Goodbye Pap, Hello Primary HPV Testing: Navigating the New Era of Cervical Cancer

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Disclosure

I have no financial interests or relationships to disclose.

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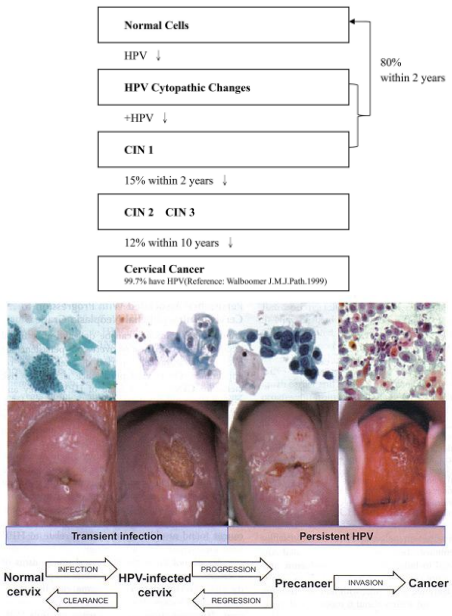
Learning Objectives

1. **Differentiate** between the three screening modalities: Primary HPV testing, Co-testing, and Cytology alone.
2. **Apply** the 2020 American Cancer Society (ACS) and updated USPSTF guidelines to determine the appropriate screening intervals for average-risk patients.
3. **Utilize** the ASCCP "Risk-Based Management" framework to determine when to "refer to colposcopy" versus "repeat in one year."
4. **Communicate** the rationale for less frequent screening to patients to alleviate anxiety regarding "missing" a cancer diagnosis.

Cervical Cancer Progression Model



AIMS

- Detect CIN 3 or higher
- Reduce morbidity from cervical cancer
- Reduce mortality from cervical cancer

The Clinical Conundrum 1

Patient: Sarah, a 31-year-old G2P2

History: No prior abnormalities; last screen 3 years ago was a "Normal" Pap (no HPV).

Today's Result: Primary HPV is **Positive** (Non-16/18). Reflex Cytology is **Negative** (NILM).

The Patient's Question: *"Wait, you found the virus that causes cancer, but you say my cells are normal? Am I sick or not? And what do we do now?"*

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The Clinical Conundrum 2

Patient: Maria, a 31-year-old G2P2

History: No prior abnormalities; last screen 3 years ago was a "Normal" Pap (no HPV).

Today's Result: Primary HPV is **Positive for HPV**16.

The Patient's Question: *"Wait, you found the virus that causes cancer? Am I sick or not? And what do we do now?"*

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The Clinical Conundrum 3

Patient: Sheila, a 57-year-old G3P3

- Establishing Care
- **History**
  - LNMP – 4 years ago
  - (+) VMS
    - Trial of Estrogen – no benefit
    - Recently had bioidentical Testosterone pellets implanted
- 8 years ago she underwent a hysterectomy for "precancer."
- She reports she has never had an abnormal pap and she has been getting "yearly evaluations for as long as she can remember."

The Patient's Question – *"Can I move to primary HPV testing instead of Pap?"*

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The New Paradigm – Primary HPV Screening

- Cytology (the Pap smear) was a 20th-century triumph, but HPV testing is the 21st-century gold standard.
  - **The Change:** Major guidelines (ACS, ACOG, ASCCP) now prefer Primary HPV testing every 5 years starting at age 25.
  - **The Rationale:** HPV testing is significantly more sensitive than cytology. A negative HPV test provides greater reassurance against CIN 3+ over the next 10 years than a negative Pap alone.
  - **The "Exit" Strategy:** Screening can typically stop at age 65 if there is a "documented adequate negative prior screening" (3 consecutive negative paps or 2 negative HPV tests within 10 years).

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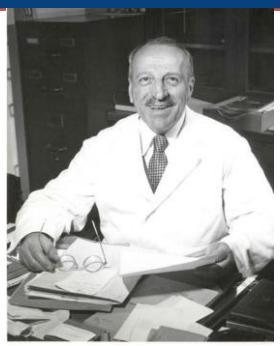
Cervical Cancer (Dysplasia) Screening

Pap Smear

First reported 1928 (technique for detecting uterine cancer using vaginal smears



Dr. Pap (1883-1962)

Initially overlooked, method gained traction following collaborative studies and publications - 1941

1950s: The test became widespread, drastically reducing mortality rates.

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Cervical Cancer (Dysplasia) Screening

Pap Smear

Pap Liquid Based Cytology

Introduced in 1996 following FDA approval of the ThinPrep System (SurePath-1999)

Standard in US by the 2010's

The method was introduced to improve upon conventional Pap smears by decreasing the number of **inadequate samples**.

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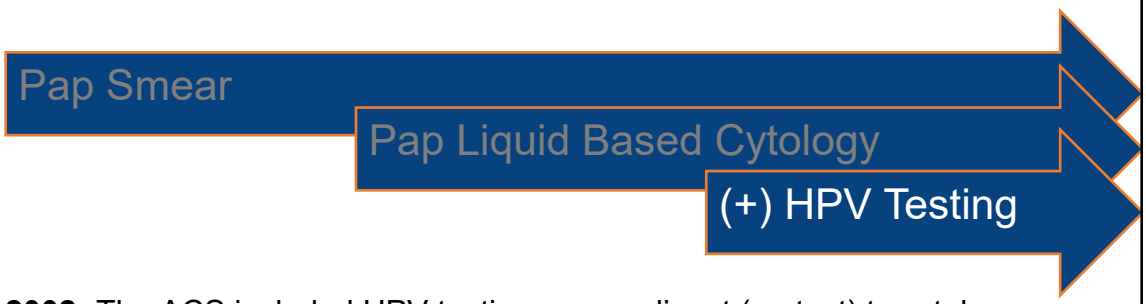
Cervical Cancer (Dysplasia) Screening



- **2002:** The ACS included HPV testing as an adjunct (co-test) to cytology for women over 30.
- **2003:** The FDA approved the Hybrid Capture II test for co-testing.
- **2012:** Updated guidelines from organizations like ASCCP strengthened recommendations for co-testing every 5 years as a preferred method.

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The New Paradigm
Primary HPV Screening

2020 (ACS)

The Change: Major guidelines (ACS, ACOG, ASCCP) now prefer Primary HPV testing every 5 years starting at age 25.

The "Exit" Strategy: Screening can typically stop at age 65 if there is a "documented adequate negative prior screening" (3 consecutive negative paps or 2 negative HPV tests within 10 years).

The Rationale: HPV testing is significantly more sensitive than cytology. A negative HPV test provides greater reassurance against CIN 3+ over the next 10 years than a negative Pap alone.

HPV testing is the 21st Century Gold Standard

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Why the Shift?

From Cytology

The "Old" Logic (1950–2020): The Pap Smear/Cytology: We looked for "bad cells" (dysplasia) under a microscope.

- The Problem: It's a snapshot in time. It tells us if disease exists today, but it's not great at predicting who will get sick tomorrow.
- The **Sensitivity** Gap: A single Pap smear can miss up to 50% of high-grade lesions.

To Virology

The "New" Logic (2026 Paradigm):

- **The HPV Test:** Look for the **cause** (the virus) rather than the **symptom** (the cell change).
- **The Predictor:** HPV testing is significantly more **sensitive**.
  - (-) High-Risk HPV, risk of developing cervical cancer in the next 5–10 years is essentially zero.
- **The Efficiency:** Because the "Negative Predictive Value" is so high, we can safely extend screening intervals to every 5 years, reducing unnecessary biopsies and patient anxiety.

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...a Long Way...

For 70 years, we played catch-up with the pap,

- trying to find abnormal cells after they already formed.

Today, we are playing defense. By testing for HPV,

- we identify the risk factor before the first abnormal cell ever appears.

We are not just finding precancer early anymore;

- we are preventing it from happening in the first place.

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ARS Question #1

A 32-year-old woman with no prior history of abnormal cervical cancer screening results presents for a wellness examination. She has been sexually active with one male partner for the past 10 years and has no significant medical history.

Which of the Following Statements Is True Regarding Screening for Cervical Cancer, Both in This Patient and in General?

A. Following a hysterectomy (including the cervix) for endometrial cancer, women should undergo yearly vaginal cytology for 20 years.
B. Current guidelines include cytology every 5 years as one screening option, beginning at age 21.
C. Current guidelines recommend stopping screening at age 75
D. The American Cancer Society recommends primary HPV testing every 5 years beginning at age 25.

