

How much could primary HPV testing reduce cervical cancer incidence and morbidity in England?

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Background

From April 2011 triage using HPV was introduced into the English screening programme with the aim of reducing the number of repeat cytology tests required.

HPV as primary screening is currently being piloted. The low 6-year cumulative incidence rate of CIN3+ among women negative for HPV suggests 6 yearly screening intervals are safe and effective.

Objectives

To assess the potential impact of **primary HPV** testing on incidence and morbidity of cervical cancer by estimating the proportion of cervical cancer diagnosed within 6 years of a negative cytology.

Methods

- Population-based case-control study of prospectively recorded data on cervical screening in England between 1988 and 2012.
- The study includes **8774** cases of invasive cervical cancer diagnosed between April 2007 and March 2012 aged 25 to 64 and **17341** controls individually matched on age and area of residency.
- **Advanced stage cancers** are defined as those known to have cancer FIGO stage 2+ and those treated by radiotherapy or chemotherapy ± radical hysterectomy (N=2256).
- We used **conditional logistic regression** to estimate the odds ratio of developing cancer within 6 years of a negative cytology test which resulted in a routine recall (i.e. next invited to cytology 3 or 5 years later), overall and by FIGO stage.
- **Assumptions:** 1) at the time of the negative cytology an HPV test would have been positive for 95% of interval cancers; 2) all these women would have attended follow-up in a timely manner; and 3) that colposcopy would have treated the disease before it became cancer.
- Official cancer statistics for England (MB1 series 2010) reported a total of **1,801 cases aged 25-64 in 2010**, corresponding to a **rate of 13.0 per 100,000 women**.

Overall

Out of 8,774 women with cancer, 38.8% had a negative cytology within 6 years of diagnosis compared to 69.9% of controls.

Table 1. Odds ratio of developing cervical cancer within 6 years of a cytology test

Test result within 6yrs of diagnosis ¹	Controls	Women with cancer	OR (95% CI)
At least one negative	12,122 (69.9%)	3,404 (38.8%)	0.24 (0.22-0.25)
Test but no negatives	1,201 (6.9%)	1,187 (13.5%)	0.88 (0.80-0.97)
No tests	4,018 (23.2%)	4,183 (47.7%)	Reference

¹Excludes tests within 6 months of diagnosis

In a co-testing scenario, assuming HPV testing has 95% sensitivity among those with negative cytology, introducing HPV as the primary screening test would identify earlier a maximum of 37% of current cases of cervical cancer in this age group. 21% of the cancer diagnosed earlier would be advanced stage.

The sensitivity of cytology in England is high. The risk of developing cancer within 6 years of negative cytology is **76%** (OR 0.24, 95% CI 0.22 to 0.25) less than the risk of those with no tests in the 6 years before diagnosis.

If HPV were to become the only screening test, we would also need to account for cancers found by cytology that would be missed by HPV testing. Assuming that HPV testing would miss 3% of those identified by cytology, this would result in the prevention or earlier diagnosis of 32.6% of cervical cancer cases in England.

In Europe, on average, the sensitivity of cytology is believed to be around 53% (Cuzick et al. Int J Cancer 2006). Assuming the proportion of negative tests in women without cancer remains the same as those presented in Table 1, and that coverage is similar to coverage in England, we estimate that the proportion of women with cancer and a negative test within 6 years of diagnosis would rise to **50.8%**.

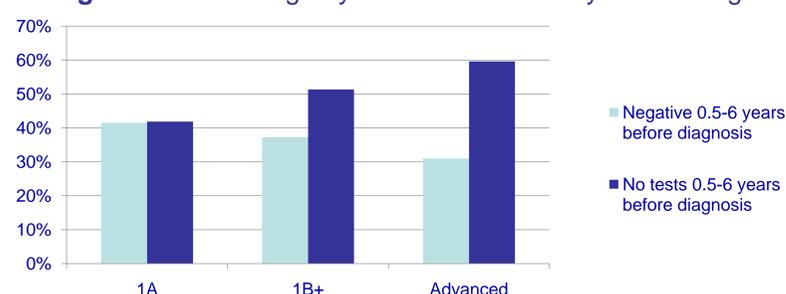
Results

By FIGO Stage

Stage was available for 90% of cases (n=7911). Of those with known stage 41.6% were FIGO stage 1A cancers.

Amongst 2256 women with **advanced cancer** 31.0% had a negative test within 6 years of diagnosis, equivalent to 8.0% of all cancers.

Figure 1. FIGO stage by test result within 6 years of diagnosis



Conclusions

Introducing HPV as the primary screening test could prevent or lead to earlier diagnosis of almost a third of current cases aged 25 to 64 in England, equivalent to **587 cancers** (or 4.2 per 100,000 women) per year in England.

In countries where cytology screening programmes are less rigorously quality assured, about half the cases would be prevented or identified earlier.