1 Year

2 Years

3 Years

4 Years

5 Years

6 Years

7 Years

8 Years

9 Years

10 Years

Extensive Aptima® HPV Longitudinal Data[18,19,23,25,26]

The Aptima HPV assay has been validated and meets the cross-sectional criteria for clinical sensitivity and specificity for CIN2+, intralaboratory reproducibility over time, and interlaboratory agreement of the international guidelines for HPV test requirements for primary screening.[27,28]

Ten years of longitudinal data are available to ensure the long-term negative predictive value of the mRNA assay is similar to DNA assays.

Reid - 3 Years

There was a very low risk of CIN2+ (<0.3%) among women tested negative by either HPV assay, suggesting that the AHPV assay can be used safely and effectively as an adjunctive test in routine cervical cancer screening.

Cook - 4 Years

There was equivalent CIN2+ sensitivity for both DNA and mRNA assays and higher specificity for the AHPV assay, supporting its use for primary screening. The 48-month exit screening round can also support the safety of the assay over a four-year period.

Iftner - 6 Years

There were no statistical differences between the assays regarding their sensitivities to CIN2 or CIN3 lesions. The specificity and positive predictive value for CIN2 were significantly improved in the AHPV assay.

Forslund - 7 Years

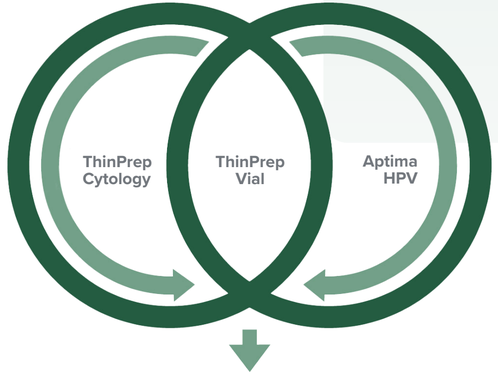
The observed performance of the HPV-mRNA assay suggests that the evaluated assay is non-inferior to HPV-DNA testing and can be used in cervical screening programmes that target women above 30 years of age for screening every 5-7 years.

Strang - 10 Years

There was a statistically similar detection of CIN2+ and CIN3+ among women who had a negative baseline HPV test by any of the assays used in the HPV FOCAL Trial.

A Complete Portfolio for all Cervical Cancer Screening Algorithms

Hologic is dedicated to advancing the accuracy and early detection of cervical cancer through clinical confidence and workflow efficiency. Just one patient sample is required for both cytology and molecular testing, and the follow-up reflex test can be directly performed from the same primary sample. The market- leading ThinPrep® Pap test and Aptima® HPV assay combined with digital cytology system, provide a comprehensive solution from sample collection to diagnosis.



Aptima® HPV Assay

Aptima® HPV 16 18/45 Genotype Assay

CE 2797 EC REP Hologic BV, Da Vincilaan 5, 1930 Zaventem, Belgium. Notified Body number wherever applicable.

