

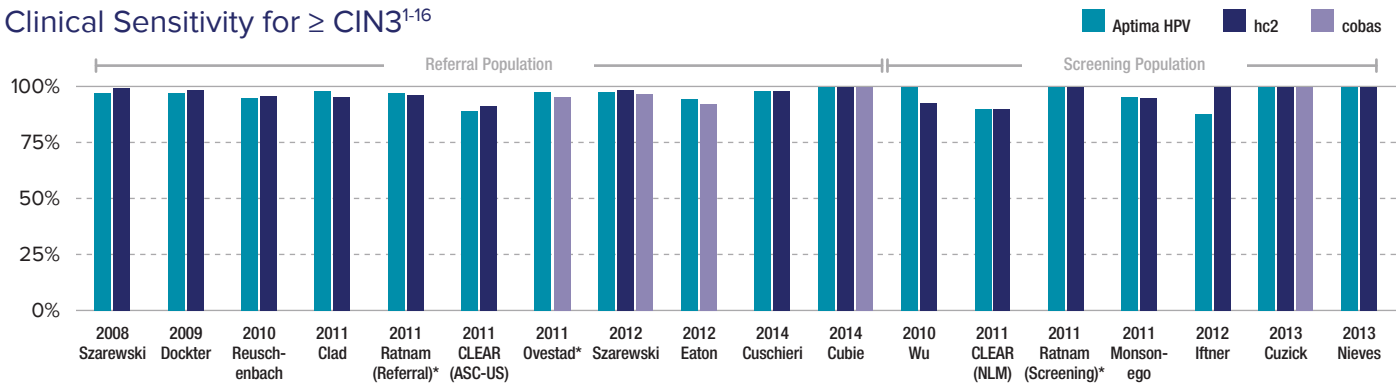
Aptima[®] HPV

E6/E7 mRNA-based tests compared to DNA-based tests.

Sensitivity

The Aptima HPV assay provides the same excellent sensitivity you've come to expect from DNA-based tests.

Clinical Sensitivity for \geq CIN3¹⁻¹⁶



*Clinical sensitivity for \geq CIN2.

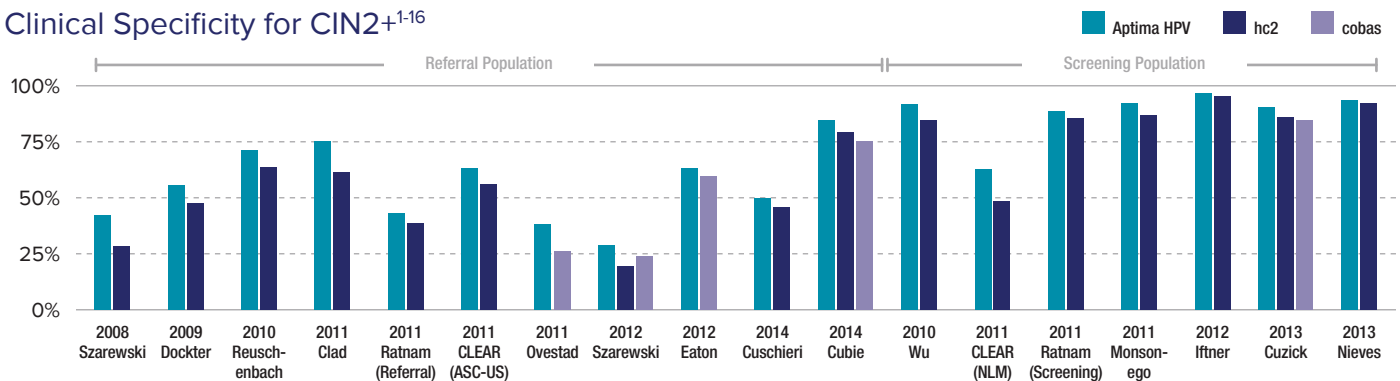
This chart is a representation of clinical data from multiple published sources. The clinical studies represented within these sources were conducted using different study designs with various assays.

Specificity

The Aptima HPV assay has been shown to deliver fewer false-positive test results compared with DNA-based tests helping to:

- Reduce uncomfortable patient conversations.
- Reduce the potential for overtreatment.

