Seeking a better solution to stratify patient risk following an HPV-positive result?

Use the QIAsure® Methylation Test.

Sample to Insight

A breakthrough in women's health

While cervical cancer affects women worldwide as one of the deadliest cancers, scientific advancements continue to improve our prevention efforts and save countless lives. In fact, over the past two decades, screening and vaccination have proven to be successful tools to prevent and detect high-risk human papillomavirus (HPV) before it becomes a danger to a woman's life or reproductive health (1).

However, while advances in technology have created highly sensitive methods for HPV detection, most HPV infections are transient and resolve without treatment. What has proven more challenging within the medical community is how to effectively identify the subset of women whose HPV infections require immediate clinical management so that they do not progress to cervical cancer (2,3).

"Effective triage of hrHPV positive screening samples constitutes one of the currently most crucial scientific issues to solve for primary HPV based screening to truly modernize cervical cancer prevention," (2).

The QIAsure Methylation Test provides additional molecular insights to aid in evaluating patient management options by accurately identifying women with markers associated with the highest short-term risk for cervical cancer.

Key benefits of the QIAsure Methylation Test

Accurate	QIAsure is a quantitative methylation-specific PCR test with high clinical sensitivity and up to 100% detection of biomarkers associated with cervical carcinoma in patients (3)
Objective	QIAsure provides objective, molecular insights that reveal whether a patient's HPV infection is actively transforming cervical cells into cancer
Efficient	QIAsure can be performed on the same sample as the primary screening HPV test using either clinician or self-collected sample QIAsure reduces unnecessary colposcopies and cervical treatments compared to triage by cytology (2)
Convenient	QIAsure can be performed on self-samples collected by the patient without a speculum exam, making it easy and convenient to be tested early without additional doctor appointments
Reliable	QIAsure provides HPV positive/methylation-negative patients and their providers with peace of mind that a wait and see policy is safe, reducing unnecessary treatment

What is QIAsure?

QIAsure is a quantitative methylation specific PCR (qMSP) test that provides molecular-level information to determine whether an HPV-positive patient or a patient with abnormal cytology is at short-term risk of developing cervical cancer. More specifically, QIAsure accurately detects the presence of biomarkers associated with cervical carcinoma and advanced transforming cervical intraepithelial neoplasia (CIN) to objectively discern transient HPV infections from ones that progress and require immediate intervention (4).

QIAsure Methylation Test clinical uses

Triage testing	Reassurance testing	Patient managment support
Primary triage test of HPV-positive women to detect markers associated with advanced or progressing CIN lesions	Due to low long-term risk of negative test, QIAsure can support extended screening intervals	Limits the over-treatment of CIN2/3 lesions, especially in young women and childbearing age
Secondary triage test in case of ASCUS-LSIL to detect markers associated with CIN3 to identify women who need a colposcopy referral • Reduces over-referral and unnecessary treatment of transient infections	In low-resource or low-access areas with longer testing intervals, QIAsure can provide insights on long-term risk and guide treatment needs	Offers objective support for treating physicians to safely apply 'wait and see' approach versus over-treatment

A closer look

QIAsure looks for methylation of host cell genes *FAM19A4 and miR124-2* in cervical-vaginal cells. Methylation of these genes indicates carcinogenic cell transformation and high short-term risk of developing cervical cancer, while absence of methylation indicates low short-term risk of developing cervical cancer (2-6). With these molecular insights, QIAsure can help reduce over-referrals and unnecessary treatments by stratifying women who need immediate intervention versus those who need only monitoring.