Diagnostic Solutions | Hologic.com | euinfo@hologic.com

References: 1. CDC. Genital HPV Infection - CDC Fact Sheet. https://www.cdc.gov/std/hpv/HPV-FS-July-2017.pdf. Published July 2017. Accessed November 10, 2023. **2.** Tinelli A, et al. HPV viral activity by mRNA HPV molecular analysis to screen the transforming infections in precancer cervical lesions. Curr Pharm Biotechnol. 2009;10(8):767-771. **3.** Cuschieri K, et al. Human Papillomavirus Type Specific DNA and RNA Persistence- Implications for Cervical Disease Progression and Monitoring. J Med Virol. 2004;73(1):65 70.doi:10.1002/mv.20062. **4.** Doorbar J. Molecular biology of human papillomavirus infection and cervical cancer. Clin Sci (Lond). 2006 May;110(5):525- 41. doi: 10.1042/CS20050369. PMID: 16597322 **5.** Aptima HPV Assay [Package Insert] AW-22202-001 Rev 001 San Diego, CA; Hologic Inc 2023. **6.** Reboli M, et al. Extension of cervical screening intervals with primary human papillomavirus testing: observational study of English screening pilot data BMJ 2022;377 :068776 doi:10.1136/bmj-2021-068776. **7.** De Sanjose S, et al. Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. Lancet Oncol.2010;11(11):1048-1056. **8.** Hopenhayn C, et al. Prevalence of human papillomavirus types in invasive cervical cancers from 7 US cancer registries before vaccine introduction. J Low Genit Tract Dis. 2014;18(2):182-189.doi:10.1097/LGT.0b013e3182a577c7. **9.** Saslow D, et al. American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology Screening Guidelines for the Prevention and Early Detection of Cervical Cancer.Am J Clin Pathol 2012;137:516-542. **10.** Wu R, et al. Human papillomavirus messenger RNA assay for cervical cancer screening: the Shenzhen Cervical Cancer Screening Trial I. Int J Gynecol Cancer. 2010;20(8):1411-1414. **11.** Ratnam S, et al. Aptima HPV E6/E7 mRNA test is as sensitive as hc2 Assay but more specific at detecting cervical precancer and cancer. J Clin Microbiol. 2011;49 (2):557-564. **12.** Monsonego J, et al. Evaluation of oncogenic human papillomavirus RNA and DNA tests with liquid-based cytology in primary cervical cancer screening: the FASE study. Int J Cancer. 2011;129(3):691-701. 13. Iftner T, et al. GAST. German Aptima Screening Trial. Comparison of Aptima and hc2 in routine screening in Germany, Symposium presentation at EUROGIN 2012. **14.** Cuzick J, et al. Comparing the performance of six human papillomavirus tests in a screening population. British J Cancer. 2013;108:908-913. **15.** Nieves L, et al. Primary Cervical Cancer Screening and Triage Using an mRNA Human Papillomavirus Assay and Visual Inspection. Int J Gynecol Cancer. 2013;23:513-518. **16.** Iftner T, et al. Head-to-Head Comparison of the RNA-Based Aptima Human Papillomavirus (HIV) Assay and the DNA-Based Hybrid Capture 2 HPV Test in a Routine Screening Population of Women Aged 30 to 60 Years in Germany. J Clin Microbiol. 2015;53(8):2509-2516. **17.** Muangto T, et al. Experience of combined liquid based cervical cytology and highrisk HPV mRNA for cervical cancer screening in Thammasat University Hospital. Asian Pac J Cancer Prev. 2016;17(9):4409-4413. **18.** Reid et al. Human Papillomavirus Oncogenic mRNA Testing for Cervical Cancer Screening. Am J Clin Pathol, 2015;144:473-483. **19.** Cook et al, Aptima HPV Assay versus Hybrid Capture® 2 HPV test for primary cervical cancer screening in the HPV FOCAL trial J. Clin. Virol. 2017;87:23-29. **20.** Cook et al. Cobas 4800 HPV and Hybrid Capture 2 comparison at baseline and 48 months in the HPV Focal trial. Poster presented at IPV 2017. **21.** Reboli et al. A daunting challenge: Human Papillomavirus assays and cytology in primary cervical screening of women below age 30 years. EU J of Cancer (2015) 51, 1456-1466. **22.** White C, et al. Performance of the HPV E6/E7 mRNA Aptima HPV assay combined with partial genotyping compared with the HPV DNA Cobas 4800 HPV test for use in primary screening: Results from the CERVIVA HPV primary screening study in Ireland [published online ahead of print, 2023 Aug 26]. Int J Cancer. 2023;10.1002/ijc.34685. doi:101002/ijc.34685. **23.** Strang T, et al. Long-term cervical precancer outcomes after a negative DNA-or RNA-based human papillomavirus test result. Am J ObstetGynecol. 2021 Nov;225(5):511.1-511. e7, doi: 10.1016/ jajog.2021.05.038. **24.** Weston G, Dombrowski C, Harvey MJ, et al Use of the Aptima mRNA high-risk human papillomavirus (HR-HPV) assay compared to a DNA HR-HPV assay in the English cervical screening programme: a decision tree model based economic evaluation. BMJ Open. 2020 Mar 8;10(3):031303. **25.** Cook et al, Comparative performance of human papillomavirus messenger RNA versus DNA screening tests at baseline and 48 months in the HPV FOCAL trial. J. Clin. Virol, 2018;108:32-37. https://doi. org/10.1016/jcv.2018.09.004. **26.** Forslund O, et al. HPV-mRNA and HPV-DNA detection in samples taken up to seven years before dysplasia of cervix uteri. Int J Cancer. 2018; doi: 10.1002/ jc.31819. **27.** Meijer et al. 2009. Guidelines for human papillomavirus DNA test requirements for primary cervical cancer screening in women 30 years and older. Int. J. Cancer 124:516-520. **28.** Arbyn et al. 2020 list of human papillomavirus assays suitable for primary cervical cancer screening. Cl. Microb, and Inf. vol 27, issue 8, Aug 2021, 1083-1095

HOLOGIC®

The Aptima® HPV Assay Targets E6/E7 mRNA

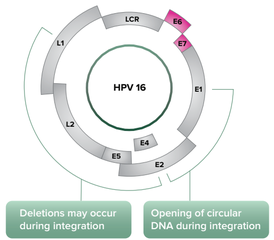
Identifies high-risk HPV infections that are present and active.

