



MEDIA KIT

ABOUT HPV TESTING

Why HPV testing?

The role of HPV in cervical cancer has been known for only 40 years. In 1976, Harald zur Hausen, a German virologist, first published his findings regarding the connections between the human papillomavirus (HPV) and cervical cancer. By 1997, Dutch researcher Jan M. Walboomers published his findings indicating a nearly 100% association between HPV infection and cervical cancer.

Does HPV infection mean that a woman will get cervical cancer?

No. In most cases, HPV infections clear up on their own. But, if the HPV persists — typically with no obvious outward symptoms — it can lead to abnormalities (dysplasia) in cervical cells that may progress in severity from mild, to moderate, to severe and to invasive cancer. This process, from infection to cancer, can take 10-15 years.

When are women tested for HPV?

The test is performed as part of routine screening for cervical cancer and may be included in their annual physical exam or obgyn visit. A list of [current guidelines](#) is available from the CDC.

Why are women screened?

Early screening programs have reduced the death rates associated with cervical cancer.

Is cervical cancer screening new?

No. The Papanicolaou (Pap) test has been a common method for cervical cancer screening since it was introduced in the 1940s. However, studies show that nearly 35% of pre-cancers are missed by Pap testing alone, giving women a false sense of security.

HPV testing can help find disease that is missed by Pap. In the [ATHENA study](#), 1 in 10 women who tested positive for HPV 16 and/or HPV 18 had cervical pre-cancer, even though their Pap test result was normal.

Co-testing — using both Pap and HPV testing to examine a single sample — has been the standard of care for more than a decade.

How do Pap testing and HPV testing differ?

In Pap testing, the sample is reviewed by human eyes through a microscope. The result can be subjective; data shows different people can interpret the same sample differently. HPV testing is more objective: HPV DNA is either detected at clinically relevant levels, or considered below this threshold.



How does the HPV test identify the virus?

The **cobas**[®] HPV Test uses polymerase chain reaction (PCR) to copy a targeted segment of HPV virus's DNA. If the DNA is present at clinically relevant levels that are correlated to presence of cervical disease (clinical threshold), then the test result is positive. If the DNA is below this threshold, the test result is called negative.

How does PCR work?

PCR copies the target DNA thousands of times in a set of repeated cycles, a process called amplification. An automated instrument is used to detect the amplified material. [Learn more](#).

THE ATHENA STUDY

What is the ATHENA study?

ATHENA stands for Addressing THE Need for Advanced HPV Diagnostics. ATHENA is the largest US prospective registrational clinical study of its kind, which evaluated the performance of the **cobas**[®] HPV Test in primary screening, ASC-US triage and co-testing in women with normal cytology. This landmark trial of more than 47,000 women ≥ 21 years of age undergoing routine cervical cancer screening, was the first clinical trial to evaluate the simultaneous real-time genotyping of 12 pooled hrHPV genotypes plus HPV 16 and HPV 18 individually.

What were the findings of the study?

Many important findings came from the ATHENA study. Several of them include:

- Women who tested negative for high-risk HPV using the **cobas**[®] HPV Test had more than twice the assurance that they would not develop high-grade cervical cancer within 3 years compared to those who had a normal Pap (NILM) result.
- Approximately 1 in 10 women who had a normal Pap (NILM) result, but tested positive for HPV 16 and/or HPV 18, were found to have high-grade cervical disease that was missed by cytology.
- Women who tested positive for HPV 16 had an almost 1 in 4 chance of developing high-grade cervical disease within 3 years.
- Women who tested positive for HPV 18 had an almost 1 in 9 chance of developing high-grade cervical disease within 3 years.
- Women aged 25-29, had a higher burden of high-grade cervical disease than women aged 40 and older. Also in this age group, 57.3% of the women who were diagnosed with high-grade cervical disease had a normal Pap result.
- The **cobas**[®] HPV Test demonstrated superior performance to liquid-based Pap cytology in primary screening.

FDA APPROVAL FOR THE COBAS® HPV TEST

When was the **cobas**® HPV Test approved for first-line, primary screening of cervical cancer?

In 2014, the U.S. Food and Drug Administration (FDA) approved the use of the **cobas**® HPV Test for first-line, primary screening, allowing it to be used in front of Pap cytology for women 25 and older. Because it not only detects high risk HPV but can also stratify HPV 16 and HPV 18 risk, the **cobas**® HPV Test is the first and only HPV test approved for primary screening in the U.S. The test was originally launched in CE mark countries in 2009. It received FDA approval in 2011 for screening patients age 21 and older with abnormal cervical cytology results and for use adjunctively with normal cervical cytology in women ages 30 and over to assess the presence or absence of high-risk HPV genotypes.