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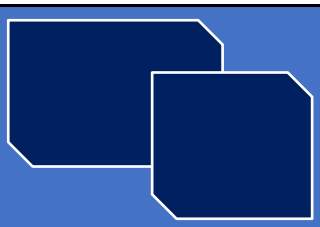

- Cytology with Reflex HPV
- Cotesting
  - ❑ provides increased sensitivity and long-term negative predictive value of high-grade CIN and cervical cancer (CIN 3 or greater [CIN3+]) compared with cytology alone.
  - ❑ HPV testing is not recommended for individuals younger than 25 years because transient HPV infections are common in this group and rarely contribute to carcinogenic outcomes.
- Primary HPV Screening

Cervical Cancer Screening Tests

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Primary HPV Screening

- Clinician-collected primary HPV screening obtains a cervical cytology sample, which can first be tested for HPV.
- Depending on the testing method screening test reports positive based on the detection of high-risk type HPV messenger RNA E6/E7 proteins or DNA

Diagnostic Accuracy for Detection of Cervical Precancer (CIN2+) of Clinician-Collected Cervical Cytology, HPV Testing Based on Clinician-Collected Cervical Specimens (Clinician HPV), and HPV Testing Using Self-Collected Vaginal Specimens (Self-HPV)		
	Pooled Sensitivity	**Pooled Specificity**
Cytology	80.4 (95% CI = 73.2-86.1)	78.5 (95% CI 69.8-85.2)
Clinician–HPV (PCR)	92.9 (95%CI = 88.6-95.5)	61.2 (95% CI = 41.2-78.1)

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Not statistically significant

Primary HPV Screening

- Clinician-collected primary HPV screening obtains a cervical cytology sample, which can first be tested for HPV.
- Depending on the testing method screening test reports positive based on the detection of high-risk type HPV messenger RNA E6/E7 proteins or DNA

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	Pooled Sensitivity	**Pooled Specificity**
Cytology	80.4 (95% CI = 73.2-86.1)	78.5 (95% CI 69.8-85.2
Self-HPV (PCR)	89.7 (95%CI 84.2-93.5)	64.7 (95% CI 44.6-80.7)
Clinician–HPV (PCR)	92.9 (95%CI = 88.6-95.5)	61.2 (95% CI = 41.2-78.1)

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Screening for Cervical Cancer*
Comparison of Screening Guidelines for Individuals as Average Risk for Cervical Cancer

Age	2024 USPSTF *(draft recommendation)*	2020 ACS and 2026 Update
< 21 years	Recommends against screening	No screening is recommended
21-24 years	Cytology alone every 3 years	No screening is recommended
25-29 years	Cytology alone every 3 years	• Primary HPV testing every 5 years with clinician-collected sample or every 3 years with self-collected sample • Cotesting* every 5 years or cytology alone every 3 years are acceptable options if primary HPV screening is limited or not available
30-65 years	• Primary HPV screening every **5 years with clinician- or patient-collected sample** • Cotesting* every 5 years or cytology alone every 3 years is an alternative to primary HPV screening	• Primary HPV screening every **5 years** with clinician-collected sample **or** every **3 years** with self-collected sample • Cotesting* every 5 years or cytology alone every 3 years is acceptable if primary HPV testing is limited or not available
> 65 Years	Recommends against screening in those who have had adequate screening and are not otherwise at high risk for cervical cancer	• **Discontinue** screening if negative primary HPV screening **(preferred)** or negative cotesting (acceptable) at 60 and 65 years of age, or three consecutive negative cytology tests performed at the recommended screening interval with last test at age 65 years (acceptable) • Self-collected primary HPV vaginal specimens should follow **3-year testing interv**al
***After* hysterectomy**	Recommends **against** screening after hysterectomy with removal of the cervix and no history of CIN2+ or cervical cancer	Individuals without a cervix and without a history of CIN2+ in the past 25 years or any history of cervical cancer should not be screened.

**Recommendations apply to all women regardless of sexual activity status.*

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US Health Resources and Services Administration
January 2026

Approved Update Guidelines from the Women's Preventive Services Initiative

- *Designate high-risk HPV testing as the preferred screening modality for women at **average risk who are 30-65 years of age***

Result

- *Private Insurance Companies are REQUIRED to cover this preventive service WITHOUT cost-sharing by 1 January 2027*

Update to the Women's Preventive Services Guidelines

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Self-Collected Vaginal Specimens for HPV Testing: Recommendations from the Enduring Consensus Cervical Cancer Screening and Management Guidelines Committee (2025)

	Recommendation
# 1	Clinician-collected cervical specimens are preferred, and self-collected vaginal specimens are acceptable for cervical cancer screening
# 2	When self-collected vaginal specimens are HPV-negative in the screening setting, repeat testing in **3 years** is recommended
# 3	When self-collected vaginal specimens are positive for HPV 16 and/or 18, direct referral for colposcopy with concurrent cytology collection is recommended
# 4	When self-collected vaginal specimen HPV test results are: a) positive for HPV (untyped), b) negative for HPV 16/18 and positive for HPV HR12 (other); or c) negative for HPV 16/18 and positive for HPV 45, 33/58, 31, 52, 35/39/68, 51 or combinations thereof, obtaining a clinician collected cervical specimen for cytology or dual stain is recommended. Subsequent management of cytology or dual-stain results per management guidelines is recommended

Wentzensen N, Massad LS, Clarke MA, Garcia F, Smith R, Murphy J, Guido R, Reyes A, Phillips S, Berman N, Quinlan J, Lind E, Perkins RB; Enduring Consensus Cervical Cancer Screening and Management Guidelines Committee. Self-Collected Vaginal Specimens for HPV Testing: Recommendations From the Enduring Consensus Cervical Cancer Screening and Management Guidelines Committee. J Low Genit Tract Dis. 2025 Apr 1;29(2):144-152. doi: 10.1097/LGT.0000000000000885. Epub 2025 Feb 21. PMID: 39982254; PMCID: PMC11939108.

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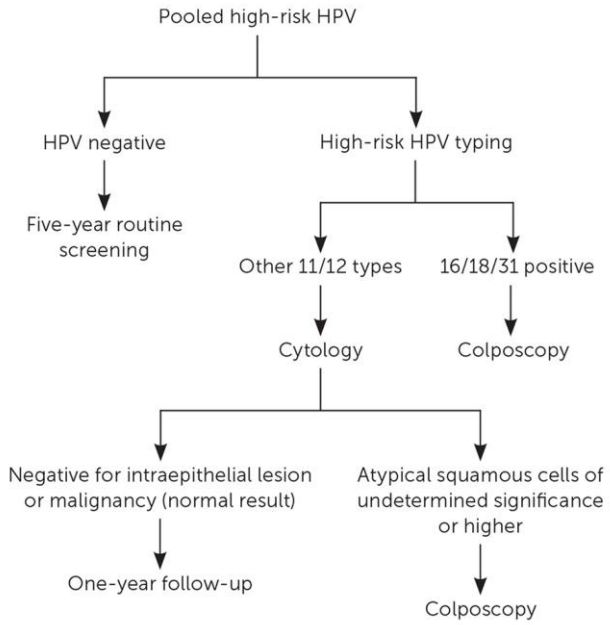
Management

Harper DM, Bettcher CM, Young AP. It Is Time to Switch to Primary HPV Screening for Cervical Cancer. Am Fam Physician. 2024 Jan;109(1):8-9. PMID: 38227863.

Risk Management of Primary HPV Screening Results Using Genotyping Triage (Preferred)



HPV = human papillomavirus.

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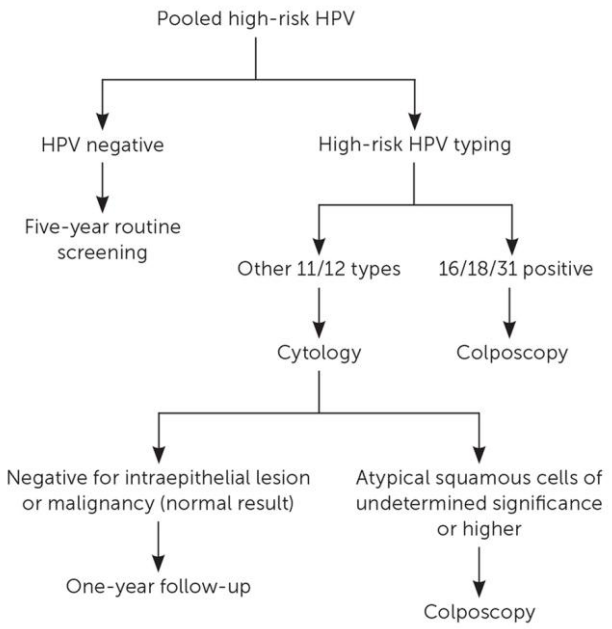
Risk Management of Primary HPV Screening Results When Genotyping Is **Unavailable**



HPV = human papillomavirus.

