCC Phase II study (Ronco 2010) all women with a positive hrHPV test were referred to colposcopy, as were those in the cytology arm who had ASC-US or LSIL+ detected. Of the women in the hrHPV arm, 7.9% tested positive compared to 3.4% of women in the cytology arm. More women in the hrHPV group underwent biopsy compared to the cytology group (3.2% vs.1.3%). The false-positive rates were 7.4 and 3.2 in the two groups, respectively.

The HPV FOCAL trial also reported a higher rate of positive hrHPV initial test results (8.2%) compared to cytology (3.6%). The referral rates for colposcopy were 8.2% and 3.6% respectively, but the rates of biopsy and false-positive results were not reported.

In the FINNISH trial (Leinonen 2012), 8% of women in the hrHPV arm and 7% in the cytology group tested positive. The referral rates for colposcopy were similar (1.2% and 1.1%), and the actual number of colposcopies and biopsies performed was not reported.

In summary:

- The overall results indicate that primary hrHPV screening detects more CIN3+ in the initial screening round compared to cytology in countries with organized screening programs and may not be applicable to countries that do not have organized screening programs.
- The hrHPV test has higher positive and false-positive rates compared to cytology. This is associated with a higher referral rate to colposcopy and, in turn, higher biopsy rates.
- The higher positive rates and referral to colposcopy were more pronounced in younger women.

- The published studies do not allow for determination of the comparative benefits and harms of primary hrHPV testing versus cytology in African American women or women in other ethnic or racial groups.
- The published studies did not have sufficient power or long-term follow-up to investigate the impact of primary hrHPV screening on reducing the incidence of cervical cancer or the related mortality.
- There is insufficient evidence to determine the optimal screening interval due to lack of direct comparison between different intervals.
- Referral to colposcopy and biopsy rates were used as surrogate outcomes for adverse effects of primary hrHPV testing.
- It is difficult to estimate the false-negative results in studies with one round of screening and short follow-up duration of negative cases.
- There is insufficient evidence to determine the outcomes of primary hrHPV testing in women vaccinated against specific types of hrHPV. As indicated earlier, the wide use of the HPV vaccine will affect the positive predictive value of cervical cancer screening tests. Only one study, conducted in Australia—which has a national, publicly funded HPV vaccination program and a high vaccination uptake among women < 33 years—suggests that primary HPV screening has a higher performance than cytology screening in settings with HPV-vaccinated populations.
- The HPV tests used in the published trials for primary testing were either not approved by the U.S. FDA or approved only for co-testing, which may limit generalization of the results. Only one study conducted in Australia on self-sampling used the cobas test approved by the FDA for primary HPV testing.

Comparative accuracy of HPV testing and cervical cytology screening for cervical cancer in women aged 21-60 years

A Cochrane systematic review (Koliopoulos 2017) examined the diagnostic accuracy of HPV testing for detecting histologically confirmed CIN2+, including adenocarcinoma in situ, in women participating in primary cervical cancer screening, and how it compares to the accuracy of cytological testing (liquid-based and conventional) at various thresholds.

The authors searched the literature through 2015 for comparative test accuracy studies in which all participants have received both HPV testing and cervical cytology followed by verification with a reference standard of combination colposcopy and histology. The analysis included a total of 40 studies with more than 140,000 women aged 20–70 years participating in a screening program. The HPV tests used in the studies were HC2 for HPV DNA testing in 27 studies, HC2+4 which tests for four additional HPV types in 20 studies (PCR in 10 studies, cobas in 2 studies, Care in 2 studies, SNIPER in 1, NASBA in 1, and Aptima in 1 study). Many of the included studies were at low risk of bias as assessed by QUAQDAS.

The authors calculated the absolute and relative sensitivities and specificities of the tests for the detection of CIN 2+ and CIN 3+ at various thresholds and computed sensitivity for each test separately.

Test comparisons were made for hybrid capture 2 (HC2) (1 pg/mL threshold) versus conventional cytology (CC) or liquid-based cytology (LBC).

Relative accuracy of the different tests for detecting **CIN2+**

HC2 versus CC

Relative sensitivity 1.52 (95% CI, 1.24–1.86); relative specificity 0.94 (95% CI, 0.92–0.96).

HC2 versus LBC

Relative sensitivity 1.18 (95% CI, 1.10–1.26); relative specificity 0.96 (95% CI, 0.95–0.97).

Relative accuracy of the different tests for detecting **CIN3+**

HC2 versus CC

Relative sensitivity 1.46 (95% CI, 1.12–1.91); relative specificity 0.95 (95% CI, 0.93–0.97).

HC2 versus LBC

Relative sensitivity 1.17 (95% CI, 1.07–1.28); relative specificity 0.96 (95% CI, 0.95–0.97).

