Innovations in screening for cervical cancer: The Australian Example

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Impact of cervical screening in Australia

In 1991 Australia introduced an organised program of 2-yearly Pap smears in women aged 18-69 years.


- 45% in women 25–49
- 54% in women 50–69
- 50% in women 70+ years
- No change in women aged 20–24 years

Rates plateaued in all age groups in the early-mid 2000’s

Smith M and Canfell K, MJA 2016
National HPV Vaccination Program

- Australia was the first country in the world to roll out a publicly-funded National HPV Vaccination Program in 2007
- Routine vaccination of 12-13 year females from 2007
- 2-year school and GP-based catch-up in 12-26 years
- Used quadrivalent HPV vaccine (HPV 16, 18, 6, 11)
- By 2016, all women aged ≤35 have been offered vaccination

Coverage data from National HPV Vaccination Register Sept 2011
Predicted drop in HPV 16 prevalence after HPV vaccination implementation in Australia 2006

Adapted from: Smith et al. Int J Cancer 2008
Observed impact in Australia
Females, early twenties

Vaccine-included HPV types
77%↓
Tabrizi S/Brotherton J et al JID 2012

Warts
73%↓
Smith M et al JID 2014

Confirmed CIN2/3
34%↓
Further impact of male vaccination

- From 2013, males aged 12-13 vaccinated at school
  - 2-year catch-up to Year 9.
- Via herd immunity, will also provide additional benefits to females


Predicted reduction in HPV incidence in females in Australia, with female-only vaccination (Strategy 1) vs. both-sex vaccination (Strategy 3)
A woman’s lifetime risk of cervical cancer now depends on vaccination...

If vaccinated, what type of vaccine?

Vaccinated after HPV exposure?

How many doses?

Unvaccinated but benefiting from herd immunity?

...how should this be factored into cervical screening decisions?
Renewal of the National Cervical Screening Program

• Announced November 2011
• Aim: “To ensure that all Australian women, HPV vaccinated and unvaccinated, have access to a cervical screening program that is acceptable, effective, efficient and based on current evidence.”
• The government's Medical Services Advisory Committee (MSAC) commissioned a systematic review of the international evidence & modelled evaluation of health outcomes and costs
  • i.e. a linked evidence approach to guide decision-making
• Process guided by an expert reference group, the Renewal Steering Committee
• Evidence report released April 28th 2014

http://www.cancerscreening.gov.au
Evidence base for HPV-based screening:

Screen-negative women

Cumulative risks over 5 years in the US Kaiser Permanente cohort according to HPV/cytology status at baseline.

Data on >1M women aged 30-64 years.

Gage et al JNCI 2014
Evidence base for HPV-based screening: Protection against invasive cervical cancer

Pooled data on invasive cervical cancer outcomes from four European trials: 176,000 women

Ronco et al, Lancet 2014
Evidence base for HPV-based screening:

Screen-positive women

- HPV 16 +ve at baseline: “Higher risk”
- Else HPV 18 +ve: “Intermediate risk”
- Else HPV other +ve: “Low risk”
- Oncogenic HPV -ve: “Low risk”

Cumulative CIN3+ in 20,514 women (median age 34 years)

Khan MJ, Castle PE, et al. JNCI 2005
Final recommendation for the renewed program in Australia

HPV screening

- Negative HPV16/18
  - Routine screening in 5 years
  - Cytology negative or low grade
    - 12 month HPV FU
      - Refer to colposcopy if any HPV +ve
      - Otherwise return to routine screening
    - Cytology high grade
      - Use the same strategy, whether or not a woman has been offered vaccination against HPV 16,18
- Other oncogenic HPV
  - Cytology high grade
    - Reflux liquid-based cytology for colposcopy management
  - Cytology negative or low grade
    - Colposcopy (diagnostic referral)

Use the same strategy, whether or not a woman has been offered vaccination against HPV 16,18.
Predicted improvements in cervical cancer rates
Final modelled estimates of long term impact, taking account of clinical guidelines

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<th>Current cytology-based program</th>
<th>Renewed HPV-based program</th>
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<tr>
<td></td>
<td>If HPV vaccination had not been introduced</td>
<td>For cohorts offered vaccination as 12 year olds</td>
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<tr>
<td>Cervical cancer cases</td>
<td>850</td>
<td>353</td>
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<tr>
<td>Cervical cancer deaths</td>
<td>227</td>
<td>94</td>
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Predicted annual numbers of cervical cancer cases and deaths for the pre-renewal NCSP and the renewed NCSP (showing differences in case numbers and relative percentage differences)

*Using the female Australian population as predicted for 2017.

Simms et al., PloSONE (in press)
HPV self-collection for underscreened women

- HPV testing on self-collected cervico-vaginal samples ("self-collection") will be funded for unscreened and underscreened women.
- Must be facilitated by a clinician who also offers mainstream cervical screening, and is restricted to women aged 30–74 years who have never been screened or are overdue for cervical screening by 2 years or more.

- A single self-collected test at age 30 will reduce a woman’s lifetime risk of cervical cancer by 40%.
- But regularly screening in the renewed program will reduce lifetime risk by >90%.
SCREENING APPROACHES FOR VACCINATED POPULATION: COMPASS TRIAL

Karen Canfell,1 Michael Caruana,1 Jessica Darlington-Brown,1 Philip Castle,1 Dorota Gertig,2 Julia Brotherton,2 Stella Heley,2 David Wrede,3 Jeffery Tan3 and Marion Saville2

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2Victorian Cytology Service Inc., Melbourne, Australia
3The Royal Women’s Hospital, Melbourne, Australia
• Compass is a large scale RCT of 5-yearly HPV vs. 2.5 yearly liquid-based cytology (LBC) screening in women aged 25-69 years in Victoria, Australia

• It is designed to provide evidence on:
  ➢ Test positivity and colposcopy referral rates in the first and subsequent rounds of screening
  ➢ Baseline CIN2+ detection in the first screening round
  ➢ Long term protection against CIN3+ (primary endpoint)
  ➢ Relative effectiveness of alternate triaging strategies for HPV positive women
Two phases:

Phase 1 (pilot) of 5,000 women, recruitment from Oct 2013 - Nov 2014.
- Baseline screening round completed, including 6 month follow-up for histology outcomes

Phase 2 (main trial) of 121,000 women:
- Recruitment commenced Jan 2015
- Stratified by cohort age-eligibility for vaccination
- 450 clinics recruiting across Victoria
- Recruitment rate 85%
Pilot results: HPV prevalence

Australia, pre-vaccination (2005-8)

1Reanalysis of data from Garland et al. BMC Medicine 2011 [Testing with LA]

Note: Data adjusted for women with both HPV16and/or18 and OHR infections
Pilot results: HPV prevalence

WHINURS (2005-8) vs. Compass (2014)

HPV 16/18

82% lower

HPV OHR

1Reanalysis of data from Garland et al. BMC Medicine 2011 [Testing with LA]

Note: Data adjusted for women with both HPV16and/or18 and OHR infections
Summary: The transformation of the National Cervical Screening Program

Pap smears
- 2-yearly; age 18-20 to 69 years
- 26 tests in a lifetime
- Reduced rates by 50% in women 25+ years, but rates now plateaued

HPV DNA testing
- 5-yearly; age 25-74 years
- 10 tests in a lifetime
- Expected to reduce cervical cancer rates by a further 20% or more, in both unvaccinated and vaccinated cohorts
The renewed cervical screening program is scheduled to start on May 1st 2017.
The future impact of vaccination and HPV screening on cervical cancer in Australia

Hall M et al., In Prep.
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