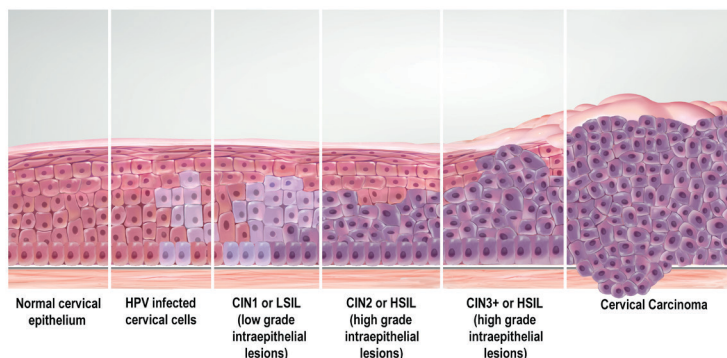
Clinical Specificity for CIN2+¹⁻¹⁶



This chart is a representation of clinical data from multiple published sources. The clinical studies represented within these sources were conducted using different study designs with various assays.

Disease Progression¹⁷

HPV mRNA levels increase while HPV DNA levels may decrease as cervical disease progresses towards cancer. Some HPV tests may provide false-negative results in more than 10% of the most severe cervical disease cases.¹⁸

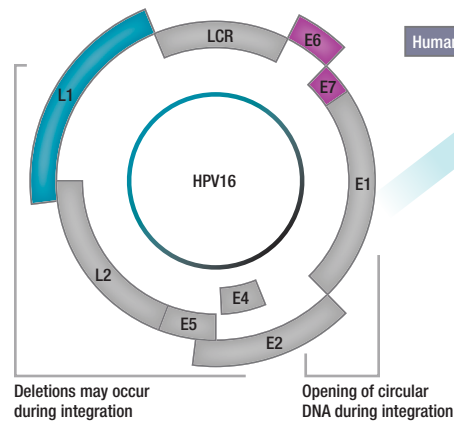


HPV DNA levels decrease
E6/E7 mRNA levels increase

Test Design

Aptima® HPV targets oncogenic activity of the HPV virus by detecting E6/E7 mRNA.⁶ Tests that target only the L1 gene are detecting an area that is not needed for disease progression and that can be deleted during integration. L1-based DNA tests have been shown to miss up to 10%-15% of the most severe disease cases.¹⁹⁻²¹

Why E6/E7



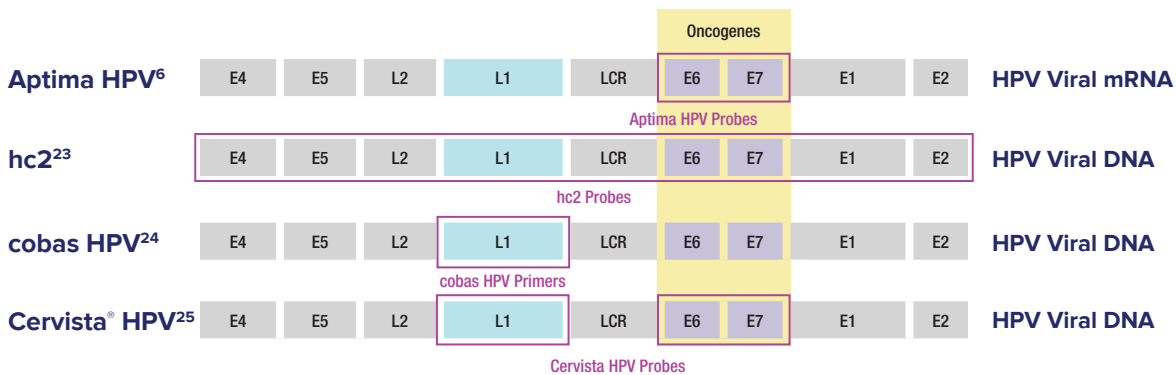
HPV genome – genotype 16 example

HPV Integration



- HPV DNA must linearize to integrate into human DNA.
- L1 region can be deleted.
- HPV assays that only target the L1 region are at risk for false negative results.²²

