HPV vaccination in Australia

Dr Julia Brotherton  
Medical Director, NHVPR  
VCS
Background: HPV

• Genital HPV is
  – Sexually transmitted
  – Extremely common
  – Usually asymptomatic and transient

Sex=HPV exposure
Monogamous women with first partner are at high risk of HPV


Figure 1. Cumulative incidence of any genital HPV infection associated with a first sex partner. The X-axis shows the no. of months from the time of first reported vaginal intercourse with a male partner (women were censored at the reported date of a second male sex partner).

49% at 3 years
Figure 2. Cumulative risk of newly detected HPV infection (any type) by age groups in women in a cohort study in Bogotá, Colombia. Adapted from [6], Copyright 2004 by the Infectious Diseases Society of America, with permission from The University of Chicago Press.
HPV and cancer

MAJOR STEPS IN CERVICAL CARCINOGENESIS

NORMAL CERVIX

HPV INFECTED CERVIX

Persistence (1 to 10 years)

CIN-3/ PRE-CANCERS

Invasion

CANCER

Infection

Clearance

Regression

MILD CYTOLOGIC ABNORMALITIES

Figure 12. Prognosis of HPV prevalent infections in Guanacaste: all carcinogenic types combined. CIN: Cervical intraepithelial neoplasia [49].

FX. Bosch et al. / Vaccine 26S (2008) K1–K16
Cumulative incidence of cervical intraepithelial neoplasia grade 3 and cancer (≥CIN-3) over a 10-year period in 7285 women younger than 30 years of age (from Khan et al JNCI 2005)
5 most frequently detected HPV types cervical cancer

Clifford 2003

Australian meta-analysis

Clifford HPV 16+18=67.3%  Australia HPV 16+18=80.1%
Human papillomavirus prevalence among indigenous and non-indigenous Australian women prior to a national HPV vaccination program

Suzanne M Garland\textsuperscript{1,2,3,4,\dagger}, Julia ML Brotherton\textsuperscript{1,5,6,\dagger}, John R Condon\textsuperscript{7}, Peter B McIntyre\textsuperscript{5}, Matthew P Stevens\textsuperscript{1}, David W Smith\textsuperscript{8} and Sepehr N Tabrizi\textsuperscript{1,2,3,4,\dagger}, for the WHINURS study group
The incidence of persistent HPV-16 infection was 3.8 per 100 woman-years at risk in the placebo group and 0 per 100 woman-years at risk in the vaccine group (100 percent efficacy; 95 percent confidence interval, 90 to 100; P<0.001). All nine cases of HPV-16-related cervical intraepithelial neoplasia grade 2 or 3, adenocarcinoma in situ, or cervical cancer related to HPV-16 or HPV-18.

Subjects were followed for an average of 3 years after receiving the first dose of vaccine or placebo. Vaccine efficacy for the prevention of the primary composite end point was 98% (95.89% confidence interval [CI], 86 to 100) in the per-protocol susceptible population and 44% (95% CI, 26 to 58) in an intention-to-treat population of all women who had undergone randomization (those with or without previous infection). The estimated vaccine efficacy against all high-grade cervical lesions, regardless of causal HPV type, in this intention-to-treat population was 17% (95% CI, 1 to 31).
National HPV Vaccination Program

- Australian Government funded from 2007
  - 12 - 13 yo girls on an ongoing basis through schools
  - 2 year “catch-up” program for 13-26 yo women through schools, GPs and community based programs
- 2007-2009 target population ~ 2.4 million
- Quadrivalent vaccine used to date
- National HPV Vaccination Program Register established
Notified coverage Victoria

As held at Sept 2011. Excludes consumers who have opted off.
HPV vaccine coverage Victoria, 12-17 year old girls
Equity in screening vs vaccination

• Victoria, Australia
  (Barbaro, Brotherton and Gertig, Med J Aust 2012; 196 (7): 445)
Notified coverage 18-26 yo by State

Monitoring vaccine impact in Australia

- **Immediate:**
  - HPV infection – sentinel surveillance model, research studies
  - Genital warts – sentinel surveillance model (+ hospital data)

- **Short-medium term:**
  - Incident Pap abnormalities – Cervical Screening Registers
  - CIN2/3 histopathology - Cervical Screening Registers
  - RRP – Australian Paediatric Surveillance Unit

- **Long term:**
  - Cervical cancer, other anogenital cancer, oropharyngeal cancer
  - Cancer registries

HPV prevalence monitoring

- Two studies in progress:
  - VACCINE: 1500 Vic women 18-25 recruited via Facebook. Survey data, verification of HPV vax status and self collected vaginal swab. (CIA S Garland. Funding VCA)
  - VIP: 1300 women aged 18-24 presenting to FPA clinics for Pap test in NSW, Vic and WA. Sentinel site model using baseline data from large sites involved in baseline WHINURS study*. Survey data, verification of HPV vax status and Dr collected cervical sample. (CIA S Tabrizi. Funding C Council and NHMRC)

http://www.biomedcentral.com/1741-7015/9/104
Interim VIP results
Women aged 18-24 years VIP n= 446

The differences remain highly significant when adjusted for age, OCP use, smoking, SES and remoteness.

In press, Tabrizi et al, JID
Genital warts sentinel surveillance

- 8 public sexual health services
- New patients only 2004-2010 - first visit to clinic. N=135,000
- No prior history of genital warts.