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Important Considerations

Individual Risk Factors: These are general guidelines. Individual risk factors (e.g., history of abnormal results, HPV infection, weakened immune system, DES exposure) may warrant more frequent screening.

Vaccination Status: Current guidelines recommend following age-based screening recommendations regardless of HPV vaccination

NO Screening

- Women greater than 65 with a history of regular normal results
- After hysterectomy for any condition OTHER THAN Cervical cancer

Don't screen with Pap cytology if under 21 years of age and pap cytology or HPV testing if over 69 years of age

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1 in 4

eligible women are not up to date with cervical cancer screening in the United States.

60%

Roughly 60%

of cervical cancer cases occur in unscreened or under-screened women, many of whom face barriers to accessing healthcare.

FEAR, ANXIETY, EMBARRASSMENT, LACK OF ACCESS, SOCIAL AND PSYCHOLOGICAL BARRIERS

may limit access

to cervical cancer screening for many women.

CDC National Health Interview Survey (NHIS) 2023; Smith et al., J Clin Epidemiol. 2021; and CDC/NIH Behavioral Risk Factor Surveillance System on screening barriers.

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Primary HPV Testing
Bottom Line

- Primary HPV screening has been thoroughly tested in 13 population-based randomized controlled trials over 15 years of follow-up.
- All trials found that primary HPV screening is as effective at detecting incident CIN 3+ as cotesting, with fewer harms.

Screening for Cervical Cancer

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AVAILABLE HPV TESTS

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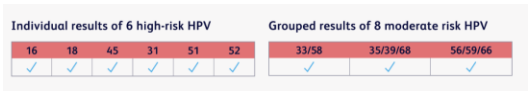
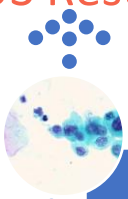
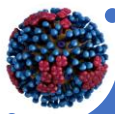
HPV Tests FDA Approved for - ☑HPV Primary Screening, ☑ Co-Testing, and ☑ Reflex Testing for ASC-US Results

Provides individual, specific results for **HPV 16, HPV 18, and HPV 45,** while grouping the remaining 11 genotypes.





Abbot Alinity m High Risk HPV Assay



BD Onclarity HPV Assay

Roche cobas HPV Assay

All three are available from the two most common Pap vials used by labs in the US -

- *BD SurePath Liquid-based Pap Test*
- *Hologic ThinPrep Pap Test*

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Primary HPV Screening Tests Approved by the U.S. Food and Drug Administration (FDA)

Primary HPV Screening Tests

Indication*	Test name	Manufacturer	Results
Primary HPV testing	Cobas HPV	Roche	Pooled 14 high-risk HPV: positive/negative Genotype specific: 16, 18, and type group (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68)
Primary HPV testing	BD HPV Onclarity	BD	Pooled 14 high-risk HPV: positive/negative Genotype specific: 16, 18, 31, 45, 51, 52, and type groups (33/58), (35/39/68), (56/59/66)
Triage after ASCUS cytology or cotesting with cytology	Cervista HPV HR	Hologic Gen-Probe	Positive, negative, indeterminate
Triage after ASCUS cytology or cotesting with cytology where the Cervista HPV HR test was used as the triage test	Cervista HPV 16/18	Hologic Gen-Probe	Positive for genotype, negative, indeterminate
Triage after ASCUS cytology	Aptima HPV	Hologic Gen-Probe	Positive, negative, invalid
Triage after ASCUS cytology or cotesting with cytology where the Aptima HPV HR test was used as the triage test	Aptima HPV 16 18/45	Hologic Gen-Probe	Positive for genotype, negative, invalid
Reflex triage after ASCUS cytology	Digene Hybrid Capture 2 HPV DNA	Qiagen	Positive/negative

ASCUS = atypical squamous cells of undetermined significance; HPV = human papillomavirus.

*—Approved by the U.S. Food and Drug Administration.

Harper DM, Bettcher CM, Young AP. It Is Time to Switch to Primary HPV Screening for Cervical Cancer. Am Fam Physician. 2024 Jan;109(1):8-9. PMID: 38227863.

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What Can We Say?

Although primary HPV screening is as effective as cotesting at detecting cervical cancer, primary HPV screening decreases the number of lifetime screenings needed.

USPSTF has modeled different screening strategies, defining harms as the lifetime number of tests, colposcopies, false-positive results, cervical cancer cases, and cervical cancer deaths.

- *Benefits were defined as life-years gained, disease detected, and cancer averted.*

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Lifetime Screening Outcomes for Three Cervical Cancer Screening Strategies per 1,000 Women

Strategy	Cytology tests	HPV tests	Total tests*	Colposcopies	Total tests/ CIN3+	Colposcopies/ CIN3+	Total workup/ CIN3+
Cyto-3y,21/ COTEST-5y,30	11,425	8,380	19,806	1,630	366.8	30.2	397
Cyto-3y,21/ HPV-5y(16/18),30	3,675	8,476	12,151	1,635	229.3	30.8	260
Cyto-3y,21/ HPV-5y(cyto),30	3,888	8,459	12,348	1,452	233.0	27.4	260

CIN 3+ = cervical intraepithelial neoplasia grade 3 (invasive squamous cell carcinoma, invasive adenocarcinoma, invasive adenosquamous carcinoma); cyto = cytology test; HPV = human papillomavirus; y = years of age.

*—Total number of cytology tests, HPV tests, and colposcopies performed to find CIN 3+.

Information from Kim JJ, Burger EA, Regan C, Sy S. Screening for cervical cancer in primary care: a decision analysis for the US Preventive Services Task Force. JAMA. 2018;320(7):706-714.

- Modeling the screening strategy of cervical cytology alone every three years for women 21 to 29 years of age, followed by cotesting every five years for women 30 to 65 years of age, led to the highest number of lifetime cytology tests per 1,000 women.
- **For the individual, primary HPV screening provides equally accurate disease detection with fewer tests.**

Harper DM, Bettcher CM, Young AP. It Is Time to Switch to Primary HPV Screening for Cervical Cancer. Am Fam Physician. 2024 Jan;109(1):8-9. PMID: 38227863.

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Primary HPV Testing

- 2020's

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Screening for Cervical Cancer

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Collection/Tests

e.g., Quest Diagnostics

Collection Is Exactly How You Have ALWAYS Done It

Test Code 14264	**HPV DNA (16, 18, Other High Risk), PCR, Cervical** This test is used for the detection of high-risk Human Papillomavirus in clinician-collected cervical samples and can be used as part of an HPV primary screening algorithm. The test detects high-risk HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68, which are reported out as HPV 16, HPV 18, and other high-risk HPV types which includes, but does not differentiate, the remaining 12 high-risk types. Interim guidance ...
Test Code 93296	**HPV DNA (16,18, Other High Risk), PCR with Reflex to ThinPrep® Automated Pap**
Test Code 14263	**HPV DNA (16, 18, Other High Risk), PCR, Vaginal Self-Collected** This test is used for the detection of high-risk Human Papillomavirus in self-collected vaginal samples and can be used as part of an HPV primary screening algorithm. The test detects high-risk HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68, which are reported out as HPV 16, HPV 18, and other high-risk HPV types which includes, but does not differentiate, the remaining 12 high- risk types. Interim ...

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Primary HPV Testing
Effective Screening Modality for Cervical Cancer in Average-Risk Women

Risk Stratification Options for Cervical Cancer Screenings	
Population	**Recommendation**
Low risk Hysterectomy including the cervix (exception cervical cancer; HGSIL) Cervix with comorbidities and decreased life expectancy	No testing
Average risk Patients (25 or) 30 to 65 years of age with a cervix	Primary HPV testing
High risk*	
Patients 30-65 years of age AND a high-risk condition (i.e., solid organ transplantation, chronic diseases marked by Janus kinase inhibitors or biologics, immunosuppressive drug treatment, HIV/AIDS postcoital bleeding, or under surveillance for prior HPV+ testing per ASCCP guidelines)	Cytology + HPV testing
** - High risk is NOT defined by smoking status, drug use, # of sex partners, or age.*	

Harper DM, Bettcher CM, Young AP. It Is Time to Switch to Primary HPV Screening for Cervical Cancer. Am Fam Physician. 2024 Jan;109(1):8-9. PMID: 38227863.

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INTEGRATION OF DUAL-STAIN BIOMARKERS EXTENDED HPV GENOTYPING

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Dual-Stain Biomarkers Robust Marker of CIN 3+

- Early 2024 – formal recognition of dual-stain cytology as an important tool for triaging HPV positive cervical cancer screening results.
- Guidelines include dual stain testing as an option in BOTH HPV primary screening and co-testing pathways.

