The Future of Cervical Screening

Jenny Ross

Protecting patients
Introduction

- Cervical cancer and the Pap smear
- History of cervical screening in Australia
- New knowledge about HPV and cervical cancer
- HPV Vaccination Program
- “The Renewal” of the National Cervical Screening Program
Cervical cancer worldwide

- One of the most preventable of all cancers
- Second most common cancer worldwide
- Around 500,000 cases and 275,000 deaths/year
- Burden highest in developing countries without screening programs
Incidence and Mortality
Australia

- Second lowest incidence and lowest mortality rate in the developed world
- 13th most common cancer
- 7 new cases per 100,000 per year
- 18th most common cause of cancer death
- 2 deaths per 100,000
- Twice the incidence and five times the mortality in ATSI women

The Pap Test

- Cheap, simple, non-invasive
- Screening tool
- Aim is to identify women with cervical abnormality
- Refer for further diagnostic testing and treatment

Around 70% squamous cell cancers are prevented
‘Organised approach’ to cervical screening

- 1960s Opportunistic screening
- 1991 Australian Institute of Health (AIH) Screening Evaluation Steering Committee report
- AHMAC: “Cervical Screening in Australia: Options for Change”
- Establishment “Organised Approach to Preventing Cancer of the Cervix”
  - Increase recruitment
  - Establish more reliable services for taking/interpreting/reporting Pap smears
  - Improve management of screen-detected abnormalities
  - Monitor and evaluate
National Cervical Screening Program

- National Screening Policy
- Two-yearly screening interval
- 18-69 years
- Mandatory laboratory standards
- Standard report format
- Standardised management guidelines
- State administered Pap Test Registries

Trends in incidence rates for Cervical cancer (ICD10 C53), Australia, 1982–2009

Female ASI rate

Cases per 100,000

Year
The Old Paradigm

“CANCER TEST”

CIN 1

CIN 2

CIN 3

CANCER

Protecting patients
Natural history of cervical cancer

- Normal
- LSIL
- HSIL
- Cancer

HPV
E6, E7

70%
98%

5 weeks
5 years
20 years

Protecting patients
Human papillomavirus (HPV)

- Small double-stranded DNA viruses
- > 100 genotypes, ~ 40 affect FGT
- Low-risk (HPV6,11) vs high-risk (HPV16,18)
- Very common in young women
- Peak incidence in early 20’s
- >95% of women will clear their HPV infection within 3 yrs (median 8-14 mths)
Human papillomavirus (HPV) and cervical cancer

- High-risk HPV present in almost all invasive cervical cancers
- Cervical cancer a rare outcome of HPV infection
- Persistent HPV infection increases by over 250 times the relative risk of cervical cancer
- Strong predictor of subsequent development of intraepithelial lesions
HPV Test

- 98% sensitivity, 99% reproducibility
- 99% negative predictive value
- Identifies women at greatest risk for disease
- HPV neg women to be managed more conservatively
HPV Vaccination

- Virus like particles specific to the L1 protein of HPV 16, 18
- Will prevent 70% of cervical cancers
- Gardasil (quadrivalent), Cervarix (bivalent)
- High immunogenicity
- 100% effective in populations neg for 16,18
HPV Vaccination

- Australian program:
  - Ongoing for 12 yr old girls (from April 2007)
  - Two-year catch up for 13-18 yr old school girls
  - GP based for women 19-26 yrs (July 2007-June 2009)
  - National Program for school aged boys (2013)

- Reduce the life time risk of cervical cancer by 48%

- National HPV Vaccination Program Register
HPV Vaccination

- Decrease in disease prevalence
- Decrease in abnormal Pap smear results
- Elimination of genital warts
- Other HPV-related cancers

Gretig et al Sex Health 2011; 8:171-8
Brotherton et al Lancet 2011;377:2085-92
Medical Journal of Australia

- Victorian Cancer Council / Victorian Cytology Service
- 2010-11 Vaccination Register data
- Pap Tests were 13% lower in vaccinated women 25-29 yrs
- Pap Tests were 10% lower in vaccinated women 20-24 yrs
- Continued participation crucial
- VIC campaign including media/letters to women 25-34 yrs
National Cervical Screening Program “The Renewal”

- Conventional Cytology
- Thin Layer Technology
- HPV Testing
- HPV Vaccination
- Screening interval
- Registries
The Renewal (What?)

- To ensure the success of the program continues and all Australian women, human papillomavirus (HPV) vaccinated and unvaccinated, have access to a cervical screening program that is based on current evidence and best practice.
The Renewal (Who?)

- Renewal Steering Committee
- Professor Ian Hammond (Chair)
- Cervical screening experts
  - gynaecological oncology
  - pathology
  - cytology
  - epidemiology
  - general practice and
  - nursing
- Input and feedback was sought from all stakeholders including industry, health professionals and consumers
- Partner Reference Group
The Renewal (Why?)

- New scientific knowledge on the development of cervical cancer
- New international and local evidence for cervical cancer prevention and screening
- New technologies
  - Liquid-based technology
  - Computer assisted image analysis
  - HPV testing
- 2007 - National HPV Vaccination Program
- Current NCSP is intensive compared to other countries
The Renewal (How?)

