Extension of cervical screening intervals with primary human papillomavirus testing: Observational study of English screening pilot data

The performance of the Aptima® mRNA-based HPV assay and the DNA-based assays is similar for the detection of CIN3+ and cervical cancer

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Introduction

- The English Cervical Cancer Screening Programme rolled-out HPV testing as the primary screening method in December 2019.
- The programme routinely invites women aged 25-49 every 3 years and women aged 50-64 every 5 years for cervical screening by HPV testing.
- Women who were HPV positive at screening are referred for colposcopy following cytology triage.

This study assessed the detection of CIN3+ and cervical cancer after two rounds of screening with either HPV testing or liquid based cytology depending on the women's age and whether the HPV test was DNA or mRNA based.

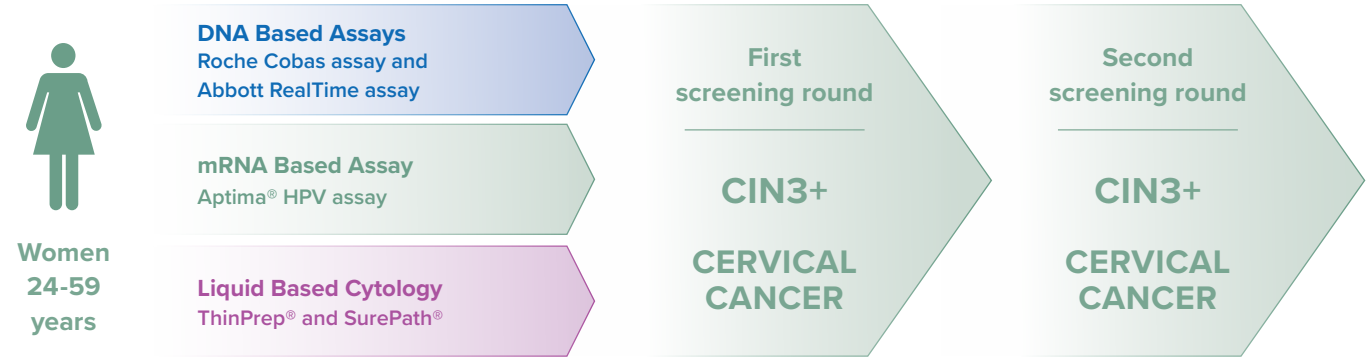
Study Design

- The study is based on real-world data collected from the English Primary HPV screening pilot.
- Women were followed up across two consecutive cervical screening rounds.
- Data represented more than four million women.
- The detection of CIN3+ and cervical cancer after a positive screening test in both screening rounds was evaluated for women screened with cytology and HPV testing.
- The difference between the mRNA-based Aptima HPV assay versus the DNA-based assays was also evaluated.

Main outcome measure

Screening Method

The detection of CIN3+ and cervical cancer after a negative HPV test.



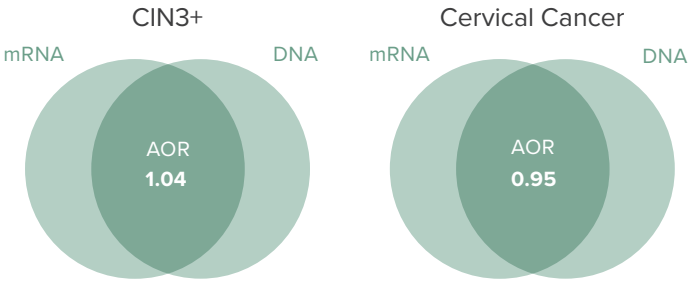
Results

1,262,510
Women 24-59 years

	First round		Second round	
	Women screened	Detected	Women screened	Detected
	HPV 379,717	**CIN3+** 5,532 **Cancer** 290	**HPV** 212,868	**CIN3+** 241 **Cancer** 2
	Cytology 882,793	**CIN3+** 8,673 **Cancer** 493	**Cytology** 282,461	**CIN3+** 1,197 **Cancer** 56

For women younger than 50 years, second round detection of CIN3+ was significantly lower after a negative HPV screen in the first round than after cytology testing, as was the risk of cervical cancer. HPV testing is more efficient to detect CIN3+ and cancer vs cytology.

Performance of mRNA verses DNA



95% CI (0.96 to 1.12)

95% CI (0.67 to 1.34)

The performance of both mRNA and DNA tests are equivalent to detect CIN3+ and cervical cancer.

Odds ratio (OR) is a relative measure of effect which allows comparison between study groups. If the outcome is the same in both groups the OR will be 1. The odds ratio was adjusted (AOR) to account for womens age, laboratory site and differences in socioeconomic deprivation.

Interval cancers diagnosed between the first and second screening rounds after a negative screen.

Interval Cancer 24-49 - hazard ratio

mRNA	*DNA*
0.35	**0.40**
95% CI, 0.04 to 2.84	**95% CI**, 0.12 to 1.33

The differences in the detection of CIN3+ and cancer between the different HPV tests are small.

In the three to five years after a negative HPV test, the risk of CIN3+ or interval cancer was not increased for the Aptima® HPV assay compared with the DNA-based tests.

One interval cancer was diagnosed after a negative test with the Aptima HPV assay versus 12 cancers after negative Cobas or RealTime tests, resulting in an adjusted ratio of **0.51** (95% CI, 0.07 to 3.91) for the Aptima HPV assay versus the DNA-based tests.

Conclusion

- The Aptima HPV mRNA test and DNA based assays have a similar performance for the detection of CIN3+ and cervical cancer, the same screening intervals can be used for both assay types.
- The low risk at three years of CIN3+ and Cervical Cancer after a negative HPV test (DNA or mRNA based) supports the extension of the three year screening interval to at least five years.
- A shorter recall interval of three years is advisable for women after early recall and who test negative and have no cytological abnormalities.

"HPV Screening Programmes have had challenges around the choice of DNA or mRNA screening tests. A major systematic review recently concluded that, compared with validated DNA assays, the Aptima mRNA-based assay was similarly sensitive, but more specific for CIN2+, Rebolj and colleagues' findings broadly agree with and add to this body of evidence"[2]

References:

1. Rebolj M, Cuschieri K, Mathews CS, et al. Extension of cervical screening intervals with primary human papillomavirus testing: observational study of English screening pilot data. BMJ 2022; 376:e068776. **2.** Canfell K, Smith M, Saville, M et al. HPV screening for Cervical cancer is reaching Maturity. BMJ 2022;377:o1303

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Aptima® HPV Assay