Technology detects the simultaneous presence of p16 and Ki-67 biomarkers in a single cell, which is a strong indicator of an HPV infection ***progressing to precancer****.*

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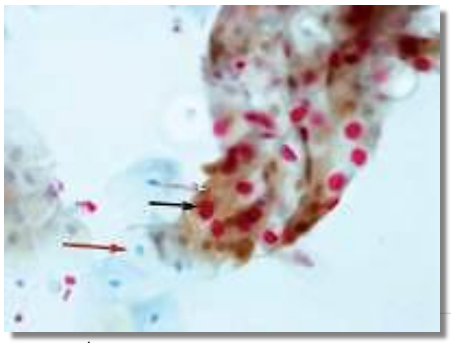
HPV Genotyping and p16/Ki-67 Test Significantly Improve Detection Rate of High-Grade Cervical Squamous Intraepithelial Lesion

Mechanism: Identifies the simultaneous expression of p16 (cell cycle arrest) and Ki-67 (cell proliferation) within a single cell—**a hallmark of HPV-mediated oncogenic transformation.**

Clinical Utility: For patients who are **hrHPV (+)** but have **Normal Cytology**, a positive Dual Stain can "up-triage" them to immediate colposcopy rather than waiting 12 months, as it is more specific for high-grade lesions.



- *Brown cytoplasmic chromogen corresponds to p16 overload (white arrow)*
- *Nuclear compartment red chromogen is a proof of high Ki-67 protein accumulation and proliferative activity (black arrow)*
- *Red arrow depicts unaffected cell (case of HPV multi-infection), magnification 40×*

DOI: 10.5114/aoms.2018.80697
Arch Med Sci 2020;16(1):87-93
With permission

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Aim of Dual-Stain Integration

- Improve early diagnosis of HPV-positive cervical precancer and cancer
- Potentially reduce the number of women diagnosed with cervical cancer
- Require fewer colposcopies compared to cytology alone for HPV+ women
- Allow clinicians to better differentiate between HPV infections that may resolve on their own and those that require intervention

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2024 ASCCP Enduring Risk-Based Management Guidelines Aim to Integrate New Technologies and Approaches that Improve Cancer Prevention for High-Risk Individuals and Decrease Unnecessary Procedures in Lower-Risk Individuals

Extended Genotyping

- Defined as the identification of individual types or groups of types beyond just HPV 16, 18 and 45. The new 2024 guidelines include HPV genotyping beyond HPV 16/18, to include management recommendations for HPV 31, 45, 33/58, 52, 35/39/68, 51 and 59/56/66.
- Provides a greater and more refined level of risk stratification than pooled HPV-positive results to more precisely determine patient management.
- HPV persistence (repeated detection of the same HPV type) is associated with a higher risk of cervical precancer compared to a single time point detection.
- Unnecessary procedures can be safely decreased in lower-risk individuals who test positive for HPV 56/59/66

file:///Users/davidweismiller/Downloads/Enduring%20Guidelines%20Extended%20Genotyping%20Summary%20032224%20(2).pdf

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Our Patients

Triage with cytology or dual stain (DS) is recommended.
If DS **(-)** or NILM cytology, repeat testing in 1 year
If DS **(+)** or cytology ≥ASC-US, colposcopy recommended.

In a primary HPV or co-testing setting patients positive for HPV 45, 33/58, 31,52, 35/39/68, 51 or combination thereof, but negative for HPV16 and HPV 18.

In a co-testing setting patients positive for 56/59/66 and no other carcinogenic types.

NILM: recommendation remains 1-year return
ASC-US and LSIL: 1 year return **instead of colposcopy.**
ASC-H, AGC, HSIL – remains colposcopy

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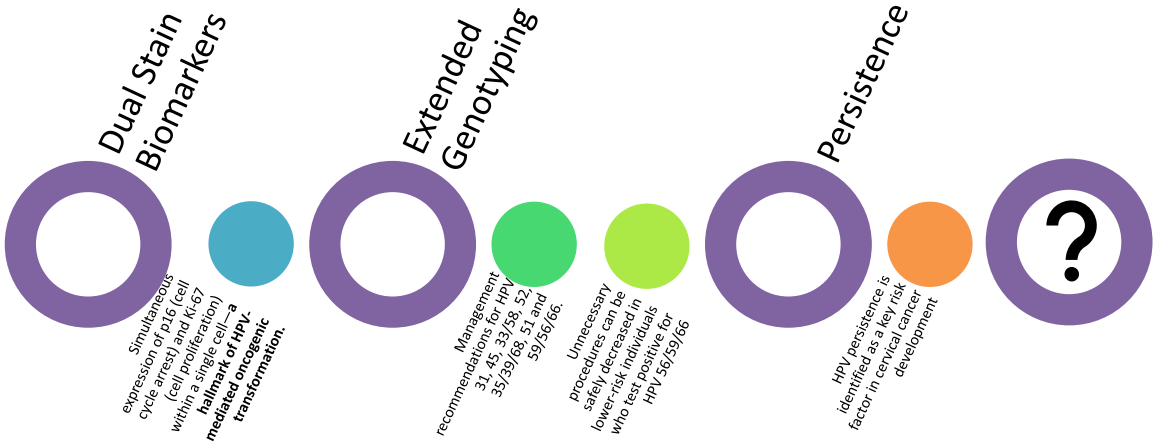
Primary HPV Testing

Refines Patient Risk Stratification and Advances the Way in Which We Screen for Cervical Cancer.



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DEVELOP A FRAMEWORK FOR IMPLEMENTING PRIMARY HPV TESTING IN CLINICAL PRACTICE, INCLUDING PATIENT EDUCATION AND FOLLOW-UP STRATEGIES

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ARS Question #2

Regarding Self-collection of Vaginal Samples for HPV Testing in Cervical Cancer Screening, Which of the Following Statements Is True?

A. Self-sampling has the potential to decrease the number of women who complete cervical cancer screening.
B. Vaginal self-sampling has demonstrated slightly inferior sensitivity compared to clinician-collected cervical os sampling for HPV detection.
C. Self-collection for HPV testing is currently only FDA approved for use both in a health care setting and at home.
D. The vaginal self sampling approach for HPV is more effective at detecting HPV than a first void urine.

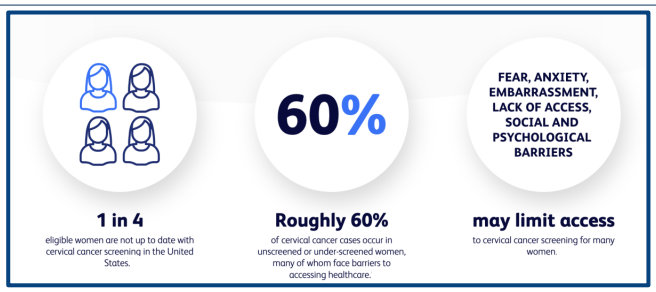
New Screening Landscape

"The cervical cancer screening landscape is rapidly changing. The use of vaginal samples, self-collected in a healthcare setting, marks a significant milestone in our joint efforts to improve accessibility and equity in healthcare."

Self-Collection

- Self-sampling is reasonable because HPV is transmitted skin-to-skin and must travel through the vagina before reaching the cervix.
- Two self-sampling approaches have been found to be effective.
  - Vaginal approach uses a device similar to a thin tampon that the patient inserts into the vagina, turns several times, places in a transport tube (some with liquid media), and returns.
  - Urine approach is similar to collection for sexually transmitted infection testing by gathering the desquamated cells coming from the cervix, vagina, and external genitalia in the first part of the urine stream.
- **Both techniques** are noninferior to clinician sampling at the os.

45



- Self-collection can improve cervical cancer screening access, especially in underserved populations.
  - In the US, Black, Hispanic and American Indian women have higher rates of cervical cancer than women of other racial groups; Black women having the highest rate of death.
- With vaginal self-collection as an option, women are more inclined to participate in such care, allowing health care providers an alternative option to identify a high-risk HPV infection in more convenient care settings.

CDC National Health Interview Survey (NHIS) 2023; Smith et al., J Clin Epidemiol. 2021; and CDC/NIH Behavioral Risk Factor Surveillance System on screening barriers.