- Assess the evidence of screening pathways – including tests, interval + age range, for HPV vaccinated and unvaccinated women.
- Determine a cost-effective screening pathway and program model.
- Improve national data collection systems and registry functions.
- Assess the feasibility and acceptability of the renewed program.
<table>
<thead>
<tr>
<th>Primary Question</th>
<th>Comparator (Current program)</th>
<th>Scenario 1</th>
<th>Scenario 2</th>
<th>Scenario 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary screening test</strong></td>
<td>Conventional cytology</td>
<td>Conventional cytology</td>
<td>LBC</td>
<td>HPV DNA testing</td>
</tr>
<tr>
<td><strong>Age range</strong></td>
<td>Women aged 18-69 years</td>
<td>Women aged 25-64 years</td>
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<tr>
<td><strong>Interval</strong></td>
<td>2 yearly</td>
<td>3 yearly (aged 25-49) and 5 yearly (aged 50-65)</td>
<td>5 yearly</td>
<td></td>
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<tr>
<td><strong>Triage options</strong></td>
<td>As per NHMRC Guidelines</td>
<td>As per NHMRC Guidelines</td>
<td>Reflex HPV DNA testing</td>
<td>Co-test LBC OR Reflex LBC</td>
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<tr>
<td><strong>Additional technology</strong></td>
<td>N/A</td>
<td>N/A</td>
<td></td>
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<tr>
<td><strong>Exit strategy</strong></td>
<td>Must have two normal cytology tests within the last 5 years</td>
<td></td>
<td>HPV DNA test at age 64 years</td>
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<td><strong>Self collection</strong></td>
<td>N/A</td>
<td>N/A</td>
<td></td>
<td>YES</td>
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<tr>
<td><strong>Call-recall system</strong></td>
<td>N/A</td>
<td></td>
<td></td>
<td>YES</td>
</tr>
</tbody>
</table>
The Renewal (When?)

- Nov 2011 – RSC inaugural meeting
- Mar 2012 – Partner Reference Group meetings
- May 2012 - Public Consultation - Renewal DAP
- Jun 2013 – Public Consultation - draft Review of Evidence
- Oct 2013 – ESC of MSAC meeting
- Nov 2013 – MSAC meeting
- Dec 2013 – SCoS meeting
- **Apr 2014 – MSAC recommendation**
- Sep 2014 – AHMAC meeting
- Sep 2014 – Policy and Implementation Plan
- 2016 ??? – Implementation + changes
MSAC Recommendation

- five yearly cervical screening interval 25 to 69 years
- primary HPV testing with partial genotyping and reflex LBC triage
- invitations and reminders to be sent from a national Register
- self-collected a HPV sample
- de-listing of existing MBS items over a 6 to 12 month transition period
- Implementation from 2016
What does this mean?

- The procedure for collecting a cervical screening sample will not change
- Placed in a vial and sent to the lab for testing
- If HPV is found, cytology testing automatically undertaken on that same sample
- no additional specimen required
HPV Tests

- Current and future tests must:
  - comply with TGA regulatory framework for IVD medical devices
  - meet Meijer et al - guidelines for HPV test requirements for primary cervical screening and validation guidelines for candidate HPV assays
  - provide a pooled result for all high risk HPV genotypes and partial HPV genotyping for HPV16 and HPV18 +/-45; and
  - not be an in-house test.

LBC solution for HPV testing

- The LBC solution needs to be validated for use with the HPV test that is being used and for subsequent LBC examination of HPV test-positive specimens.

- Important to ensure that reflex LBC triage testing can occur using the same specimen and thus avoid the need to obtain another specimen.

- Different types of LBC solution available including ThinPrep PreservCyt Solution, SurePath medium, Specimen Transport Medium (STM) and brand specific solutions for HPV testing.
HPV self-collection

- International studies show that HPV self-sampling increases screening participation rate for never and under-screeners

- In Australia – self collection for STIs eg chlamydia

- Facilitated by a medical or nurse practitioner (or on behalf of a medical practitioner) who also offers mainstream cervical screening, for an under screened or never screened woman

- The accuracy of HPV self-collection varies for different types of sampling devices and HPV tests;

- Only for never and under-screened women
Estimated Volume changes /year

- Pap tests ~ 2.4M to 0.
- HPV tests ~ 55K to 1.3M+
- LBC tests ~ ? to 340K
- Colposcopies ~ 82K to 102K
Young women

- HPV is prevalent in young women and regresses
- Cervical cancer is very rare < 25 yo
- Screening has not decreased mortality < 25 yo
- HPV vaccination has reduced the risk of high grade abnormalities in young women
- Starting at 25yo reduces over treatment and minimises harms such as future pregnancy loss
Cytology

- Highly trained and tertiary educated personnel
- Specific and specialised skill set
- Gynaecological cytology comprises ~80% workload
- Workload reduction approx 86% (MSAC); 50-90% (Cyto labs)
- Reduction in staff 75-95% (or close completely)
- Main impact on private and large cytology laboratories
- Impact on Scientists, Pathologists, Lab Prep staff, Clerical staff
Cytology

- Diagnostic rather than screening test
- Enriched population of abnormalities
- Liquid based only
- Stringent quality monitoring
- Changes in NPAAC Requirements
- Retraining
Opportunities

- More lives saved
- Less testing and improved participation
- Improved national registries and data collection
- Improved evaluation of both the NCSP and HPV vaccination
- Continued leadership and innovation
  - 1st HPV vaccine,
  - 1st national HPV school based immunisation program,
  - 1st national cervical screening using primary HPV test
Next steps

- AHMAC September 2014
- Steering Committee for the Renewal Implementation Project (SCRIP)
  - MBS items: Addition, deletion and transition
  - National Registers / HPV Vaccination Register
  - Workforce and practice change
  - Quality Framework
  - Quality and Safety Monitoring Committee (QSMC)
  - Communication and information

msac.gov.au
cancerscreening.gov.au
George Papanicolaou
1883-1962
Thank you