



## Human Papillomavirus (HPV) and Cervical Cancer Fact Sheet

### Fast Facts

- Human papillomavirus (HPV) is a common infection transmitted during sexual contact and those affected often do not show symptoms.<sup>1</sup>
- Almost all cervical cancers – more than 99 percent – are caused by HPV.<sup>2</sup>
- There are more than 118 genotypes of HPV and 14 are considered high risk for cervical cancer. Two of these, HPV genotypes 16 and 18, are considered the highest risk and responsible for approximately 70 percent of cervical cancers.<sup>3</sup>
- In an overview of more than 60,000 women, HPV testing was substantially more sensitive in detecting cervical disease than cytology (96.1% vs. 53.0%).<sup>4</sup> By finding precancerous lesions early, clinicians can prevent cancer from developing.

### Overview

Human papillomavirus, also known as HPV, is a common virus that can be transmitted through skin-to-skin contact. Approximately 80 percent of women will have an HPV infection by age 50.<sup>5</sup> There are more than 118 HPV genotypes, about 40 of which can infect the genitals, mouth, and throat in both males and females.<sup>6</sup> Most people with HPV are unaware that they have it, and are equally unaware that they may be passing it on to others.<sup>7</sup>

There is currently no cure for HPV infection; however, a vaccine is available for boys and girls and young men and women, ages 9-to-26, to protect against four types of HPV. Treatments are also available that can partially treat the conditions that some types of HPV can cause, such as genital warts and cervical cancer.

The Centers for Disease Control and Prevention estimates that more than 90 percent of all HPV infections are cleared by the body's immune system within two years without causing any serious health

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<sup>1</sup> Centers for Disease Control. Genital HPV Infection – Fact Sheet. Retrieved from <http://www.cdc.gov/std/hpv/stdfact-hpv.htm> on February 25, 2011.

<sup>2</sup> Centers for Disease Control. Epidemiology and Prevention of Vaccine-Preventable Diseases. The Pink Book: Course Textbook - 12th Edition Second Printing (May 2012). Retrieved from <http://www.cdc.gov/vaccines/pubs/pinkbook/hpv.html> on March 3, 2013.

<sup>3</sup> de Sanjose S, Quint WG, Alemany L, et al. Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. *Lancet Oncol.* 2010;11:1048-1056.

<sup>4</sup> Cuzick J, Clavel C, Petry K, et al. Overview of the European and North American studies on HPV testing in primary cervical cancer screening. *Int J Cancer.* 2006;119(5):1095-1101.

<sup>5</sup> Centers for Disease Control. Epidemiology and Prevention of Vaccine-Preventable Diseases. The Pink Book: Course Textbook - 12th Edition Second Printing (May 2012). Retrieved from <http://www.cdc.gov/vaccines/pubs/pinkbook/hpv.html> on March 3, 2013.

<sup>6</sup> Steben et al *Gyn Onc.* Volume 107, Issue 2, Supplement, November 2007, Pages S2-S5.

<sup>7</sup> Kerker SC et al. Human papillomavirus infection in asymptomatic population. *Sex Reprod Health.* 2011 Jan;2(1):7-11.



problems.<sup>8</sup> Not every woman who tests positive for HPV will show symptoms or develop cervical cancer. However, problems may occur if HPV persists.

## HPV and Cervical Cancer

In women, high-risk HPV genotypes, such as HPV 16 and HPV 18, can cause low-grade and high-grade cell changes, or pre-cancers, in the cells of the cervix. Health care professionals are more concerned with high-grade changes because these are more likely to progress into cancer over time, while low-grade changes typically regress without treatment.

Cervical cancer is the second most common cancer in women worldwide with more than 500,000 new cases and 270,000 related deaths each year.<sup>9</sup> In nearly all cases, cervical cancer is caused by a persistent high-risk HPV infection. More than 99 percent of cervical cancer cases are associated with approximately 14 HPV genotypes.<sup>10</sup> HPV 16 and 18 have been identified as the highest-risk genotypes, and cause approximately 70 percent of all cervical cancers.<sup>11</sup>

## Current Diagnosis and Screening Guidelines

Medical guidelines in the U.S. currently recommend that all women 21 years old and older be regularly screened for cervical cancer and allow for cytology testing every three years as the initial screening test to determine the risk of cervical cancer. For women age 30 - 65, the preferred screening option is cytology in conjunction with HPV DNA testing every five years. However, Pap testing every three years is still considered an acceptable option in this age group.

