THE IMPACT OF HPV PRIMARY SCREENING ON COLPOSCOPY.

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BAC Annual Scientific Meeting
October 2015
Aims:

An evaluation of primary HPV screening commenced in Sheffield in May 2013.

This lecture considers both the prior impact of HPV triage and test of cure on colposcopy services in Sheffield and throughout the UK, and the impact of Primary HPV screening.
Historic Events Related to HPV

- **1907** - Viral nature of genital warts first recognised (*Ciuffo*)
- **1972** - Connection between HPV and skin cancer (*Ginsburg-Jabłońska*)
- **1976** – Hypothesis that HPV associated with cervical cancer (*zur Hausen*)
- **1983** – HPV 16 detected in cervical cancer (*zur Hausen*)
- **1984** - HPV 18 detected in cervical cancer (*zur Hausen*)
- **2006** – Sentinel Sites Study (*Kitchener*)
- **2008** – HPV Immunisation introduced in UK
- **2011** – Introduction of HPV triage and test of cure
- **2013** – Introduction of HPV Primary Screening
Borderline changes or low-grade dyskaryosis tested for high-risk human papillomavirus (HR HPV).

- If HR HPV positive – Refer to Colposcopy

- If HR HPV negative - Discharge to routine screening.
Introduction of HPV Test of Cure  
Sheffield: Feb 2008

If both cytology and HPV testing are negative at six months then return to routine recall

Where
If cytology negative HPV positive refer to colposcopy

[The risk of CIN 2+ over the next two years quoted as <0.5%.]
HPV Triage

Caused anxiety amongst colposcopists:

>>Essentially the limiting factor is colposcopy<<

- If normal colposcopy should you biopsy?
- If normal colposcopy what should you biopsy?
- If normal are you happy to directly discharge to routine screening?
- What is going to happen to my colposcopy referrals!!
Introduction of Primary HPV Screening
Sheffield: April 2013

- Samples Tested for HPV
- If HPV –ve discharged to routine recall
- If HPV +ve Reflex cytology Performed.
- If hrHPV +ve cytology negative – Repeat in 12 months.
- If hrHPV +ve with abnormal cytology – Refer to colposcopy.
Amendments to HPV Primary Screening

- April 2013 Introduced

- April 2014 – Started referring HPV 16/18 cytology negative at 12 months

- April 2015 – Started referring HRHPV Other cytology negative at 24 months.
The Prediction: Year 1: 2013

- Overall HPV positive rate, in Sheffield = 16% of the screened population
- 25% of the 16% had abnormal cytology thus referred to colposcopy.
- Provided a referral rate to colposcopy of 4% of the screened population continues – unchanged since the introduction of primary HPV screening.
Data from the ARTISTIC study and other non-UK studies suggest that over a 24-month period, 66% of women will cure their HPV infection but 33% will not.

Therefore at 24 months, we can expect 4% of the screened population to still be HPV positive and have to be referred to colposcopy.

This 4% will represent a doubling of referral to the Sheffield colposcopy clinic.
The Prediction Year 2: 2014

- **Protocol change** - From May 2014 all the women who are still HPV16/18 positive / cytology negative will be seen at 12 months rather than at 24 months.

- Based on the number of screening samples for Sheffield, 30,000/year, we expect an increase in referrals of 400 cases for next year.

- Approximately 35-50% of the women with HPV16/18 cytology negative will still be HPV16/18 positive 12 months later.
The Prediction Year 3: 2015

- From May 2015 we will have to see the women who are non 16/18 positive (HPV Other) women who are still cytology negative at 24 months.
- Accounts for approx. 800 new referrals.
- In addition we need to see the 400 HPV16/18 positive cases from the women invited or recalled to the screening programme in 2014.
- Thus giving a total number of extra referrals in 2015 of 1200.
And the Lead Colposcopist Says

‘Oh My GOD’
‘Oh My GOD’
‘Oh My GOD’

(or indeed something a little less polite!!)
The Reality
Sheffield Screening Time Lines

- Introduced direct referral February 2008
- Introduced HPV triage March 2008: We had always seen women with mild dyskaryosis on first sample but women with borderline had to have persistent changes i.e. second or third borderline or worse
- Introduced HPV primary screening April 2013
  - April 2014: Started referring HPV16/18 cytology negative at 12 months
  - April 2015: Started referring HR-HPV O cytology negative at 24 months
- Introduced Separate Symptomatic clinic (PCB Clinic) June 2014
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<tbody>
<tr>
<td><strong>New Referrals</strong></td>
<td>Total</td>
<td>Total</td>
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<td>New referrals where referral reason is recorded</td>
<td>1823</td>
<td>1595</td>
<td>1565</td>
<td>1605</td>
<td>1652</td>
<td>1355</td>
<td>1358</td>
<td>941</td>
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<td><strong>Negative cytology HRHPV</strong></td>
<td>282</td>
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<td><strong>Moderate or worse referrals</strong></td>
<td>539</td>
<td>444</td>
<td>402</td>
<td>374</td>
<td>224</td>
<td>287</td>
<td>405</td>
<td>339</td>
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<tr>
<td><strong>Borderline or mild referrals</strong></td>
<td>997</td>
<td>775</td>
<td>674</td>
<td>803</td>
<td>781</td>
<td>689</td>
<td>720</td>
<td>391</td>
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<tr>
<td><strong>Number of women undergoing treatment</strong></td>
<td>613</td>
<td>516</td>
<td>525</td>
<td>421</td>
<td>412</td>
<td>477</td>
<td>456</td>
<td>400</td>
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<tr>
<td><strong>Number of women on follow up</strong></td>
<td>374</td>
<td>502</td>
<td>676</td>
<td>643</td>
<td>1164</td>
<td>830</td>
<td>669</td>
<td>639</td>
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Effects on All Referrals:

- HPV Triage
- HPV Primary screening
- Direct Referral
- Symptomatic Clinic
- Jade Goodie

Graph showing trends for:
- All referrals
- Cytology referrals
- Cytology and HPV pos cytology negative referrals
- Clinical referrals

Data spans from 2003/4 to 2014/15.
Effects on All Referrals

- Other
- Clinical - non urgent
- Clinical - urgent
- Glandular
- Invasive
- Severe
- Moderate
- Mild
- Borderline
Effects on Cytology +ve or –ve hrHPV +ve

Effect of HPV Triage

Effect of HPV Primary Screening
Effects on Cytology +ve or –ve hrHPV +ve
Effects on Cytology Referral

Effect of HPV Triage

Effect of HPV Primary Screening
Effects on Appointments

Trends in Type of Appointment

- New cytology referrals
- Follow up - treatment
- Follow up - colposcopy
- Total
Effects on Appointments

Total Number of Appointments

Percentage Type of Appointment

Follow up - colposcopy
Follow up - treatment
New cytology referrals
Effects on Number of Cytology Referrals:

**Average number of cytology referrals**

- HPV Primary Screening
- HPV Triage

**Average no. referrals cytology + HPV pos/cyto negative**

- HPV Primary Screening


Notes:
- Average number of cytology referrals
- Average no. referrals cytology + HPV pos/cyto negative
Effects on See & Treat Rates:

S&T rate

Introduction of Zedscan
Effects on Waiting Times

High Grade seen within 2 weeks

Low Grade seen within 4 weeks
Key Challenges: HPV Triage

**Impact on colposcopy:**

- Impact on workload related to local colposcopy practice and local referral guidelines for women with low-grade dyskaryosis.
- Largest increase in referrals seen in laboratories referring on second mild dyskaryosis and third borderline change.
- Sheffield saw an initial increase in low grade referrals, but a vast reduction in follow up rates due to discharge of women with normal findings to routine recall and the discharge of women to primary care for performance of test of cure.
- Increase in workload therefore temporary, as seen in most clinics throughout the UK, and referrals and workload have since stabilised.
Key Challenges: HPV Triage

Impact based on lab reporting:

- Colposcopy units practising under the umbrella of laboratories with a higher percentage of low-grade referral rates found a lesser increase in workload as, when tested for hrHPV, those found to be negative were discharged to routine recall as opposed to referral for colposcopy.

- Both pilot and sentinel site studies demonstrated significant variations between cytology laboratories.

- Different HPV platforms used at different laboratory sites.

- Different cytology platforms used at different laboratory sites.

- Difficult to ascertain the precise impact of differing HPV platforms on colposcopy referral rates.

- Studies have identified significant variation between assays, particularly in cytologically negative samples, which might result in a significant variation in the number of colposcopy referrals.
Key Challenges: HPV Triage

Impact on colposcopists:

- if colposcopy was normal should a biopsy be performed, and if so, what should they biopsy when no acetowhite changes were apparent.
- Individuals confidence in their own colposcopy ability also came into question.
- Not all colposcopists were, or indeed are, comfortable discharging low-grade hrHPV, colposcopy negative women to routine recall without a biopsy proven absence of CIN.
- new HPV pathways rendered national guidelines inadequate; colposcopy databases in need of upgrading; and KC65 data collection, used to nationally monitor the performance of colposcopy clinics on local, regional and national levels, no longer fit for purpose.
Key Challenges: Primary HPV Screening

- hrHPV rates vary across the sites at between 11% and 16%, and the overall referral rate to colposcopy currently lies at around 4-5%.
- We must also consider the use of different HPV platforms on referral numbers.
- We must consider individualised practices in cytology laboratories.
- We must accept as a possible consequence that prior knowledge of hrHPV status might naturally lead to overcall of low-grade dyskaryosis.
- We already know that practices vary throughout laboratories in the UK hence we must be vigilant, particularly when considering low-grade referral rates, subsequent colposcopy referral rates, and patient outcomes.
Key Challenges: Primary HPV Screening

- As for colposcopists, training, education, and reaccreditation of practice perhaps lie at the forefront of our speciality as essentially in all these pathways, although little discussed, colposcopy remains the rate limiting factor.
- Audit and benchmarking of individuals and colposcopy services on the whole will be essential for us to maintain the excellent cervical cancer screening programme we currently provide within the UK.
- Colposcopy is no longer the second screening tool in the cervical screening programme, but the third when used as an adjunct to HPV testing and cytology.
- What seems likely however, in the next few years, is that new technologies or, a fourth screening tool, will become increasingly utilised throughout colposcopy services to improve the detection of high grade CIN at first visit; improve the management of women treated at first visit; and improve the management of women who do not have high grade CIN.
Key Challenges: Primary HPV Screening

- We have yet to receive any significant information as regards to colposcopy outcome data in terms of detection of high grade CIN in primary HPV screening and the study is only just obtaining data on the percentage of women who have persistent high risk HPV infection, so results must be patiently awaited.

- In the long-term however we also remain uncertain as to the effect of HPV immunisation programmes on HPV screening and colposcopy referral rates in England, thus future workload and consequent workforce planning in colposcopy will remain for the time being difficult to predict.