Nearly all sexually active women and men will have an HPV infection at some point in their lives. Very few will go on to develop cancer.[1]

Cervical Cancer Progression Model

E6/E7 mRNA expression is indicative of the HPV infections most likely to lead to disease.[2,3,4]

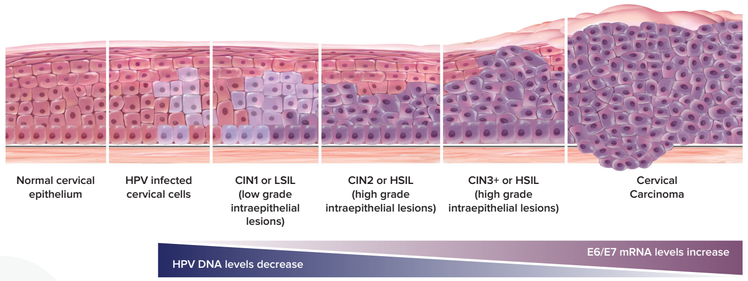
HPV Genome – Genotype 16 Example



HPV Viral mRNA

The Aptima HPV assay targets E6/E7 viral messenger RNA from 14 high-risk HPV types,[5] targeting the infections most likely to lead to cervical cancer and helping healthcare professionals maximise the benefits of screening while minimising potential harm.

Studies show mRNA identifies the presence and activity of a high-risk HPV infection. HPV DNA assays detect transient/inactive infection, of any of the 14 high-risk types.



HPV Detection Strategies[5,6]

DNA vs. mRNA assays

Improved Specificity	DNA Tests	mRNA Tests
High Sensitivity	✓	✓
Improved Specificity		✓
Low Colposcopy Referral rate		✓
Negative predictive value 10 years	✓	✓

A Targeted Approach with Aptima® 16 18/45 Genotype Assay

Aptima® HPV Detects All 14 HR HPV Genotypes[5]

Aptima HPV 16 18/45 Genotype Assay

16 | 18 | 45 | 31 | 51 | 52 | 33 | 58 | 35 | 39 | 68 | 56 | 59 | 66

HPV types 16, 18 & 45 associated with[7]

- Up to 75% of Squamous Cell Carcinomas
- 94% of HPV-related cervical Adenocarcinomas

HPV type 45[7,8]

- Only prevalent in 0.4% of women with normal cytology
- Third most common HPV type in invasive cervical cancer
- Identifies more women at risk for Adenocarcinoma, with minimal impact to colposcopy

HPV type 16 associated with[7]

- 62% of Squamous Cell Carcinomas
- 50% of Cervical Adenocarcinomas

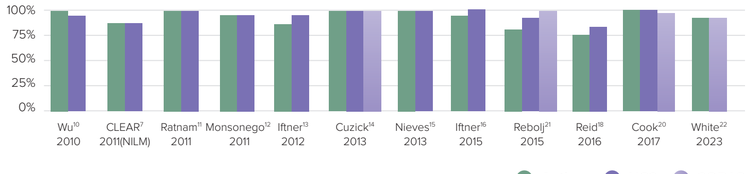
"The optimal screening strategy should identify those cervical cancer precursors likely to progress to invasive cancers (maximising the benefits of screening) and avoid the detection and unnecessary treatment of transient HPV infection and its associated benign lesions that are not destined to become cancerous (minimising the potential harms of screening)."

— Saslow, et al.[9]

Maximising Benefits and Minimising Harms in Screening and Referral Populations[5,9,10-22]

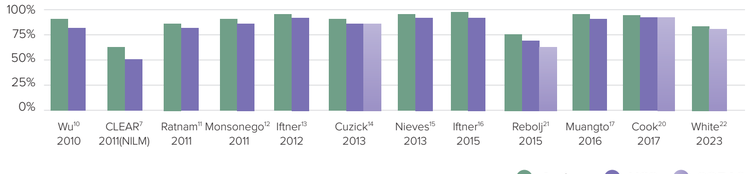
HPV Test Clinical Sensitivity for ≥CIN3

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



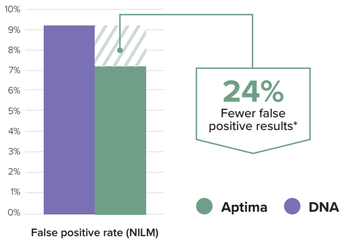
HPV Test Clinical Specificity for <CIN2

The Aptima HPV assay shows equivalent sensitivity to DNA-based tests with superior specificity.



Fewer false-positive results minimise the potential for over treatment.

The Aptima HPV assay shows less false positive results compared to DNA- based assays.



* Data adapted from the Aptima HPV assay package insert table 13[5]

Precision targeting identifies active and clinically relevant infection.

Superior performance provides long-term protection even after 10 years.[23]

Less false positive results and potential reduction in over treatment Improve the patient experience.[6]

Minimising unnecessary procedures and patient follow -up lead to health economic savings.[24]