Since the introduction of the Pap test in the 1940s, a microscopic examination of cells by a cytotechnician or pathologist, the test has played a critical role in diagnosing women's cervical diseases, and is still a valuable part of women's health care. However, the cytology, while specific, is unable to identify if HPV DNA is present. It can also miss about 50 percent of cervical pre-cancer in a single round of screening.<sup>12</sup>

For this reason, medical guidelines in many countries around the world have begun to recommend HPV testing to verify the presence of high-risk HPV DNA as the primary screen for cervical cancer prevention. Research has shown that HPV DNA testing can help identify the risk of cervical cancer in the pre-cancer stages and help health care providers identify disease missed by cytology. Although HPV itself cannot be treated, the cellular changes that come from an infection can be treated, especially if they are caught early.<sup>13</sup> HPV DNA testing allows a clinician to test for specific high-risk genotypes of HPV, including those

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<sup>8</sup> World Health Organization. Human papillomavirus and cervical cancer fact sheet. Retrieved from <http://www.who.int/mediacentre/factsheets/fs380/en/> on March 3, 2014.

<sup>9</sup> World Health Organization. Human papillomavirus and cervical cancer fact sheet. Retrieved from <http://www.who.int/mediacentre/factsheets/fs380/en/> on March 3, 2014.

<sup>10</sup> Bouvard [www.thelancet.com/oncology](http://www.thelancet.com/oncology) Vol 10 April 2009.

<sup>11</sup> de Sanjose S, Quint WG, Alemany L, et al. Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. *Lancet Oncol.* 2010;11:1048-1056.

<sup>12</sup> Cuzick J et al. *Int J Cancer* 2006; 119:1095-1101.

<sup>13</sup> Centers for Disease Control. Genital HPV Infection – Fact Sheet. Retrieved from <http://www.cdc.gov/std/hpv/stdfact-hpv.htm> on February 25, 2011.



associated with the highest risk for cervical cancer, HPV 16 and HPV 18. This allows for earlier identification of women most at risk as well as more specific testing and potential treatment of cervical disease before it develops into cervical cancer.

In April 2014, the **cobas**<sup>®</sup> HPV Test was approved by the FDA as a first-line primary screening tool in women aged 25 years and older to assess cervical cancer risk, based on the presence of clinically relevant high-risk HPV DNA. The **cobas**<sup>®</sup> HPV Test is the first HPV test indicated as a first-line primary screen for cervical cancer in the United States.

In October 2015, the Netherlands announced that it will become the first country in the world to transition its national cervical cancer screening program from the Pap test to primary HPV screening. Roche won the HPV primary screening tender in the Netherlands for the **cobas**<sup>®</sup> HPV Test after an extensive public process in which diagnostic providers were assessed on their ability to meet performance, quality and pricing criteria.

### **The HPV Vaccine and HPV Testing**

The two currently approved vaccines are designed to protect against the two most common types of high-risk HPV, HPV 16 and 18, but not the other high-risk HPV genotypes that are responsible for approximately 30 percent of cervical cancers.<sup>14</sup> In addition, HPV vaccination has not been widely adopted in many regions and protection is limited to those with no prior exposure to the HPV virus. As such, testing for high-risk HPV genotypes continues to play an important role in cervical cancer screening.

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<sup>14</sup> Centers for Disease Control. Epidemiology and Prevention of Vaccine-Preventable Diseases. The Pink Book: Course Textbook - 12th Edition Second Printing (May 2012). Retrieved from <http://www.cdc.gov/vaccines/pubs/pinkbook/hpv.html> on March 3, 2013.



## cobas® HPV Test Fact Sheet

### Fast Facts

- Roche has been awarded a 5-year contract by the National Institute for Public Health and the Environment (RIVM) in the Netherlands for implementation of the **cobas**® HPV Test as the first-line, primary screening test in the national cervical cancer screening program. The Netherlands is the first country in the world to fully transition its national cervical cancer screening program from the Pap test to primary HPV screening.
- The **cobas**® HPV Test was approved by the FDA in April 2014 as a first-line primary screening tool in women 25 years and older to assess cervical cancer risk, based on the presence of clinically relevant high-risk HPV DNA.
- The **cobas**® HPV Test provides three results in one test, with one patient sample. It individually identifies HPV 16 and 18, the two genotypes responsible for about 70 percent of cervical cancers, while simultaneously detecting 12 other high-risk genotypes as a pooled result.<sup>15</sup>
- The **cobas**® HPV Test helps physicians know more about their patients' risk for developing cervical cancer, so they can make earlier, more accurate decisions about patient care, ultimately preventing many women from developing the disease.
- In the landmark ATHENA trial, which studied more than 47,000 women in the U.S., it was shown that a negative **cobas**® HPV Test result provides more reassurance that high grade cervical disease (CIN3+) will not develop within 3 years versus a negative Pap test result.<sup>16</sup>

### HPV Testing in Cervical Cancer Screening

HPV is known to cause at least 99 percent of cervical cancer worldwide with nearly 12,000 women diagnosed in the U.S. each year.<sup>17,18</sup> Early detection is important for women at higher risk of developing cervical cancer as HPV infections are more likely to lead to cervical cancer if left untreated over time. In an overview of more than 60,000 women, HPV testing was substantially more sensitive in detecting cervical disease than cytology (96.1% vs. 53.0%).<sup>19</sup> By finding precancerous lesions early, clinicians can prevent cancer from developing.