QIAsure clinical performance

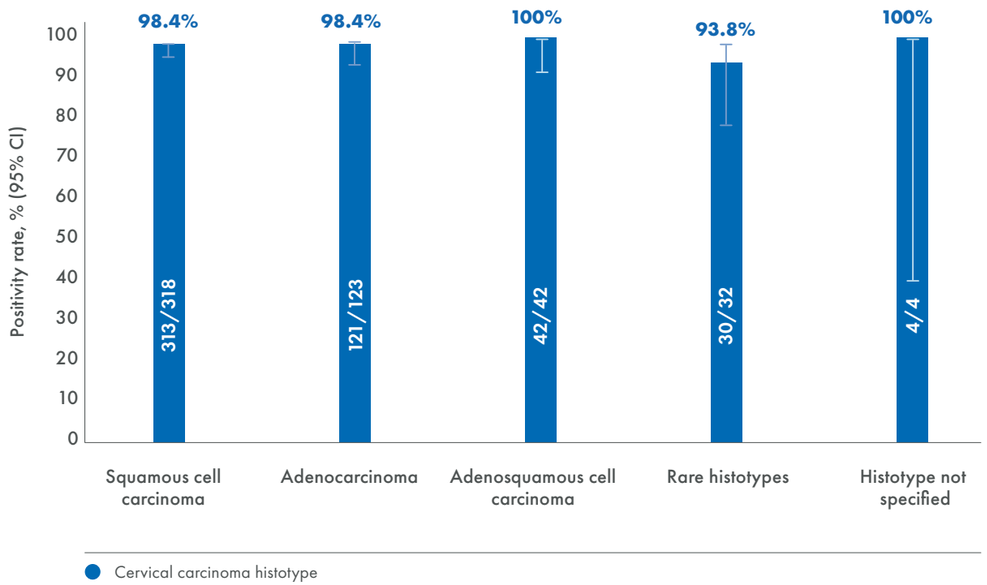
The value of QIAsure in identifying progressive cervical disease

Abnormal patterns of DNA methylation have been implicated in various cancers, including cervical cancer where promoter hypermethylation of the tumor suppressor gene *FAM19A4* and/or *miR124-2* indicates the presence of precancer or cancer (2-6). QIAsure examines promoter hypermethylation in bisulfite-converted DNA isolated from cervical-vaginal specimens using a multi-plex real-time PCR test. Positive results correlate with the presence of carcinogenic cells and advanced transforming CIN lesions.

Independent research confirms the effective use of *FAM19A4/miR124-2* methylation analysis for detection of cervical carcinomas and advanced CIN 2/3 lesions across cervical histotypes (3).

The below chart represents positivity rates among 519 cervical cancer cases tested retrospectively in a global multicenter study (3).

QIAsure Methylation Test: positivity rates by histotype



- Of the 519 cervical cancer specimens, 510 tested positive, yielding a positivity rate of 98.3% (95% CI: 96.7–99.2); consistent over all histotypes, FIGO stage, HPV genotype and geography

The value of QIAsure to stratify risk following an HPV-positive result

A large multicenter retrospective clinical performance study examined the performance of *FAM19A4/miR124-2* (QIAsure) as a triage for HPV-positive women across different countries and using various sample collection media, DNA extraction methods, and HPV screening tests (2).

Results demonstrate that among these differences, CIN3 sensitivity of QIAsure remained consistent at 77%, indicating appropriate use as a triage for HPV-positive women, in place of or in conjunction with cytology.

QIAsure performance in HPV-positive women with CIN3+

	Proportion (pooled value)	n / N
Sensitivity (CIN3)*	77.2%	176/228
Specificity (≤CIN1)	78.3%	1,575/2,012
NPV (CIN3+)	28.3%	1,641/1,694
PPV (CIN3+)	28.3%	195/690

- QIAsure shows reliable clinical performance for CIN3+ in HPV-positive women, comparable to cytology
- Verification bias for cytology results in slightly higher sensitivity and PPV for cytology

> "Substituting cytology in triage of hrHPV positive screening samples with an objective molecular biomarker test with a high PPV for ≥CIN2 or ≥CIN3 such as FAM19A4/miR124-2 methylation, colposcopy referrals can be markedly reduced while maintaining good sensitivity for cervical cancer and advanced CIN," (2).