What was the basis of the FDA decision?

The decision came after a unanimous recommendation from the Microbiology Devices Panel of the FDA's Medical Devices Advisory Committee. It was based on the findings of the ATHENA study showing that the **cobas**® HPV Test is a safer, more effective way to screen for cervical cancer in women 25 and older.

How is the **cobas**® HPV Test different from other HPV tests?

The **cobas**® HPV Test gives three results in one test:

- Pooled high-risk HPV types (HPV 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68)
- HPV 16
- HPV 18

Additionally, the **cobas**® HPV Test has an internal control feature to confirm the presence of human DNA sample.

Why is it important to give separate results for HPV 16 and HPV 18?

HPV 16 and HPV 18 are the highest risk HPV types, responsible for about 70% of all cervical cancers. Identifying the presence or absence of HPV 16 or HPV 18 means a more accurate assessment of cervical cancer risk.

What does the approval mean for women?

The findings show that the **cobas**® HPV Test has significantly higher sensitivity in the identification of women who are at risk for developing cervical cancer. Women with a negative **cobas**® HPV Test result will have increased assurance that they are at low risk of developing cervical cancer.

ADDITIONAL HPV REFERENCES

Centers for Disease Control and Prevention

- Cervical cancer screening guidelines for average-risk women: <http://www.cdc.gov/cancer/cervical/pdf/guidelines.pdf>
- Human papillomavirus (HPV): <http://www.cdc.gov/hpv/>
- HPV vaccines: <http://www.cdc.gov/hpv/vaccine.html>
- HPV and cancer: <http://www.cdc.gov/hpv/cancer.html>
- HPV-associated cancer statistics: <http://www.cdc.gov/cancer/hpv/statistics/>
- Incidence, prevalence and cost of sexually transmitted infections in the United States: <http://www.cdc.gov/std/stats/STI-Estimates-Fact-Sheet-Feb-2013.pdf>

Clinical Studies of Interest

- Ronco G, Dillner J, Elfström KM, et al. Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four European randomised controlled trials. *Lancet*. 2014 Feb 8;383(9916):524-32. doi: 10.1016/S0140-6736(13)62218-7. Epub 2013 Nov 3.
- Dillner J, Rebolj M, Birembaut P, et al. Long term predictive values of cytology and human papillomavirus testing in cervical cancer screening: joint European cohort study. *BMJ*. 2008;377:1-8.
- Khan MJ, Castle PE, Lorincz AT, et al. The elevated 10-year risk of cervical pre-cancer and cancer in women with human papillomavirus (HPV) type 16 or 18 and the possible utility of type-specific HPV testing in clinical practice. *J Natl Cancer Inst*. 2005;97(14):1072-1079.
- Castle PE1, Stoler MH, Wright TC Jr, Sharma A, Wright TL, Behrens CM. Performance of carcinogenic human papillomavirus (HPV) testing and HPV16 or HPV18 genotyping for cervical cancer screening of women aged 25 years and older: a subanalysis of the ATHENA study. *Lancet Oncol*. 2011 Sep;12(9):880-90.
- Cox JT, Castle PE, Behrens CM, Sharma A, Wright TC Jr, Cuzick J, Athena HPV Study Group. Comparison of cervical cancer screening strategies incorporating different combinations of cytology, HPVtesting, and genotyping for HPV 16/18: results from the ATHENA HPV study. *Am J Obstet Gynecol*. 2013 Mar;208(3):184.e1-184.e11.
- Mayrand MH, Duarte-Franco E, Rodrigues I, Walter SD, Hanley J, Ferenczy A, et al. Human papillomavirus DNA versus Papanicolaou screening tests for cervical cancer. *N Engl J Med*. 2007 Oct 18;357(16):1579-88.
- Silverloo I, Andrae B, Wilander E. Value of high-risk HPV-DNA testing in the triage of ASCUS. *Acta Obstet Gynecol Scand*. 2009;88(9):1006-10.
- Solomon D, Schiffman M, Tarone R, ALTS Study Group. Comparison of three management strategies for patients with atypical squamous cells of undetermined significance: baseline results from a randomized trial. *J Natl Cancer Inst*. 2001 Feb 21;93(4):293-9.