HPV Detection Strategies



| | Aptima HPV ⁶ | hc2 ²³ | cobas ²⁴ | Cervista ²⁵ |
|--|-------------------------|----------------------|---------------------|------------------------|
| Detects HPV mRNA | ✓ | | | |
| Targets the E6/E7 Oncogenes | ✓ | ✓ | | ✓ |
| No Cross Reactivity with Common Low Risk Types | ✓ | | ✓ | ✓ |
| Inclusion of Type 45 in Genotyping Assay | ✓ | | | |
| Genotyping in a Separate Reaction <small>Genotyping not recommended for ASC-US cytology result.²⁶</small> | ✓ | *no genotyping assay | | ✓ |
| Internal control | ✓ | | ✓ | ✓ |
| 3 years of Longitudinal data | ✓ | ✓ | ✓ | ✓ |

References: 1. Szarewski A, et al. *Cancer Epidemiol Biomarkers Prev.* 2008;17(11):3033-42. 2. Dockter J, et al. *J Clin Virol.* 2009;45(S1):S55-S61. doi:10.1016/S1386-6532(09)70009-5. 3. Reuschenbach M, et al. *Gynecol Oncol.* 2010;119(1):98-105. doi:10.1016/j.ygyno.2010.06.011. 4. Clad A, et al. *J Clin Micro.* 2011;49(3):1071-6. doi:10.1128/JCM.01674-10. 5. Ratnam S, et al. *J Clin Micro.* 2011; 49(2): 557-64. doi:10.1128/JCM.02147-10. 6. Aptima HPV Assay [package insert]. #503789. Hologic, Inc., 2013. 7. Ovestad IT, et al. *Gynecol Oncol.* 2011;123(2):278-83. doi:10.1016/j.ygyno.2011.07.024. 8. Szarewski A, et al. *J Clin Microbiol.* 2012;50(6):1867-73. doi:10.1128/JCM.00181-12. 9. Eaton B, et al. Comparison of the Aptima HPV assay and the cobas HPV test in an ASC-US population [abstract]. International Papillomavirus Conference; Nov. 30 – Dec. 6, 2012; San Juan, Puerto Rico. 10. Cuschieri K et al. *J Clin Virol.* 2014;59(2):104-8. doi:10.1016/j.jcv.2013.12.001. 11. Cubie HA, et al. *J Clin Pathol.* 2014;67(6):458-63. doi:10.1136/jclinpath-2013-202014. 12. Wu R, et al. *Int J Gynecol Cancer.* 2010;20(8):1411-4. doi:10.1111/IGC.0b013e3181f29547. 13. Monsonego J, et al. *Int J Cancer.* 2011;129:691-701. doi:10.1002/ijc.25726. 14. Iftner T et al. Comparison of Aptima and HC2 in a routine screening trial in Germany with follow up [abstract]. International Papillomavirus Conference; Nov. 30 – Dec. 6, 2012; San Juan, Puerto Rico. 15. Cuzick J, et al. *British J Cancer.* 2013;108(4):908–913. doi: 10.1038/bjc.2013.22. 16. Nieves L, et al. *Int J Gynecol Cancer.* 2013;23(3):518-8. doi:10.1097/IGC.0b013e318280f3bc. 17. Doorbar J. *J Clin Virol.* 2005;32(S1):7-15. doi:10.1016/j.jcv.2004.12.006. 18. Wright TC, et al. *Am J Obstet Gynecol.* 2012;206(1):46.e1-11. doi: 10.1016/j.ajog.2011.07.024 (Study included non-imaged ThinPrep®, cobas HPV, Hybrid Capture 2 assay) 19. de Sanjose et al. *Lancet Oncol.* 2010;11(11):1048-56. doi: 10.1016/S1470-2045(10)70230-8. 20. Wheeler CM, et al. *J Natl Cancer Inst.* 2009;101(7):475-87. doi:10.1093/jnci/djn510. 21. Coutlée F, et al. *J Med Virol.* 2011;83(6):1034-41. doi:10.1002/jmv.22081. 22. Morris BJ. *Clin Chem Lab Med.* 2005;43(11):1171-7. doi:10.1515/CCLM.2005.203. 23. Hybrid Capture 2 [package insert]. #L00665. QIAGEN, Inc. 24. cobas c4800 [package insert]. #05641268001-0N. Roche Molecular Systems, Inc. 25. Cervista HPV HR [package insert]. #15-3100.Hologic, Inc. 26. Massad L, et al. *J Low Genit Tract Dis.* 2013;17(5S1):S1-S27. doi:10.1097/LGT.0b013e318287d329.

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