Women <=26 years of age (2007)


Updated data presented courtesy of B Donovan
Proportion of Australian-born women with genital warts by age group, 2004-2011

Updated data presented courtesy of B Donovan
Proportion of Australian-born heterosexual men with genital warts by age group, 2004-2011

Updated data presented courtesy of B Donovan
Proportion of Australian-born MSM with anogenital warts, 2004-2011

p=0.098

Updated data presented courtesy of B Donovan
Almost 90% decline in genital warts in women and HSM < 21 years since July 2007

Adjusted OR pre and post July 2007 (no. of sex partners)

- Females <21
  - Pre: 1.11 (0.9-1.4)
  - Post: 0.44 (0.3-0.6)
- MSW <21
  - Pre: 1.32 (0.9-1.9)
  - Post: 0.42 (0.3-0.6)

Non residents excluded


©2011 by BMJ Publishing Group Ltd
## AIS/CIN2+ Histopathology: Smoothed Curves

**Victoria 2003-2009 by Age Group**

- **17 years & younger**
  - Apparent decline in youngest age groups
  - Significant post vax women <18 years
  - Incidence Rate Ratio per quarter 0.87, p=0.01
  - Difference in pre/post IRR per quarter 1.14, p=0.05

- **18-20 years**

- **21-25 years**

- **26-30 years**

- **31 years and older**

---

**J Brotherton et al.**

Trends in high-grade abnormalities, 2000-2011, Victoria

Source: VCCR statistical report 2011, *in press*
Trends in high-grade abnormalities, 2004-2010, Australia

<table>
<thead>
<tr>
<th>Year</th>
<th>&lt;20</th>
<th>20-24</th>
<th>25-29</th>
<th>All ages</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>14.5</td>
<td>20.3</td>
<td>17.7</td>
<td>7.7</td>
</tr>
<tr>
<td>2005</td>
<td>13.2</td>
<td>20.2</td>
<td>17.7</td>
<td>7.7</td>
</tr>
<tr>
<td>2006</td>
<td>13.2</td>
<td>19.9</td>
<td>17.7</td>
<td>7.8</td>
</tr>
<tr>
<td>2007</td>
<td>11.6</td>
<td>18.9</td>
<td>17.8</td>
<td>7.7</td>
</tr>
<tr>
<td>2008</td>
<td>10.8</td>
<td>21.3</td>
<td>19.3</td>
<td>8.3</td>
</tr>
<tr>
<td>2009</td>
<td>8.9</td>
<td>19.9</td>
<td>19.0</td>
<td>8.1</td>
</tr>
<tr>
<td>2010</td>
<td>7.8</td>
<td>19.7</td>
<td>19.9</td>
<td>8.5</td>
</tr>
</tbody>
</table>

Source: CSA report 2009-2010, AIHW
Pap screening and vaccination

• 234 Victorian women 18-28 CATI survey 2009
• 94% heard of Pap tests, 60% ever had one
• Among women aware of the vaccine, 96% knew Pap tests still needed if vaccinated
• **No** vaccinated woman who hadn’t had a Pap test said ‘I don’t need Pap tests because I’ve been vaccinated’
• **All** vaccinated women who hadn’t had a Pap test intended to have a PT in future

Brotherton and Mullins, Cancer Epi 2012
But....

- 19% thought the ‘vaccine prevents all cervical cancers if given early enough’ (7.7% unsure)
- 9% thought the ‘vaccine can be used to treat women who have cervical cancer or cervical abnormalities’ (14% unsure)
- 17% of unvaccinated women agreed that ‘Knowing the vaccine is available makes me less likely to have a Pap test in the future’ (2% unsure)
- 8% of vaccinated women agreed that ‘Having had the vaccine makes me less likely to have a Pap test in the future.’ (1% unsure)
- 31% of women agreed that ‘I am not really concerned about getting cervical cancer’ (5% unsure)
  - No difference by vaccination status; 33% vaccinated vs 30% unvaccinated; p=0.7
Where to now?

• Disease control
  – **Optimise current program**
  – **Male vaccination** 12-13 yo school program + catch up two cohorts
    • Start date? Communication strategy? Uptake?
  – **Nonavalent vax V503** in Phase III RCT (Types 6, 11, 16, 18, 31, 33, 45, 52, 58) Game changer?
  – **Renewal** of cervical screening program underway

• Surveillance
  – **Data linkage** vaccine registers with PTRs
  – **VACCINE** study is HPV **typing** 500 **CIN3** lesions from vaccine age eligible Victorian women using laser capture microdissection technique – prospective specimens from VCS and RWH lab included
  – **Cancers** not yet routinely typed
  – **RRP surveillance** and typing commenced APSU Oct 2011
  – **Males** HPV surveillance strategy - ?urine testing
Acknowledgements

• VIP investigators (CIA Sepehr Tabrizi, CIB Julia Brotherton, CIC Rachel Skinner, AIs Deborah Bateson, Kathleen McNamee, Maria Garefalakis, John Kaldor, Suzanne Garland.) Special thanks to Bette Liu and Eleanor Cummins for work on the interim analysis.

• Young Women’s Health Survey co-investigators – Bette Liu, Basil Donovan, John Kaldor, Marion Saville

• Basil Donovan

• Dorota Gertig, Marion Saville, Genevieve Chappell and Bianca Barbaro

The National HPV Vaccination Program Register is owned by the Commonwealth Department of Health and Ageing and operated by the Victorian Cytology Service www.hpvregister.org.au

Contact details: Julia Brotherton jbrother@vcs.org.au