 Primary HPV screening: The current state of the science - UK

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Disclosures

• No financial relationships or conflict of interest to disclose
HPV primary screening – UK

Talk will cover:

- HPV testing – triage and post treatment ‘test of cure’
- Sentinel site Project
- Preliminary Findings
- Implementation plan
Triage of Borderline/low grade abnormalities

England, Wales, Northern Ireland
Implemented HPV triage in 2012/3

Scotland-did not implement triage
so acceptable to refer for colposcopy if:
Borderline nuclear change x 3
Low grade dyskaryosis x 2
Management of BNA/ Low grade Dyskaryosis

If Colposcopy adequate and normal:
- Discharge to GP for routine cytology 3-5 years

If Colposcopy Low grade/ biopsy proven CIN 1:
- Repeat cytology, HPV, colposcopy in 12 months
- Community cytology and HPV in 12 months

If Colposcopy High grade:
- Treat
Effects of HPV triage on colposcopy

Increase in low grade referrals → workload /capacity issues

Increase in High grade referrals and treatments → earlier detection and management of HG disease

Reduction of follow-ups if pathway followed
Approved HPV platforms in UK

Qiagen Hybrid Capture 2 High-Risk HPV DNA test
Abbott RealTime High Risk HPV test
Roche Cobas 4800 HPV system
Hologic Aptima HPV Assay
Hologic Cervista HPV HR test
BD Onclarity HPV test
Cepheid Xpert HPV assay
HPV Testing in Wales – current status

HPV Test of Cure (Sept 14/Dec 15)
HPV triage of low grade abnormalities (May 16)

Other factors

• Vaccinated women just entering the screening programme
• Cervical smear numbers falling
  • Extended intervals
  • Reduced repeat smears
• Reduced prevalence of CIN in screened population
Scotland

No data – no pilot sites or early implementers.

Several meetings to put together a full business case as instructed by Scottish government.

If approved, will go to full primary HPV implementation.
Northern Ireland

Triage and TOC - follow England guidance

Will see how England and Wales get on.

Have established a committee – but will not be implementing HPV primary screening before 2019.
13,000 women attending for primary screening Invited to take part in research by smear taker

Cytology based primary screening (CWUIH)

HPV DNA (cobas HPV) HPV E6/E7 mRNA (APTIMA HPV)

Residual smear material (<20mls)

HPV DNA Positive

Second Round Test
Cytology
HPV 16/18 (cobas HPV) E6/E7 mRNA (APTIMA HPV) p16/Ki-67 (CINtec PLUS) Methylation makers (CADM1 MAL mir124)

Patients longitudinally followed for up to 10 years

Final clinical outcome after 10 years

Managed by routine CervicalCheck guidelines

Republic of Ireland: CERVIVA HPV Primary Screening Pilot
Evidence supporting HPV Primary screening

ARTISTIC (A Randomised Trial in Screening To Improve Cytology)
Manchester based trial, ages 20-65
Evaluated effectiveness of HR HPV screening
Compared LBC and HPV testing
Over 3 screening rounds, HPV-PS
  • Showed increased sensitivity to detect CIN 2+
  • Gave longer protection after a negative result
Six English sentinel sites

Initially evaluated HPV triage

For primary HPV screening:
- Only partial conversion to maintain cytology expertise
- Local models for conversion to primary HPV screening are variable
- Different hr-HPV testing platforms
  - Roche – Norwich, Sheffield, Manchester
  - Genprobe – Bristol, Liverpool
  - Abbot – Manchester, London
- Triage by reflex cytology
  - Thin prep or Surepath

Bristol
Manchester
Sheffield
Liverpool
London
Norwich
Pilot started in April 2013
Amendments to Algorithm for primary HPV screening

April 2014 – started referring HPV 16/18 cytology negative to colposcopy at 12 months

April 2015- started referring HR-HPV other cytology negative at 24 months
HPV Primary Screening Pilot
Colposcopy Management Recommendations Algorithm

Version 2.0 January 2015

Colposcopy Examination

Inadequate

Index HR-HPV +ve
- cytology 3low grade

Repeat colposcopy
in 12m

Consider LLETZ –
patient choice

Index HR-HPV +ve
- cytology 2high grade

LLETZ

Normal and adequate

No biopsy or biopsy <CIN1

Index HR-HPV+ve/
cytology 3low grade

Discharge to 3y recall

Index HR-HPV+ve/
cytology 2high grade

Discussion at MDT
within 2m

Abnormal Biopsy CIN+

Manage according to
‘abnormal colposcopy
examination’ see
page 2
HPV Primary Screening Pilot
Colposcopy Management Recommendations Algorithm