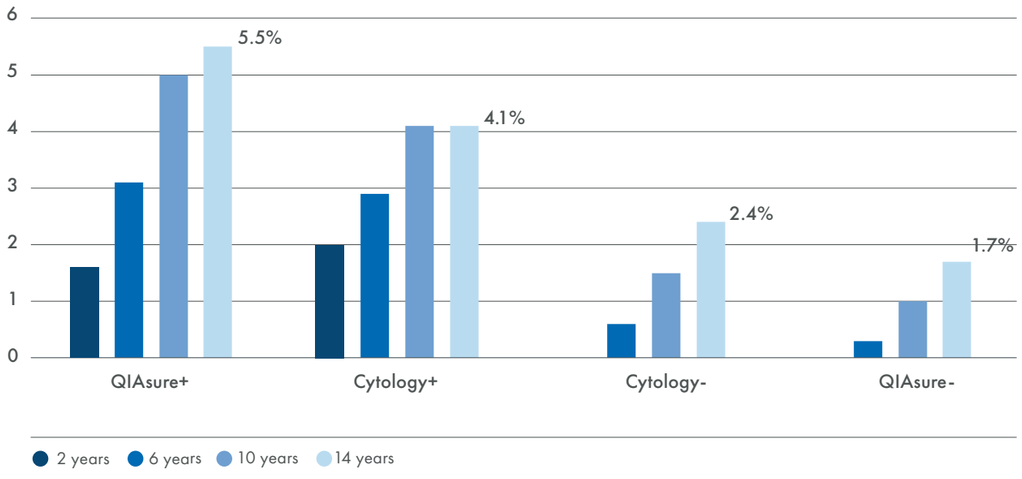
The value of QIAsure for assessing long-term cancer risk

Long-term longitudinal data published in 2018 examined the fourteen-year cumulative incidence of cervical cancer among HPV-positive women stratified by *FAM19A4/mir124-2* methylation or cytology test result at baseline (5).

Overall, women who were *FAM19A4/mir124-2*-negative at baseline had the lowest long-term cancer risk, meaning that a negative QIAsure test is a reliable indicator that an HPV-positive patient is at low risk for progressive cervical disease in the short term.

"The low cervical cancer risk conferred by a negative test supports the use of this DNA methylation test as a safe triage alternative in HPV-based screening programs," (5).

Long-term cancer risk by HPV-positive strategy (5)



QIAsure is effective at identifying cancer risk, with positive *FAM19A4/mir124-2* results suggesting immediate colposcopy, and negative results indicating lower risk for cancer compared to cytology (5).

QIAsure has also proven effective at identifying CIN3+ risk, with FAM19A4/mir124-2-positive results suggesting immediate colposcopy, while methylation-negative results indicating low long-term CIN3 risk, similar to that of cytology (6).

Improving clinical assurance – for you and for her

Current cervical screening algorithms lack an objective, accurate, and accessible test to identify cervical precancer or cancer before it becomes problematic. Implementing the QIAsure Methylation Test as a triage strategy following an HPV-positive result can quickly identify women at highest risk for cervical disease or cancer, while reducing unnecessary referrals and over-treatment.

"A methylation-based triage assay may offer several advantages over cytology: it is objective, directly applicable to the DNA isolates that are generated during most HPV-based screening workflows, has a high repeatability as shown herein, allows higher throughput, could be adapted to intermediate and low resource settings, and it can be directly applied to self-collected samples," (5).

References

1. World Health Organization (2022). Cervical cancer fact sheet https://www.who.int/news-room/fact-sheets/detail/cervical-cancer
2. Bonde, J., et al. (2021) Methylation markers FAM19A4 and miR124-2 as triage strategy for primary human papillomavirus screen positive women: A large European multicenter study. Int J Cancer, 148, 396–405.
3. Vink, F.J. (2019) FAM19A4/miR124-2 methylation in invasive cervical cancer: A retrospective cross-sectional worldwide study, Int J Cancer, 147, 1215-1221.
4. QIAsure Methylation Test IFU: https://www.qiagen.com/de/resources/resourcedetail?id=d4851ddc-405d-4d93-be9a-a343c8576d64&lang=en
5. De Strooper, L.M.A., et al., (2018) Cervical cancer risk in HPV-positive women after a negative FAM19A4/mir124-2 methylation test: A post hoc analysis in the POBASCAM trial with 14 year follow-up. Int J Cancer. 143, 1541 – 1548.
6. Dick, S. et al. (2019) Long-term CIN3+ risk of HPV positive women after triage with FAM19A4/miR124-2 methylation analysis. Gynecol Oncol., 154, 368-373.

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