The Scottish HPV vaccine programme - why is it a success story?

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Cervical cancer by deprivation
Scotland

Cancer of the cervix uteri (ICD-10 C53)
Age-standardised incidence and mortality rates by SIMD 2012 deprivation quintile

Uptake 3 doses vaccine,
HPV vaccines in Scotland

- Girls aged 12-13 (S2) routinely immunised from September 2008
- Catch-up campaign for girls up to 18 (2008-2011)
  - Some of these may have had prior HPV exposure

- Bivalent
  - HPV 16 and 18  Sept 2008-Aug 2012
  - AS04-type adjuvant

- Quadrivalent
  - HPV 6, 11, 16 and 18  Sept 2012- present
  - Alum adjuvant
# Vaccine uptake

<table>
<thead>
<tr>
<th>S2 in school year</th>
<th>Dose 1</th>
<th>Dose 2</th>
<th>Dose 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008/09</td>
<td>94.5</td>
<td>93.8</td>
<td>92.4</td>
</tr>
<tr>
<td>2009/10</td>
<td>93.6</td>
<td>92.5</td>
<td>90.9</td>
</tr>
<tr>
<td>2010/11</td>
<td>92.9</td>
<td>92.0</td>
<td>90.1</td>
</tr>
<tr>
<td>2011/12</td>
<td>94.2</td>
<td>93.4</td>
<td>91.4</td>
</tr>
<tr>
<td>2012/13</td>
<td>94.4</td>
<td>93.4</td>
<td>91.4</td>
</tr>
<tr>
<td>2013/14</td>
<td>94.4</td>
<td>92.5</td>
<td>88.8</td>
</tr>
</tbody>
</table>

Source: CHSP/SIRS

- Routine uptake > 90%
- Catch-up vaccine uptake from 65-75%
Adverse event monitoring

• Two systems
  – UK - MHRA – yellow card system
  – Scotland – SMR01 system
• ‘Blue hands’
• ‘Pain at injection site’
• No increase in over 60 conditions associated with either vaccine
  – Includes POTS, CFS and other neurological conditions
• Excellent safety profile
Impact of not having an AEFI strategy

Vaccine uptake rates (%)

- Dose 1
- Dose 2
- Dose 3

Birth cohort year:
- n=8598 1994
- n=8267 1995
- n=8165 1996
- n=8002 1997
- n=7977 1998
- n=7731 1999
- n=7705 2000*

Eligible for free vaccination before suspension of proactive recommendation
Data linkage ensures robust analyses

"NCCIAS" - Colposcopy clinical system

"SCCRS" - Screening system

"CHSP-S" - Immunisation records

CHI

Screening population

CIN2+ Biopsies
20-24 year olds

Incidence & Prevalence
HPV related Disease

Secondary testing
Residual LBC
20 year olds

SCCRS = Scottish Cervical Call and Recall System
NCCIAS = National colposcopy clinical information and audit system
CHSP-S = Child Health Systems Programme - School
Scottish HPV Ref Lab (SHPVRL)

- Women attending their 1st cervical smear appointment (from age 20 in Scotland)
- HPV DNA testing of ~ 1000 anonymised residual liquid based cytology (LBC) samples
- Genotyping data for HPS surveillance since 2009 with current assay
  - High risk or putative high-risk types: 16,18,26,31,33,35,39,45,51,52,53,56,58,59,66,68,73,82
  - Low risk types: 6,11,42,43,44 & 70
  - Generates numeric value for HPV type(s) in sample
HPV type from anonymised LBC samples, 2009-2014
non-vaccinated vs fully vaccinated
### Evidence of herd protection in unvaccinated females?

<table>
<thead>
<tr>
<th>Study year</th>
<th>HPV 16 or 18</th>
<th>HPV31 or 33 or 45</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>2009</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>2010</td>
<td>1.128</td>
<td>(0.95, 1.339)</td>
</tr>
<tr>
<td>2011</td>
<td>1.045</td>
<td>(0.846, 1.291)</td>
</tr>
<tr>
<td>2012</td>
<td>1.175</td>
<td>(0.879, 1.57)</td>
</tr>
<tr>
<td>2013</td>
<td><strong>0.669</strong></td>
<td><strong>(0.468, 0.956)</strong></td>
</tr>
</tbody>
</table>
Effectiveness of < 3 doses