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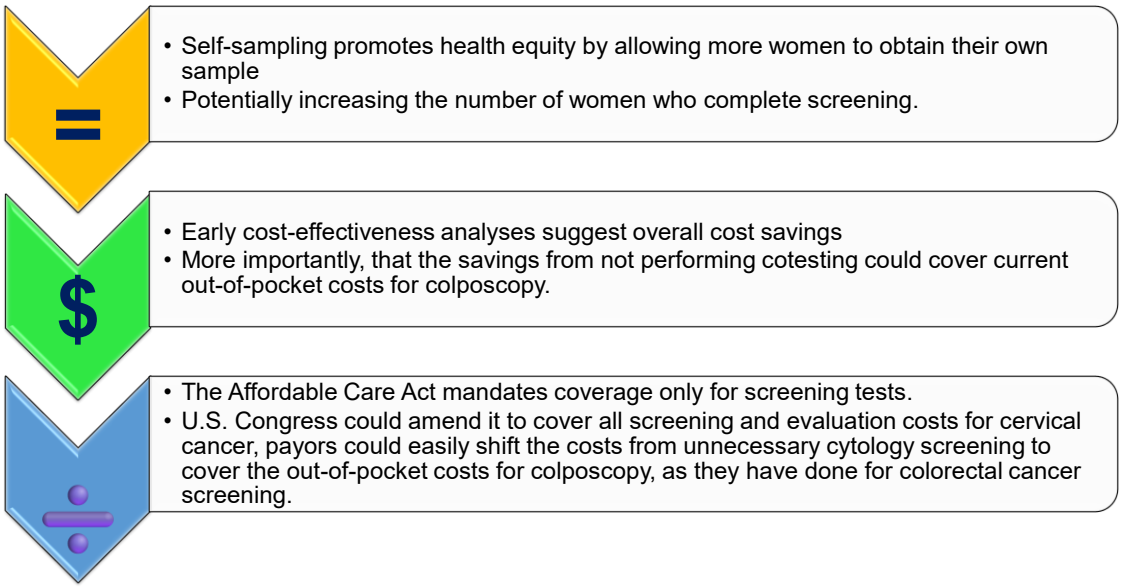
Benefits to Self-Collection



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The STEP Randomized Clinical Trial (2026 Analysis)

- New economic and longitudinal data from the **STEP trial** (Self-Testing options in the Era for Primary HPV screening) was published in early 2026.
- **Key Finding**
  - Directly mailing HPV kits to overdue individuals **increased screening rates by over 14%.**
  - Analysis confirmed this approach is not only cost-effective but **cost-saving** compared to traditional office-based Pap cytology.

Economic Analysis of Mailed Primary HPV Self-Testing Kits in a Large Integrated Health System. **JAMA Network Open (March 2026).**

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Primary HPV Screening Tests Approved by the FDA

Test (year approved)	Genotyping	Approved for Self Collection
Roche cobas HPV test (2014)	HPV 16 and 18 Detects 12 other high-risk HPV types: 31/33/35/39/45/ 51/52/56/58/59/66/68 (pooled results)	Yes, using Evalyn brush, Copan 522C.80 swab (FLOQSwab), or Teal Wand
BD Onclarity HPV Assay (2018)	HPV 16, 18, and 45 Detects 11 other high-risk HPV types: 31, 51, 52, 33/58, 35/39/68, and 56/59/66 (pooled results)	Yes, using Copan 522C.80 swab
Abbott Alinity m High Risk HPV Assay (2023)	HPV 16, 18, and 45 genotyping not provided but can be added as additional testing; 11 others can also be added: 31/33/52/58 and 35/39/51/56/59/66/68	Yes, using simpli-COLLECT HPV Collection Kit or Evalyn brush

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Primary HPV Screening Tests Approved by the FDA

Test (year approved)
Roche cobas HPV test (2014) Evalyn brush, Copan 522C.80 swab (FLOQSwab), or Teal Wand
BD Onclarity HPV Assay (2018) Copan 522C.80 swab
Abbott Alinity m High Risk HPV Assay (2023) simpli-COLLECT HPV Collection Kit or Evalyn brush

Evalyn Brush

Copan 522C.80 Swab

Teal Wand

Simpli-COLLECT HPV

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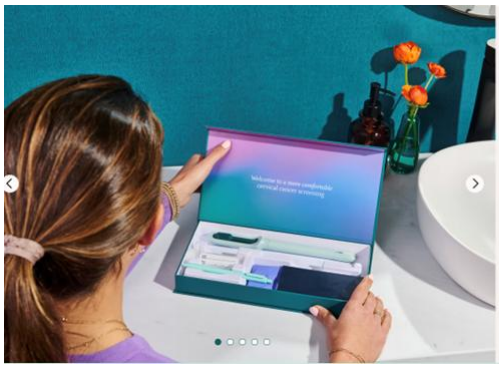

Teal Wand

Clinical Sensitivity – 96% (Equal) to That of Clinician Collection

F.D.A. Approves First At-Home Alternative to the Pap Smear

The tool will allow women to screen for HPV, which causes almost all cases of cervical cancer, without visiting a doctor.

Wall Street Journal May 9, 2025

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ACS – 2025 Teal Wand

American Cancer Society Includes Teal's At-Home Self-Collection for Primary HPV Testing in New Cervical Cancer Screening Guidelines

December 4, 2025

(2026), Screening for cervical cancer. CA Cancer J Clin, 76: e70049. https://doi.org/10.3322/caac.70049

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Teal Health

Patients will label a vial with the sample in it, and then mail it out for processing.

After a sample is collected, the swab is detached from the wand and returned in the vial.

- Allow patients to order the test online, speak with a telehealth provider, collect a sample and then mail it to be tested for HPV.
- Company is working with insurers to secure coverage and with donors to try to subsidize the cost for people without insurance.
- If the test is positive, the patient will be referred to an in-person provider for a cytologic sampling or colposcopy.
  - Teal plans to mail an initial round of tests to customers in California in June before expanding to other states.

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HPV DNA (16, 18, Other High Risk), PCR, Vaginal Self-Collected

Test Code

14263

CPT Code(s)*

87626

Test Details

Methodology

Polymerase Chain Reaction (PCR)

Reference Range(s)

HPV 16	Not Detected
HPV 18	Not Detected
HPV Other	Not Detected

Alternative Name(s)

Primary Screening,HPV alone,HPV Vaginal Collection,HPV self-collect

Preferred Specimen(s)

1 ThinPrep® vial sample collected with COPAN FLOQSwab 552C.RM

Alternative Specimen(s)

1 ThinPrep vial sample collected with Evalyn Brush

Minimum Volume

1.5 mL

Collection Instructions

Patient should follow instructions provided with the self-collection device.

The collection device should be immediately transferred to ThinPrep following provided instructions.

Transport Container

ThinPrep® vial

Transport Temperature

Room temperature

e.g., **Quest Diagnostics**

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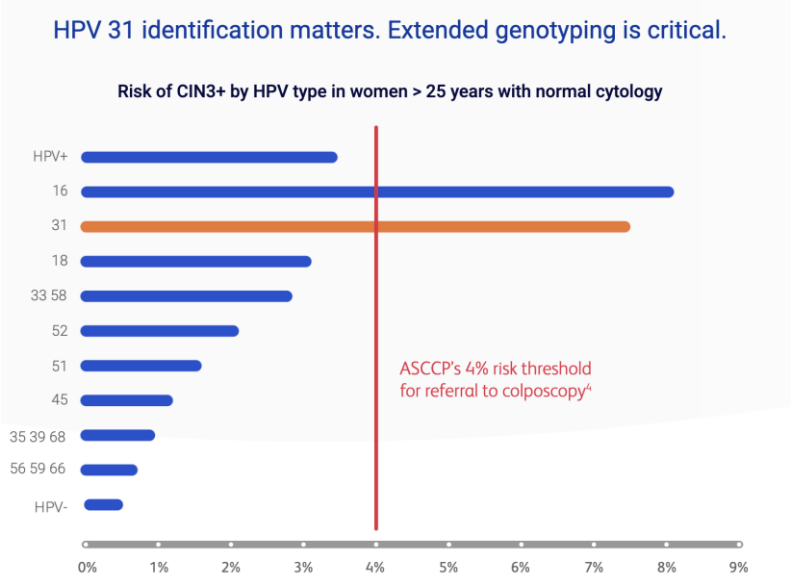
HPV 31 POSES A HIGHER RISK FOR CERVICAL PRECANCER AS COMPARED TO HPV 18



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LIVING GUIDELINES

*The 2025–2026 management landscape for **Primary HPV testing** has shifted from "test results" to **individualized risk-based triage**. The core principle is "Equal Risk, Equal Management," where a patient's prior history now carries as much weight as their current HPV status.*