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<sup>15</sup> de Sanjose S, Quint WG, Alemany L, et al. Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. *Lancet Oncol.* 2010;11:1048-1056.

<sup>16</sup> Roche Molecular Systems, data on file.

<sup>17</sup> CDC: Epidemiology and Prevention of Vaccine-Preventable Diseases. The Pink Book: Course Textbook - 12th Edition Second Printing (May 2012). Retrieved from <http://www.cdc.gov/vaccines/pubs/pinkbook/hpv.html> on March 3, 2014

<sup>18</sup> Centers for Disease Control. Inside Knowledge Cervical Cancer Fact Sheet. Retrieved from [http://www.cdc.gov/cancer/cervical/pdf/cervical\\_facts.pdf](http://www.cdc.gov/cancer/cervical/pdf/cervical_facts.pdf) on March 3, 2014.

<sup>19</sup> Cuzick J, Clavel C, Petry K, et al. Overview of the European and North American studies on HPV testing in primary cervical cancer screening. *Int J Cancer.* 2006;119(5):1095-1101.

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Since its introduction in the 1940s, the Pap test and the microscopic examination of cells by a cytotechnician or pathologist has played a critical role in diagnosing cervical diseases and is still a valuable part of women's health. However, cytology is unable to identify if HPV DNA is present and can miss about 50 percent of cervical pre-cancer in a single round of screening.<sup>20</sup>

In October 2015, Roche won the HPV primary screening tender in the Netherlands for the **cobas**<sup>®</sup> HPV Test after an extensive public process in which diagnostic providers were assessed on their ability to meet performance, quality and pricing criteria. The RIVM evaluated a number of HPV tests through their stringent and comprehensive criteria, one of which was to utilize DNA PCR-based technology. A national HPV screening program like the one being developed in the Netherlands will lead to a more efficient and effective use of resources. Most importantly, it will lead to fewer women developing cervical cancer, which is a highly, if not completely preventable cancer.

Screening women with an HPV DNA test that includes HPV genotyping for the highest-risk HPV genotypes gives healthcare professionals more specific information on which to base patient care decisions. Identifying women at the highest risk for cervical disease allows physicians to better manage their patients before cervical cancer develops.

### The **cobas**<sup>®</sup> HPV Test

The **cobas**<sup>®</sup> HPV Test is the first and only HPV test in the United States indicated as a first-line primary screening tool in women 25 years and older to assess cervical cancer risk, based on the presence of clinically relevant high-risk HPV DNA. The **cobas**<sup>®</sup> HPV Test is also approved by the FDA to screen patients, age 21 and older, with abnormal cytology results.

The **cobas**<sup>®</sup> HPV Test is the only FDA-approved test that can individually identify HPV 16 and 18, the two genotypes responsible for 70 percent of all cervical cancers, while simultaneously detecting 12 other high-risk genotypes of HPV as a pooled result in a single test.<sup>21</sup> By identifying women at higher risk for developing cervical cancer, the **cobas**<sup>®</sup> HPV Test allows healthcare professionals to make earlier, more informed decisions about patient care, ultimately helping to prevent many women from developing the disease.

In the landmark ATHENA trial, which studied more than 47,000 women, one in 10 women age 30 and older who tested positive for HPV 16 or 18 with the **cobas**<sup>®</sup> HPV Test had evidence of cervical pre-cancer, even though their Pap result was normal.<sup>22</sup> The robustness of this data led to the original approval in the US for co-testing and ASC-US testing in 2011, and the first and only primary screening claim in 2014.

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<sup>20</sup> Cuzick J et al. *Int J Cancer* 2006; 119:1095–1101.

<sup>21</sup> de Sanjose S, Quint WG, Alemany L, et al. Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. *Lancet Oncol.* 2010;11:1048-1056.

<sup>22</sup> Wright TC Jr, Stoler MH, Sharma A, et al. Evaluation of HPV-16 and HPV-18 genotyping for the triage of women with high-risk HPV+ cytology-negative results. *Am J Clin Pathol.* 2011;136(4):578-586.

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## The ATHENA Trial

The **cobas**® HPV Test has been clinically validated by the ATHENA study, which was the largest U.S. cervical cancer registration study ever conducted in the U.S. and involved more than 47,000 women. The study was designed to answer current medical and scientific questions about the importance of testing for high-risk HPV genotypes in cervical cancer screening and to provide clinical information about the specific HPV genotypes that place women at highest risk for developing cervical cancer. Results of ATHENA have been extensively published in scientific peer-reviewed journals and cited on numerous occasions by the medical community. Additional data and studies have shown when HPV DNA tests are used as the primary test and Pap cytology as secondary, significantly more cervical disease was identified compared to Pap cytology-based screening alone.<sup>23</sup>

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<sup>23</sup> Ronco G, et al. Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four European randomized controlled trials, *The Lancet* - 8 February 2014 (Vol. 383, Issue 9916, Pages 524-532).