<table>
<thead>
<tr>
<th>No. of Doses</th>
<th>Unadjusted VE [% (95 CI's)]</th>
<th>P value</th>
<th>Adjusted VE [% (95 CI's)]</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV 16/18</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td></td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>25.1 (-5.7, 48.0)</td>
<td>0.1093</td>
<td>48.2 (16.8, 68.9)</td>
<td>0.0075</td>
</tr>
<tr>
<td>2</td>
<td>36 (15.3, 52.3)</td>
<td>0.0023</td>
<td>54.8 (30.7, 70.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>3</td>
<td>70.2 (65.0, 74.7)</td>
<td>&lt;0.0001</td>
<td>72.8 (63.8, 80.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HPV 31/33/45</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td></td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>-15.9 (-74.6, 25.9)</td>
<td>0.4978</td>
<td>-1.62 (-85.1, 45.3)</td>
<td>0.9588</td>
</tr>
<tr>
<td>2</td>
<td>41.4 (12.1, 62.8)</td>
<td>0.0143</td>
<td>48.3 (7.6, 71.8)</td>
<td>0.0287</td>
</tr>
<tr>
<td>3</td>
<td>55.5 (45.1, 64.1)</td>
<td>&lt;0.0001</td>
<td>55.2 (32.6, 70.2)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Effect of vaccination on cervical intraepithelial neoplasia (CIN)

- Assessment of screened cohort for women born 1988-1994
  - 1991-94 – post-vaccine
- Omission of small number of episodes (referred to colposcopy before screening)
- Inclusion of incident abnormal (CIN1-3) cases in 1st year after 1st screen, by cohort year
- Poisson regression model adjustment for birth cohort and deprivation
- **3495** individuals censored to December 2015
<table>
<thead>
<tr>
<th></th>
<th>CIN1</th>
<th></th>
<th>CIN2</th>
<th></th>
<th>CIN3</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1</td>
<td>0.75 (0.45-1.25)</td>
<td>0.270578</td>
<td>1.10 (0.74-1.63)</td>
<td>0.64964</td>
<td>1.08 (0.7-1.68)</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td>1.03 (0.74-1.43)</td>
<td>0.854938</td>
<td>0.92 (0.67-1.27)</td>
<td>0.60862</td>
<td>0.80 (0.55-1.16)</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>0.82 (0.69-0.98)</td>
<td><strong>0.027616</strong></td>
<td>0.49 (0.41-0.59)</td>
<td><strong>&lt;0.0001</strong></td>
<td>0.41 (0.33-0.51)</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Birth year</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1988</td>
<td>1</td>
<td>0.90 (0.76-1.07)</td>
<td>0.242296</td>
<td>0.99 (0.84-1.18)</td>
<td>0.9177</td>
<td>0.80 (0.66-0.97)</td>
</tr>
<tr>
<td>1989</td>
<td></td>
<td>0.86 (0.72-1.03)</td>
<td>0.098124</td>
<td>0.93 (0.78-1.11)</td>
<td>0.43691</td>
<td>0.95 (0.79-1.14)</td>
</tr>
<tr>
<td>1990</td>
<td></td>
<td>0.74 (0.59-0.92)</td>
<td><strong>0.006367</strong></td>
<td>0.89 (0.72-1.11)</td>
<td>0.30228</td>
<td>0.94 (0.75-1.19)</td>
</tr>
<tr>
<td>1991</td>
<td></td>
<td>0.67 (0.53-0.85)</td>
<td><strong>0.000973</strong></td>
<td>0.70 (0.55-0.90)</td>
<td><strong>0.00477</strong></td>
<td>0.69 (0.52-0.9)</td>
</tr>
<tr>
<td>1992</td>
<td></td>
<td>0.76 (0.60-0.95)</td>
<td><strong>0.016985</strong></td>
<td>0.81 (0.64-1.03)</td>
<td>0.08217</td>
<td>0.57 (0.43-0.75)</td>
</tr>
<tr>
<td>1993</td>
<td></td>
<td>0.62 (0.47-0.82)</td>
<td><strong>0.000576</strong></td>
<td>0.61 (0.45-0.82)</td>
<td><strong>0.00128</strong></td>
<td>0.47 (0.33-0.68)</td>
</tr>
<tr>
<td><strong>Deprivation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SIMD1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SIMD2</td>
<td></td>
<td>0.88 (0.75-1.03)</td>
<td>0.109791</td>
<td>0.82 (0.70-0.95)</td>
<td>0.00875</td>
<td>0.96 (0.81-1.14)</td>
</tr>
<tr>
<td>SIMD3</td>
<td></td>
<td>0.82 (0.70-0.97)</td>
<td><strong>0.020784</strong></td>
<td>0.61 (0.52-0.73)</td>
<td><strong>&lt;0.0001</strong></td>
<td>0.74 (0.62-0.9)</td>
</tr>
<tr>
<td>SIMD4</td>
<td></td>
<td>0.76 (0.64-0.91)</td>
<td><strong>0.00245</strong></td>
<td>0.64 (0.53-0.76)</td>
<td><strong>&lt;0.0001</strong></td>
<td>0.61 (0.5-0.75)</td>
</tr>
<tr>
<td>SIMD5</td>
<td></td>
<td>0.78 (0.66-0.92)</td>
<td><strong>0.003065</strong></td>
<td>0.45 (0.37-0.54)</td>
<td><strong>&lt;0.0001</strong></td>
<td>0.43 (0.34-0.53)</td>
</tr>
</tbody>
</table>