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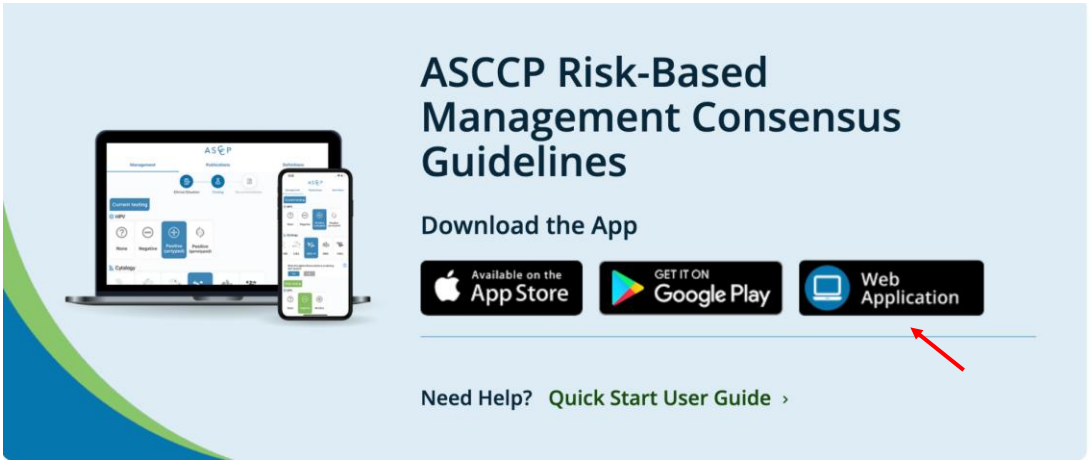

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ASCCP Living Guidelines (Risk-Based Management)

We no longer treat the result; we treat the risk -

- **What are "Living" Guidelines?** The ASCCP moved to a web-based/app-based model because the data is updated in real-time. It uses the "Equal Management for Equal Risk" principle.
- **The 4% Threshold:** If a patient's 5-year risk of CIN 3+ is < 4%, we can usually follow up in 1, 3, or 5 years. If the risk is ≥ 4%, a Colposcopy is recommended.
- **Why it Matters:** Prevents over-treatment in low-risk patients (like young women with transient HPV) while catching high-risk patients who might have had a "negative" Pap but carry HPV 16 or 18.
- **History is important** – it is ideal to have 10 years, 5 years works.

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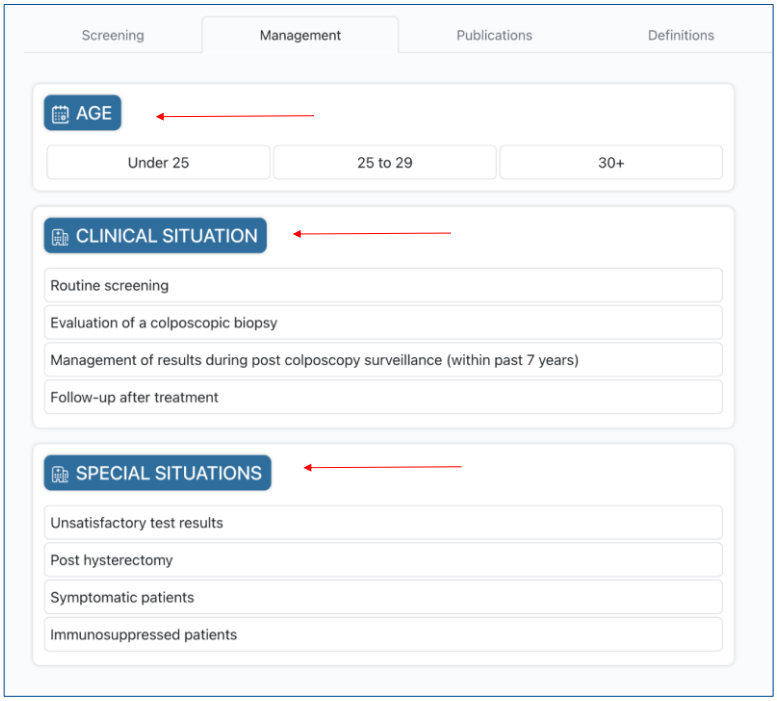
Application



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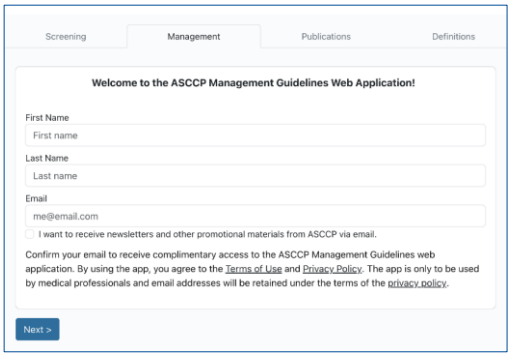
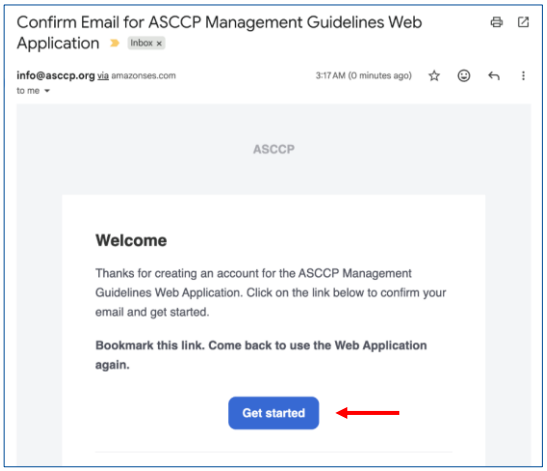
Web Application





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The "Treat" Threshold

- When do we skip the biopsy and go straight to the LEEP?
  - **Expedited Treatment (See-and-Treat)**: If the immediate risk of CIN 3+ is >25% (e.g., HPV 16 positive with HSIL cytology), the guidelines now allow for moving directly to treatment (LEEP) without a biopsy first, especially in patients over 25 who have completed childbearing.
  - **The Goal**: Reduce the "loss to follow-up" an

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Summary of Management for Positive HPV Screening Test Results with Self-collected and Clinician-collected Specimens for Settings Using Cytology (Either as a Cotest or Triage Test)

ASCCP

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HPV test result	Management of clinician- vs. self-collected collected specimens	Current HPV test result	Current cytology result	Past history	Management
HPV 16/18	Clinician-collected: Laboratory performs cotest or reflex cytology. Self-collected: Colposcopy recommended. Collect cytology at colposcopy.	16	HSIL	Noncontributory	Treatment preferred; colposcopy acceptable
		16	ASC-H	Noncontributory	Treatment or colposcopy
		16	NILM, ASC-US, LSIL, AGC, or no cytology	Noncontributory	Colposcopy[1]
		18	HSIL	Noncontributory	Treatment or colposcopy
		18	NILM, ASC-US, LSIL, ASC-H, AGC, or no cytology	Noncontributory	Colposcopy[1,2]
HPV 45, 33/58, 31, 52, 35/39/68, 51 Untyped or "other" types when 16 and 18 are not present	Clinician-collected: Laboratory performs cotest or reflex cytology. Self-collected: Patient returns for collection of cytology unless current test is 2nd consecutive HPV+ in which case colposcopy recommended.	45, 33/58, 31, 52, 35/39/68, 51 or untyped/other	HSIL, ASC-H, AGC	Noncontributory	Colposcopy[1,2]
		45, 33/58, 31, 52, 35/39/68, 51	ASC-US, LSIL	Noncontributory	Colposcopy
		Other/untyped	ASC-US, LSIL	Documented HPV negative screen in past 5 years or colposcopy <CIN2 within past 1 year	Repeat HPV test in 1 year
		Other/untyped	ASC-US, LSIL	Any history other than above	Colposcopy
		45, 33/58, 31, 52, 35/39/68, 51 or untyped/other	NILM	Normal[3] or colposcopy <CIN2 within past 1 year	Repeat HPV test in 1 year
		45, 33/58, 31, 52, 35/39/68, 51 or untyped/other	Not available	HPV+ without colposcopy (i.e. current test is 2nd consecutive HPV+)	Colposcopy
HPV 59/56/66	Clinician- collected: No additional immediate testing needed. Laboratory may run cytology if cotesting is performed.[4] Self-collected: No additional immediate testing needed	59/56/66	ASC-H, AGC, or HSIL	Noncontributory	Colposcopy[1,2]
		59/56/66	No cytology or NILM, ASC-US, LSIL	Normal or colposcopy <CIN2 within past 1 year	Repeat HPV test in 1 year
		59/56/66	Not available	HPV+ without colposcopy (i.e., current test is 2nd consecutive HPV+)	Colposcopy