The results did not differ by age group (younger or older than 30 years).
The authors concluded that while HPV tests are less likely to miss cases of CIN 2+ and CIN 3+, these tests do lead to more unnecessary referrals. However, a negative HPV test is more reassuring than a

negative cytological test, as the cytological test has a greater chance of being falsely negative, which could lead to delays in receiving the appropriate treatment. Evidence from prospective longitudinal studies is needed to establish the relative clinical implications of these tests.

Accuracy of human HPV testing on self-collected versus clinician-collected samples

Arbyn and colleagues (2014) performed a meta-analysis pooling the results of 36 studies with 154,556 women. Eligibility criteria for inclusion in the meta-analysis were:

- Cervical cell sample was self-collected by a woman followed by a sample taken by a clinician.
- An hrHPV test was done on the self-sample (index test) and HPV testing or cytological interpretation was done on the specimen collected by the clinician (comparator tests).
- The presence or absence of cervical intraepithelial neoplasia grade 2 (CIN2) or worse was verified by colposcopy and biopsy in all enrolled women or in women with one or more positive tests.

The outcomes of the analysis were the absolute accuracy of the index and comparator tests for finding CIN2+ or CIN3+, as well as the relative accuracy of the index versus the comparator tests.

The pooled results showed that the sensitivity and specificity of HPV testing using self-samples were lower than with clinician-taken samples:

Relative sensitivity: 0.88 (95% CI, 0.85–0.91) for CIN2+ and 0.89 (95% CI, 0.83-0.96) for CIN3+
Relative specificity: 0.96 (95% CI, 0.95–0.97) for CIN2+ and 0.6 (95% CI, 0.93-0.99) for CIN3+

While the meta-analysis had generally valid methodology and analysis, it only assessed the accuracy of the tests and did not evaluate the effect of self-sampling on the incidence of cervical cancer or precancer in a population.

Effect of HPV self-sampling on improved participation in cervical cancer screening

Several studies showed that self-collecting HPV testing improves participation in cervical cancer screening and that the majority of women who have been under-screened but who tested HPV-positive in a self-obtained sample visited a clinic for follow-up diagnosis and management.

Racey and colleagues' systematic review and meta-analysis (2013) of 10 studies showed that self-collecting HPV testing improves participation in cervical cancer screening (overall relative compliance of HPV self-collected testing versus Pap testing was 2.14 (95% CI, 1.30–3.52).

A large RCT, iPap (Sultana 2016), was conducted in Australia among 8,160 women aged 30–69 years to determine whether HPV self-sampling increases participation in cervical cancer screening by never- and under-screened (not screened in the past 5 years) women compared with a reminder letter for a Pap test.

The study used the Roche cobas 4800 test to measure the presence of HPV DNA. The primary outcome was participation, as indicated by returning a swab or undergoing a Pap test. The secondary outcome was undergoing appropriate clinical investigation for women in the self-sampling arm with a positive HPV test.

The results showed that participation was significantly higher in the self-sampling arm with 20.3% versus 6.0% for never-screened women, absolute difference 14.4% (95% CI, 12.6–16.1%, $p < 0.001$), and 11.5% versus 6.4% for under-screened women, difference 5.1% (95% CI, 3.4–6.8%, $p < 0.001$).

Of the 1,649 women who returned a swab, 45 (2.7%) were positive for HPV16/18 and 95 (5.8%) were positive for other high-risk HPV types. Within 6 months, 28 (62.2%) women positive for HPV16/18 had colposcopy as recommended and 9 (20%) had cytology only. Of women positive for other high-risk HPV types, 78 (82.1%) had a Pap test as recommended.

Overall, the published studies indicate that self-sampling for HPV increases the cervical cancer screening participation rate. However, self-sampling may potentially decrease the opportunity of direct contact between the patient and clinician. The lack of appropriate follow-up and clear instructions on interpreting a positive test result may increase patient anxiety, especially with the likelihood that many GreeHPV infections may clear spontaneously. Patient education is thus of great importance before offering women the choice between self-sampling or clinician-performed testing (Gupta 2018).

References (KPWA review)

Arbyn M, Verdoodt F, Snijders PJ, et al. Accuracy of human papillomavirus testing on self-collected versus clinician-collected samples: a meta-analysis. *Lancet Oncol*. 2014 Feb;15(2):172-183.

Canfell K, Caruana M, Gebski V, et al. Cervical screening with primary HPV testing or cytology in a population of women in which those aged 33 years or younger had previously been offered HPV vaccination: Results of the Compass pilot randomised trial. *PLoS Med*. 2017 Sep 19;14(9):e1002388.

Gupta S, Palmer C1, Bik EM, Cardenas JP, et al. Self-Sampling for Human Papillomavirus Testing: Increased Cervical Cancer Screening Participation and Incorporation in International Screening Programs. *Front Public Health.* 2018 Apr 9;6:77.

Koliopoulos G, Nyaga VN, Santesso N, et al. Cytology versus HPV testing for cervical cancer screening in the general population. *Cochrane Database Syst Rev.* 2017 Aug 10;8:CD008587. doi: 10.1002/ 14651858. CD008587.pub2.

