

HPV mRNA

Test Codes:

HPV mRNA - 718

HPV mRNA w/Reflex Genotypes 16, 18/45 if HPV is Positive - 438

Pap, ThinPrep® w/HPV mRNA - 719

Pap, ThinPrep® w/Reflex HPV mRNA if ASC-US - 704



Specimen Requirements

Using a cervical broom or brush and plastic spatula, collect a sample and rinse the device vigorously in the CytoLyt fluid in the ThinPrep vial. Print patient's complete last name and first name or initial and unique identifier on the vial.

CPT Codes*

HPV mRNA: 87624

HPV Genotypes 16, 18/45: 87625

ThinPrep® Pap: 88175

Reflex tests are performed at an additional charge and are associated with an additional CPT code.

Clinical Use

- Screen for cervical cancer in women 30-65 years of age (in conjunction with cervical cytology)
- Determine need for colposcopy in women 21-29 years of age with ASC-US (atypical squamous cells of uncertain significance) cervical cytology results

Clinical Background

Human papilloma virus (HPV) infection has been shown to be the etiological agent in more than 99% of cervical cancers.¹ Of the more than 100 HPV genotypes, 14 have been linked to the development of cervical cancer and are therefore termed high-risk genotypes.² Although the majority of HPV infections spontaneously resolve within 2 years, individuals with persistent high-risk HPV infection are at high risk of developing cervical intraepithelial neoplasia (CIN) and cervical carcinoma.^{2,3}

Cervical cytology (ie, Pap test) has been used to screen for premalignant and malignant cervical lesions since its introduction in the 1950s, and its use has reduced the incidence of cervical cancer; however, it is limited by relatively low sensitivity and specificity.⁴ Numerous studies have shown that testing for high-risk HPV DNA is significantly more sensitive (high negative predictive value) than cytology for the detection of high-grade CIN (ie, CIN 2 or greater).^{5,6} Though current high-risk HPV DNA testing methods provide adequate sensitivity, specificity is lacking (low positive predictive value) leading to false-positive results and unnecessary invasive procedures such as colposcopy and biopsy.⁷

HPV E6/E7 oncoproteins mediate the development of cervical cancer. Their overexpression, which can be measured as E6/E7 messenger RNA (mRNA) transcripts, is associated with a significantly increased risk of CIN and cervical cancer.^{8,9} This test determines the presence of E6/E7 mRNA from 14 high-risk HPV genotypes.

In a study of 800 women referred for colposcopy, the sensitivity and specificity of this test were shown to be >92% and 99%, respectively, for detection of high-risk HPV types and 91% and >55%, respectively, for the detection of CIN2+.¹⁰ In women undergoing routine screening (N=1,373), the sensitivity and specificity for the detection of CIN2+ were 100% and 88.3%, respectively.¹¹

Individuals Suitable for Testing

- Women 30-65 years of age
- Women 21-29 years of age who have an ASC-US, LSIL, or more severe cervical cytology result

Method

- Transcription-mediated amplification (TMA)
 - Detects E6/E7 mRNA from 14 high-risk HPV genotypes
- Analytical sensitivity:
 - <100 copies mRNA/reaction (types 16, 18, 31, 33, 35, 39, 45, 58, 59, 66, 68)
 - 100-300 copies mRNA/reaction (types 51, 52, 56)
- Analytical specificity: cross-reacts with low-risk HPV genotypes 26, 67, 70 and 82, but not with any bacteria, yeast, or fungi tested
- Results reported: HPV mRNA detected or not detected; does not differentiate the genotypes

Reference Range

Not detected

Interpretive Information

A “not detected” result is consistent with the absence of high-risk HPV E6/E7 mRNA, a level of HPV mRNA below the detection limit of the assay, or presence of a genotype other than those listed above. It suggests a low risk of cervical cancer.

A “detected” result indicates the presence of high-risk HPV E6/E7 mRNA and is suggestive of an increased risk of cervical cancer.

Results may be affected by polyquaternium 15 (found in personal lubricants) and by the antifungal tioconazole. Performance in HPV-vaccinated women has not been evaluated. Results should be interpreted in conjunction with other clinical and laboratory data.

Following is a summary of follow-up recommendations for specific combinations of HPV and cervical cytology results.¹² Guidelines do not distinguish between high-risk HPV testing methods, which may have variable sensitivity and specificity.

Age 30-65 years

- Pap test negative or ASC-US/high-risk HPV negative: Routine screening with Pap and high-risk HPV at 5-year intervals (preferred)
- Pap test negative/high-risk HPV positive: Repeat Pap test and high-risk HPV test at 12 months; or perform HPV genotype 16, 18/45 test
- Pap test ASC-US/ high-risk HPV positive: Colposcopy
- Pap test ASC-H, LSIL, HSIL, cancer: Colposcopy

Age 21-29 years

- Pap test ASC-US/ high-risk HPV negative: Routine screening with Pap test at 3-year intervals
- Pap test ASC-US/ high-risk HPV positive: Colposcopy
- Pap test ASC-H, LSIL, HSIL, cancer: Colposcopy

References

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