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Summary of Management for Positive HPV Screening Results with Self-collected and Clinician-collected Specimens for Settings Using Reflex Testing with p16ink4a/Ki-67 Dual Stain

ASCCP

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HPV test result	Management of clinician- vs. self-collected collected specimens	Current HPV result	Current dual stain result	Past history	Management
HPV 16/18	Clinician- and self-collected: same management	16 and/or 18	Noncontributory	Noncontributory	Colposcopy *with collection of cytology if available*
HPV 45, 33/58, 31, 52, 35/39/68, 51 or untyped	Clinician-collected: Laboratory performs reflex dual stain. Self-collected: Patient returns for collection of dual stain.	45, 33/58, 31, 52, 35/39/68, 51 or untyped	Dual stain negative[1]	Normal[2] or colposcopy <CIN2 within past 1 year	Repeat HPV test in 1 year
		45, 33/58, 31, 52, 35/39/68, 51 or untyped	Dual stain positive[3]	Noncontributory	Colposcopy
		45, 33/58, 31, 52, 35/39/68, 51 or untyped	Noncontributory	HPV+ without colposcopy (i.e., current test is 2nd consecutive HPV+)	Colposcopy
HPV 59/56/66	Clinician- and self-collected: same management	59/56/66	Noncontributory	Normal[2] or colposcopy <CIN2 within past 1 year	Repeat HPV test in 1 year[1]
		59/56/66	Noncontributory	HPV+ without colposcopy (i.e., current test is 2nd consecutive HPV+)	Colposcopy

Wentzensen N, Massad LS, Clarke MA, Garcia F, Smith R, Murphy J, Guido R, Reyes A, Phillips S, Berman N, Quinlan J, Lind E, Perkins RB; Enduring Consensus Cervical Cancer Screening and Management Guidelines Committee. Self-Collected Vaginal Specimens for HPV Testing: Recommendations From the Enduring Consensus Cervical Cancer Screening and Management Guidelines Committee. J Low Genit Tract Dis. 2025 Apr 1;29(2):144-152. doi: 10.1097/LGT.0000000000000885. Epub 2025 Feb 21. PMID: 39982254; PMCID: PMC11939108.

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Key 2026 Action Thresholds

Management decisions are now mathematically guided by "Immediate Risk" of CIN3+:	
Risk	Management
≥ 60%	Expedited treatment (LEEP) is preferred.
25-59%	Expedited treatment or colposcopy is acceptable.
4.1-24%	Colposcopy is required
0.15-4%	1-year follow-up.
< 0.15%	Return to 5-year screening.

*These thresholds are calculated dynamically via the **ASCCP Management Guidelines App**, which was updated in January 2026 to include longitudinal data from over 1 million patients in the Kaiser Permanente-Northern California cohort.*

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RETURN TO OUR CASES

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The Clinical Conundrum
Question 3

Patient: Sarah, a 31-year-old G2P2

History: No prior abnormalities; last screen 3 years ago was a "Normal" Pap (no HPV).

Today's Result: Primary HPV is **Positive** (Non-16/18). Reflex Cytology is **Negative** (NILM).

The Patient's Question: *"Wait, you found the virus that causes cancer, but you say my cells are normal? Am I sick or not? And what do we do now?"*

ARS Question #3

Based on the 2026 ASCCP "Living" Guidelines, What Is the Most Appropriate Next Step for Sarah?

A. Immediate Colposcopy
B. Repeat co-testing (HPV + Pap) in 1 year
C. Repeat Primary HPV testing in 1 year
D. Pap Cytology with reflex HPV in 1 year

CONTINUING EDUCATION COMPANY

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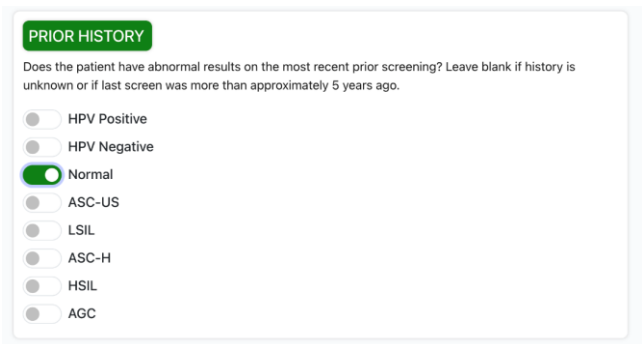
Patient Data



https://www.asccp.org/mobile-app/

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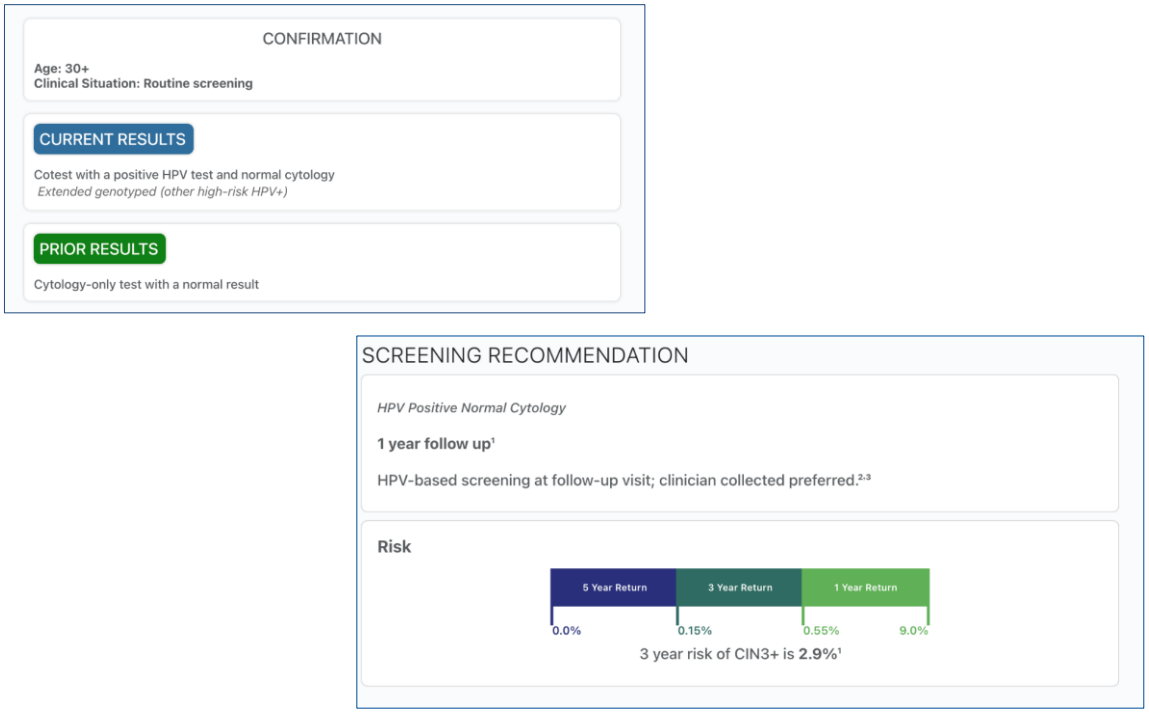
Recommendation



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The Answer and Rationale

- Correct Answer:
  - **The 4% Rule**: Sarah's immediate risk of CIN 3+ is well below the 4% threshold required for a colposcopy.
  - **The "Why"**: Most HPV infections in healthy 30-somethings are transient. By waiting 12 months, we allow for "viral clearance."
  - **The Nuance**: If we did a colposcopy today, we would likely find nothing or a low-grade lesion (LSIL/CIN 1) that would resolve on its own. We would be "over-diagnosing" and causing unnecessary cervical trauma.
  - **The Next Step**: If she is still HPV positive in one year, her risk rises above the 4% threshold, and then we perform the colposcopy.

Sarah is the most common patient in your 2026 inbox. If you send every Sarah to colposcopy, you'll have a backlog of procedures and a lot of anxious patients. If you use the ASCCP app, you give her a evidence-based 'green light' to wait for her immune system to do its job

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The Clinical Conundrum
Question 4

Patient: Maria, a 31-year-old G2P2

History: No prior abnormalities; last screen 3 years ago was a "Normal" Pap (no HPV).

Today's Result: Primary HPV is **Positive for HPV 16**

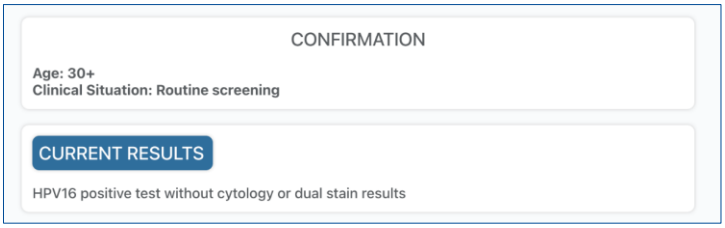
The Patient's Question: *"Wait, you found the virus that causes cancer? Am I sick or not? And what do we do now?"*

ARS Question #4

Based on the 2026 ASCCP "Living" Guidelines, What Is the Most Appropriate Next Step for Maria?

