HPV Testing in Cervical Screening - What’s Taking So Long?

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Why is HPV testing an attractive option for cervical cancer screening?

* More sensitive than the Pap test
* More “upstream” in the carcinogenic process, thus enabling a longer safety margin for screening intervals
* Can be automated, centralized, and be quality-checked for large specimen throughput
* May be more cost-effective than cytology if deployed for high volume testing, such as in primary screening
* A more logical choice for screening women vaccinated against HPV infection

E Franco, National Symposium on Infectious Agents & Cancer
Toronto, March 11, 2010

HPV in Primary Testing

Prediction #1
- HPV is more sensitive (but less specific) than a Pap test
- HPV can detect lesions earlier than a Pap test
HPV for cervical cancer screening (HPV FOCAL): Complete Round 1 results of a randomized trial comparing HPV-based primary screening to liquid-based cytology for cervical cancer

Lisa S. Lippert1, B. van den Brule1, Laura N. S. Gorter2, Gisela C. van den Brule1, K. C. E. van der Velden1, Lienke M. M. van der Velden1, R. W. M. van der Linden3, J. E. N. J. v. der Linden3, A. van der Linden3, M. E. J. van Steenbergen1, and W. J. K. van den Brule1

Int. J. Cancer: 140, 440-448 (2017)
• HPV based screening resulted in significantly lower CIN2+ at 48 mos compared with LBC
• Cumulative CIN2+ incidence showed no significantly different disease detection
• Cumulative colposcopy referral rates were similar
• Women who were HPV negative at baseline had a significantly lower risk of CIN2+ compared with cytology-negative women
**HPV in Primary Testing**

**Prediction #1**
- HPV is more sensitive (but less specific) than a Pap test
- HPV can detect lesions earlier than a Pap test
- NPV = Longer Screening Intervals
- Less loss to follow up (?)

**HPV in Primary Testing**

**Prediction #2**
- HPV testing is a more logical choice for screening women vaccinated against HPV infection

"HPV vaccination will make the existing approach of high-frequency screening by cytology too costly and inefficient"

EL Franco Vaccine: 2006

**The screening population is changing.**
Screening Test Performance

STATS 101
Prevalence affects the predictive value of any test. The same diagnostic test will give you different information according to the clinical setting in which you apply it.

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>PPV 95%</th>
<th>PPV 50%</th>
<th>PPV 25%</th>
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<tr>
<td>1%</td>
<td>99%</td>
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Falling Prevalence Leads To False Positive Results

Early effect of the HPV vaccination programme on cervical abnormalities in Victoria, Australia: an ecological study

Summary

Background: Introducing a school-based human papillomavirus (HPV) vaccination programme with the quadrivalent HPV vaccine for all women aged 12-26 years between 2007 and 2008. The purpose was to assess cervical abnormalities in the population.

Methods: Data from the Victorian Cervical Cytology Register between 2005 and 2015 were used to assess the incidence of abnormal cytology, defined as high-grade cervical abnormalities (HGCAs), among women in several immunisation strata. The HPV vaccine was initially introduced in 2007 and the second dose was given in 2008. The effectiveness of the programme was estimated using a difference-in-difference approach.

Results: After the introduction of the vaccination programme, there was a 96% reduction in the incidence of HGCAs in women aged 12-17 years. No similar temporal decline was recorded for CIN2 or CIN3.

Conclusion: This is the first longitudinal assessment of the impact of HPV vaccination on cervical abnormalities in an immunised population. The results support the effectiveness of the vaccination programme in reducing the incidence of cervical abnormalities.
Prevalence of cervical disease at age 20 after immunisation with bivalent HPV vaccine at age 12-13 in Scotland: retrospective population study

Tim Palmer, Lynn Wallace, Kevin G Pollard, Kate Dochiar, Chris Robertson, Kim Kavanagh, Margaret Cruickshank

- Routine immunisation using the bivalent HPV vaccine against high grade cervical disease was found to be highly effective
- In the setting of high uptake and a catch-up programme, unvaccinated women also show a reduction in disease, possibly because of herd protection

British Journal of Cancer (2016) 114, 582–589

HPV immunisation and cervical screening—confirmation of changed performance of cytology as a screening test in immunised women: a retrospective population-based cohort study

J J Palmer, M McDougal, K G J Pollard, K Kavanagh, K Dochiar, M Cruickshank, S Connor, S Nisar and C Robertson

- Significant reductions in PPV for CIN2+ were observed.
- Significant increase in the number of women referred to colposcopy to detect one case of CIN2+

Conclusions: The lower incidence of disease in vaccinated women alters the key performance indicators of cervical cytology

British Journal of Cancer (2016) 114, 582–589

HPV in Primary Testing

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