Leinonen MK, Nieminen P, Lönnberg S, et al. Detection rates of precancerous and cancerous cervical lesions within one screening round of primary human papillomavirus DNA testing: prospective randomised trial in Finland. *BMJ*. 2012;345:e7789.

Melnikow J, Henderson JT, Burda BU, Senger CA, Durbin S, Weyrich MS. Screening for Cervical Cancer With High-Risk Human Papillomavirus Testing: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. Rockville (MD): Agency for Healthcare Research and Quality (US); 2018 Aug. Report No.: 17-05231-EF-1.

Ogilvie GS, Krajden M, van Niekerk D, et al. HPV for cervical cancer screening (HPV FOCAL): Complete Round 1 results of a randomized trial comparing HPV-based primary screening to liquid-based cytology for cervical cancer. *Int J Cancer*. 2017 Jan 15;140(2):440-448.

Ogilvie GS, van Niekerk D, Krajden M, et al. Effect of Screening With Primary Cervical HPV Testing vs Cytology Testing on High-grade Cervical Intraepithelial Neoplasia at 48 Months: The HPV FOCAL Randomized Clinical Trial. *JAMA.* 2018 Jul 3;320(1):43-52.

Racey CS, Withrow DR, Gesink D. Self-collected HPV testing improves participation in cervical cancer screening: a systematic review and meta-analysis*. Can J Public Health*. 2013 Feb 11;104(2):e159-66.

Ronco G, Giorgi-Rossi P, Carozzi F, et al; New Technologies for Cervical Cancer Screening (NTCC) Working Group. Efficacy of human papillomavirus testing for the detection of invasive cervical cancers and cervical intraepithelial neoplasia: a randomised controlled trial. *Lancet Oncol*. 2010;11(3):249-257.

Sultana F, Gertig DM, Wrede CD, et al. A pilot study to compare dry cervical sample collection with standard practice of wet cervical samples for human papillomavirus testing. *J Clin Virol.* 2015 Aug; 69:210-213.

FDA-approved HPV tests and their intended uses

Instrument (manufacturer)	Summary of the test	Test principle	Intended use
Hybrid Capture 2 High Risk HPV DNA test (Digene)	Identifies genetic DNA from HPV in cervical cells	Uses a DNA-Probe-Hybrid immunoassay technique and is used combined when a woman's Pap test results are mildly abnormal	• Detection of high-risk HPV (HR-HPV) • Follow up test when a PAP smear is mildly abnormal
Cervista HPV HR and Genfind DNA Extraction (Hologic)	Identifies DNA from 14 high-risk genital HPV types commonly associated with cervical cancer	Uses DNA-probe technology	• Determine a patient's risk for developing cervical cancer
Cervista HPV 16/18 (Hologic)	Identifies HPV types 16 and 18 in cervical samples	Uses specific DNA-probe technology and may be used in combination or as a follow-up to the Cervista HPV HR test	• Determine a patient's risk for developing cervical cancer • Used for women age 30 and over or any age with borderline cytology results to determine the need for additional follow up procedures
cobas HPV test (Roche Molecular Systems)	Used on the cobas 4800 system to identify DNA from 14 high-risk genital HPV types commonly associated with cervical cancers. Specific for HPV types 16 and 18 but also identifies other high-risk types	Uses fluorescent labeled DNA probes	• Provides information on a patient’s risk for developing cervical cancer • For women age 30 or over or women age 21 and older with borderline cellular results to assess the need for additional follow-up and diagnostic procedures
APTIMA HPV Assay (Gen-Probe)	Used with the Tigris DTS system to identify RNA from 14 high-risk genital HPV types commonly associated with cervical cancer. Detects messenger RNA from two HPV viral oncogenes, E6 and E7	Uses RNA capture and amplification of HPV RNA	• Determine a patient's risk for developing cervical cancer • Used for women age 30 and over or any age with borderline cytology results to determine the need for additional follow up procedures

Guideline Development Process and Team

Development process

The Cervical Cancer Screening Guideline was developed using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis. For details, see Evidence Summary and References.

This edition of the guideline was approved for publication by the Guideline Oversight Group in May 2019.

Team

The Cervical Cancer Screening Guideline development team included representatives from the following specialties: family medicine, gynecologic oncology, obstetrics/gynecology, pathology, and preventive care.

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Disclosure of conflict of interest

Kaiser Permanente requires that team members participating on a guideline team disclose and resolve all potential conflicts of interest that arise from financial relationships between a guideline team member or guideline team member's spouse or partner and any commercial interests or proprietary entity that provides or produces health care–related products and/or services relevant to the content of the guideline.

Team members listed above have disclosed that their participation on the Cervical Cancer Screening Guideline team includes no promotion of any commercial products or services, and that they have no relationships with commercial entities to report.