A. Immediate Colposcopy
B. Repeat co-testing (HPV + Pap) in 1 year
C. Repeat Primary HPV testing in 1 year
D. Expedited treatment (LEEP)

Data Entry



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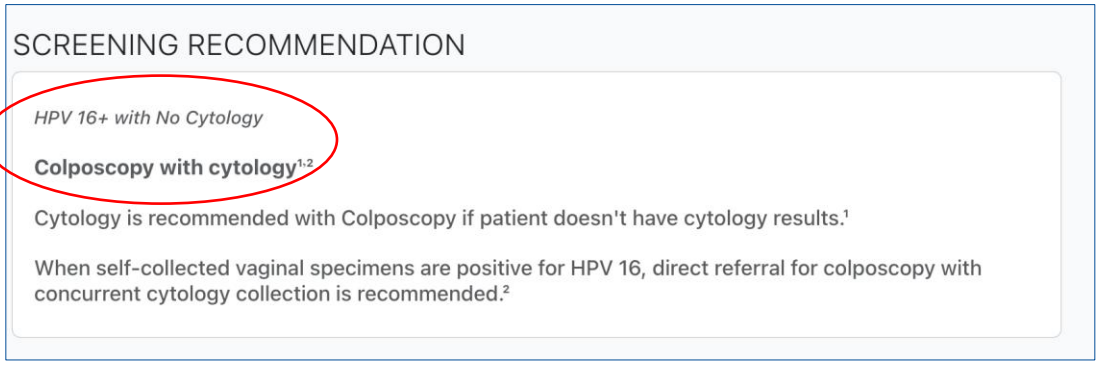
Screening Recommendation



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The Answer and Rationale

- Correct Answer:
  - **The 4% Rule**: Maria's immediate risk of CIN 3+ is well above the 4% threshold required for a colposcopy.
  - **The "Why"**: the presence of **HPV 16** (or 18) carries an immediate risk of high-grade disease that is **higher than 4%**.

The genotype is our 'urgency' marker. Sarah and Maria have the exact same Pap result, but their clinical path is totally different because of the DNA of the virus they are carrying. That is the heart of 2026 precision screening.

The "Living" Guideline algorithm sees Maria's history as a sign of **persistent** HPV. Persistence is the true driver of cancer

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The Clinical Conundrum 3

Patient: Sheila, a 57-year-old G3P3

- Establishing Care
- **History**
  - LNMP – 4 years ago
  - (+) VMS
    - Trial of Estrogen – no benefit
    - Recently had bioidentical Testosterone pellets implanted
  - 8 years ago she underwent a hysterectomy for "precancer."
  - She reports she has never had an abnormal pap and she has been getting "yearly evaluations for as long as she can remember."

The Patient's Question – *"Can I move to primary HPV testing instead of Pap?"*

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The Script for the Skeptical Patient

"I know it feels strange to skip the Pap smear, but we've actually upgraded our technology. We are now testing for the HPV virus itself rather than just looking for the cell changes it causes. Think of it like a security system: the old Pap smear looked for 'signs of a break-in' (cell changes), while the new test checks to see if 'the intruder is even at the door' (the virus). Because this test is so much more accurate at predicting your risk over the next several years, it is actually safer to wait longer between tests. We are still doing your pelvic exam and health check today—we're just being smarter about how we screen for cancer."

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Summary Checklist for the Modern Clinician

We've Moved from 'What Does This Pap Mean?' to 'What Is This Patient's 5-Year Risk?' that Is a Massive Win for Patient Safety and Reducing Over-Treatment."

	Parameter
✓	Switch to Primary HPV: Start at age 25 if your lab supports it.
✓	Download the App: Use the ASCCP Management Guidelines app—don't try to memorize the tables.
✓	History is King: You cannot manage a current abnormal result without knowing the last 10 years of the patient's screening history.
✓	Genotyping Matters: 16 and 18 are the "bad actors." They always require closer scrutiny than other high-risk types.

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"Cervical cancer screening recommendations have changed over time, driven by improved understanding of the disease's natural progression, the recognized role of high-risk HPV infection, and advancements in screening technologies"

SUMMARY

- Primary HPV screening benefits patients by limiting unnecessary testing, benefits physicians by providing a simpler strategy for management, and benefits society by making cervical cancer screening more accessible.
- Now is the right time for clinicians to shift our cervical cancer screening strategy from cotesting to primary HPV screening for average-risk, asymptomatic women.

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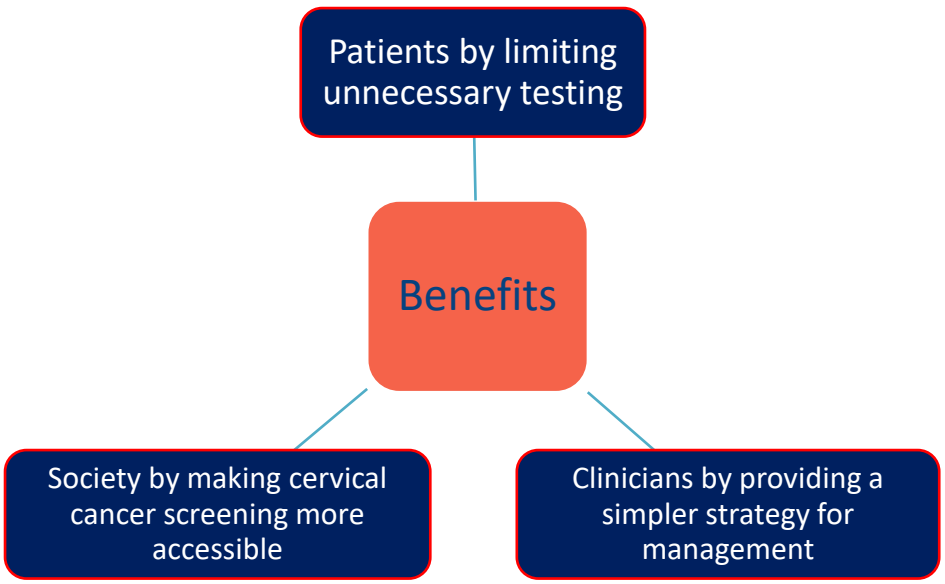
Primary HPV Screening



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Practice Recommendations

Recommendation	SOR
Join the movement, increase access to cervical cancer screening. Use Primary HPV Testing. Contact your reference lab for collection specifics and ordering.	-
All trials found that primary HPV screening is as effective at detecting incident CIN 3+ as cotesting, with fewer harms.	A
Screening recommendations: (ASCCP/USPSTF – 21) (ACS- 25) **Ages 21-24:** Cytology (Pap test) every 3 years **Ages 25-65:** Primary HPV Testing every 5 years (clinician-collected) or 3 years (self-collected)	A
Two Sampling approaches have been found to be effective for Primary HPV Testing self collection – Vaginal Approach and Urine (first catch) approach. Home self-collection is also now available.	B
Dual stain biomarkers integration allows clinicians to better differentiate between HPV infections that may resolve on their own and those that require intervention.	B
Extended genotyping provides a greater and more refined level of risk stratification than pooled HPV-positive results to more precisely determine patient management.	B

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References

1. Marcus, Jenna Z. MD[1]; Cason, Patty RN, MS, FNP-BC[2]; Downs, Levi S. Jr. MD, MS[3]; Einstein, Mark H. MD, MS[1]; Flowers, Lisa MD[4]. The ASCCP Cervical Cancer Screening Task Force Endorsement and Opinion on the American Cancer Society Updated Cervical Cancer Screening Guidelines. Journal of Lower Genital Tract Disease 25(3):p 187-191, July 2021. | DOI: 10.1097/LGT.0000000000000614
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3. Schiffman, Mark MD1; Wentzensen, Nicolas MD1; Perkins, Rebecca B. MD2; Guido, Richard S. MD3. An Introduction to the 2019 ASCCP Risk-Based Management Consensus Guidelines. Journal of Lower Genital Tract Disease 24(2):p 87-89, April 2020. | DOI: 10.1097/LGT.0000000000000531
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5. Self-collected vaginal specimens for human papillomavirus testing and guidance on screening exit: An update to the American Cancer Society cervical cancer screening guideline. CA: A Cancer Journal for Clinicians (2025).

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