Version 2.0 January 2015

Colposcopy Examination

Abnormal

CIN1 untreated

Recall in 12m

HR-HPV -ve

3y recall

HR-HPV +ve

Cytology negative – 12m recall

HR-HPV -ve

Cytology negative – Refer to colposcopy

HR-HPV +ve

Cytology negative – Refer to colposcopy

HR-HPV +ve/ cytology normal or abnormal

3y recall

Cytology abnormal – Refer to colposcopy

HR-HPV +ve/ cytology normal or abnormal

12m recall

Cytology abnormal – Refer to colposcopy

HR-HPV -ve

12m repeat test

HR-HPV +ve

Cytology abnormal – Refer to colposcopy

CGIN

Treatment

Recall in 6m

HR-HPV -ve

3y recall

HR-HPV +ve

Cytology negative – Refer to colposcopy

HR-HPV +ve/ cytology normal or abnormal

Refer to colposcopy

HR-HPV +ve/ cytology abnormal

12m recall

Cytology negative – Refer to colposcopy

*Women who have been adequately treated (complete excision margins) for CGIN or SMILE. Women without complete excision margins will receive annual HPV testing for 10 years.
**After 3 years women will begin a new screening episode according to the HPV Primary Screening Protocol Algorithm.

2 of 2
Primary HPV Screening

• All women aged 25 – 65

• 314,244 women underwent primary HPV testing to Dec 2015

• 651,307 women underwent primary cytology testing to July 2015

• hr-HPV positive rates
  • Average 12.7%, range 10.5 – 15.0%
  • HPV 16/18 4.0%
  • Age 24-29 27.6%
  • Age 50-64 5.5%
Infection with multiple hr-HPVs are associated with higher rates of abnormal cytology.
## Changes in colposcopy referrals in Sheffield

<table>
<thead>
<tr>
<th></th>
<th>% of women screened referred to colposcopy</th>
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</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>4</td>
</tr>
<tr>
<td>12 month retest</td>
<td>1</td>
</tr>
<tr>
<td>24 month retest</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>7</td>
</tr>
<tr>
<td>Primary cytology</td>
<td>4</td>
</tr>
</tbody>
</table>

**Primary hr-HPV screening increases referral to colposcopy by 68%**
Changes in colposcopy referrals at Sheffield

hr-HPV Primary Screening

hr-HPV Triage

Jade Goody

Symptomatic clinic

All referrals
Cytology referrals
Cytology and HPV pos cytology negative referrals
Clinical referrals

IFCPC 2017 World Congress
Proportions of non-negative cytology primary and non-primary cases July 2013 to May 2016

- Negative non-primary HPV = 90.19%
- Negative primary HPV = 93.81%
Northwick Park (London) experience

Colposcopy referral rates 2013 - 2016

<table>
<thead>
<tr>
<th>Year</th>
<th>Primary HPV</th>
<th>Non-primary HPV</th>
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<tbody>
<tr>
<td>2013 %</td>
<td>5.54</td>
<td>6.46</td>
</tr>
<tr>
<td>2014 %</td>
<td>6.03</td>
<td>5.61</td>
</tr>
<tr>
<td>2015 %</td>
<td>7.18</td>
<td>4.85</td>
</tr>
<tr>
<td>2016 %</td>
<td>7.41</td>
<td>4.49</td>
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National implementation of HPV primary screening

Public Health Minister for England announced HPV primary screening will be implemented into English cervical screening programme by 2019
Primary HPV screening implementation: Laboratory reconfiguration

<table>
<thead>
<tr>
<th>Objective</th>
<th>Weight</th>
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<tbody>
<tr>
<td>Quality</td>
<td>18</td>
</tr>
<tr>
<td>Staffing Feasibility</td>
<td>15</td>
</tr>
<tr>
<td>Effective IT Connectivity</td>
<td>15</td>
</tr>
<tr>
<td>Cost of Safe Delivery</td>
<td>15</td>
</tr>
<tr>
<td>Linkage to Local Services</td>
<td>10</td>
</tr>
<tr>
<td>Delivery During Transition</td>
<td>6</td>
</tr>
<tr>
<td>Adequate Clinical Support</td>
<td>6</td>
</tr>
<tr>
<td>Service Sustainability</td>
<td>6</td>
</tr>
<tr>
<td>Specimen Transport Feasibility</td>
<td>5</td>
</tr>
<tr>
<td>Commissioning Feasibility</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
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Options appraisal for laboratory reconfiguration

Current system
59 laboratories across England
4. Centralisation of HPV testing and cytology testing as a single seamless service, using:
   - a minimum number of 4 to 5 centralised services performing both HPV testing and cytology screening (option 4a)

   a maximum number of 10 to 15 centralised services performing both HPV testing and cytology screening (option 4b)
Future UK-National Screening Committee Decisions

• Primary HPV Geno-typing,
• Extended screening intervals following Primary HPV testing implementation,
• Screening HPV positive women beyond the age of 65
• Self sampling and how this impacts on coverage
• How to deal with increase in colposcopy workload

Expected decisions Summer 2017
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