Table 1: Relative risk of CIN 1, 2 and 3 by number of doses of HPV vaccine received adjusted by birth cohort year and deprivation.
So why is it successful?

• Local implementation group

  Collaboration with the national project to lead and co-ordinate the local implementation of HPV vaccine programme by:

  – monitoring the introduction of the programme and provision of reports to the National Project Manager as appropriate
  
  – local implementation of scheduling of appointments
  
  – ensuring the dissemination of publicity and that information resources are available locally for young people, parents and professionals
  
  – advising local services and professionals on the evidence base for the HPV vaccine programme
  
  – ensuring that local teaching/training is provided to those providing immunisation
  
  – ensuring infrastructure is in place to order, store and distribute HPV vaccine in accordance with legislation and manufacturers recommended storage requirements
Good communication with Local Boards

Example presentation
together we can fight cervical cancer
There is now a vaccine to help protect against cervical cancer

Together we can fight cervical cancer
From 1 September 2008 girls aged 12 to 17 will be offered the Human Papilloma Virus (HPV) vaccine

Together we can fight cervical cancer
Most girls will hear more about the HPV immunisation programme through their school.

Together we can fight cervical cancer.
Girls who have already left school will be contacted later in the year by their local NHS

Together we can fight cervical cancer
Girls will hear more about it through TV, radio, cinema, press and online advertising during August and September.

The ‘Hero Girl’ features in the TV advertising, posters and leaflets.

Together we can fight cervical cancer.
One-day **roadshows** will also take place throughout Scotland

The Public Health Minister with girls from the TV advert and girls who will be immunised this year, at the first roadshow in Paisley

Why not go along to the [city] roadshow at [venue] on [date] to find out more about the HPV immunisation programme…

Together we can fight cervical cancer
Find out more at

www.fightcervicalcancer.org.uk

or call the NHS helpline

0800 22 44 88
Choice of vaccine

• Cervarix chosen as ‘cancer vaccine’
• Avoided sexualisation i.e. no discussion relating to genital warts
• Fears of reduced uptake in Catholic schools not realised
• BUT
• Many girls not sure what HPV is and how relates to screening
Jade Goody effect

Top 25 of most influential people, Heat magazine (2007)

Told of diagnosis in Big Brother house in August 2008

Metastasis Feb 2009

Married partner 22 Feb 2009

Died March 2009 Aged 27
**Strengths:**
Coordination
Communication
Local buy-in
Scottish Immunisation Programme (SIP)

**Weaknesses:**
Better catch-up uptake – GP services not effective (30%)

**Opportunities:**
Project and programme management key to success
Collaboration
SHINe

**Threats:**
Adverse events
Anti-vax campaigners
Conclusions

• Government support
• Importance of local implementation groups
• Importance of school-based programme
  – Teacher buy-in
  – School nurses
• Considered communication plan
• ‘Cancer vaccine’
  – Cervical, vulval, penile, anal and oropharyngeal
• Raised awareness of disease
• Dissemination of impact across all media
HPV vaccine ‘reduces cervical cancer symptoms’

A young girl receives the HPV vaccine. Picture: Sanofi Pasteur MSD/PA