Best practice in cervical cancer immunisation

Report of a roundtable discussion about the impact of the human papillomavirus vaccine in Australia

Discussion and recommendations
March 2008
Executive summary

On 18 April 2007, The Cancer Council Australia convened a national roundtable discussion on human papillomavirus (HPV) immunisation and its impact on the National Cervical Screening Program. The aim was to bring leaders in immunisation and screening together to share their expertise, examine the latest evidence and develop recommendations for policy makers. The Australian Government (Commonwealth Department of Health and Ageing) co-sponsored the event.

The roundtable was convened in response to the emergence of a vaccine that prevents two strains of HPV that cause approximately 70% of cervical cancer. While HPV vaccination has the potential to significantly reduce the impact of cervical cancer, its introduction in Australia must be managed in a way that ensures Australia’s successful cervical cancer screening program continues to protect women who, for reasons documented in this report, would not benefit from the vaccine.

The event gathered together the nation’s leaders in cervical cancer policy and implementation, with the key objectives to: identify what information is currently available for health professionals and the community about the HPV vaccine; lead discussion around the impact of HPV vaccination on the National Cervical Screening Program; and generate outcomes and recommendations that can help inform policy and practice.

A key component of the roundtable was a workshop facilitated by Professor Terry Nolan, Head of School, School of Population Health, University of Melbourne, which identified: potential barriers to the successful rollout of the HPV vaccination program; potential barriers to ensuring the National Cervical Screening Program delivers optimal results following the introduction of HPV immunisation; and research questions that need to be addressed in the short and long term. The workshop rated the significance of key interventions under each of these headings, as documented in this report.

The roundtable also featured formal presentations from experts in a range of fields related to cervical cancer control, which are summarised in Attachment 1.

Following lengthy discussion, roundtable participants agreed on five principles around which a set of more detailed recommendations, and agencies with remit to explore them, are documented:

1. Review the National Cervical Screening Program;
2. ‘Central’ overseeing to monitor the HPV vaccine’s impact on the National Cervical Screening Program;
3. Develop an Indigenous ‘package’ for screening and vaccination;
4. Undertake post-implementation evaluation of the National HPV Vaccination Program; and
5. Address information systems issues.

This report lists these recommendations and summarises the discussion and presentations from the roundtable. Publication was deferred to enable additional expert input and to coincide with the subsequent development of the HPV immunisation chapter of The Cancer Council Australia’s National Cancer Prevention Policy.
Overview

After more than three decades of opportunistic screening for cervical cancer in Australia, the Australian Federal Government, in partnership with the states and territories, introduced the National Cervical Screening Program in 1991.

Between 1991 and 2002, the incidence rate of cervical cancer among women aged 20 to 69 almost halved. Between 1991 and 2004, the cervical cancer mortality rate in Australia declined by more than 50% and is now among the lowest in the world. These declines in cervical cancer incidence and mortality can, in part, be attributed to the success of the National Cervical Screening Program. (In 2003, there were 725 new cases of cervical cancer in Australia and 239 deaths, which equated to 1.7% of total cancer incidence and 0.6% of total cancer mortality.)

The National Health and Medical Research Council last reviewed guidelines for the National Cervical Screening Program in 2006. Australia’s current screening policy recommends that all sexually active women aged 18-69 have a Pap test every two years.

In 1991, a research team based in the University of Queensland had begun developing a vaccine for HPV, which is identified in 99.7% of cervical cancer specimens. Clinical trials showed the vaccine to be 100% effective in preventing HPV types 16 and 18, responsible for up to 70% of cervical cancers.

In July 2006, the Therapeutic Goods Administration (TGA) approved Australia’s first HPV vaccine, Gardasil, for use in girls and women aged 9 - 26 and boys aged 9-15. A second vaccine, Cervarix, was being assessed for TGA approval for use in females, reportedly up to the age of 45, at the time of the national HPV roundtable.

The Australian Government recently included Gardasil on the National Immunisation Program. Ongoing from April 2007, Gardasil is available to girls aged 12-13 (first year of secondary school). Additionally, for a two-year catch-up period the vaccine is available for girls and women aged 13 - 26.

Subsequent to the HPV immunisation roundtable, in May the TGA granted Cervarix its first license in a major market for the prevention of cervical cancer and precancerous lesions caused by HPV types 16 and 18 for use in females ages 10-45 years.

Rationale for convening roundtable

The Cancer Council Australia welcomed the development of HPV vaccination as a major step forward in reducing cervical cancer incidence and mortality, both globally and in Australia. In a media statement in June 2006, the Cancer Council stated that TGA approval of Gardasil was “an exciting prospect”, particularly for future generations, while urging women who had been sexually active to continue participating in the cervical screening program. This position reflects the complexity of HPV immunisation in a country like Australia that has a successful cervical cancer screening program; this complexity motivated The Cancer Council Australia to convene the HPV immunisation roundtable.

Evidence shows that the vaccine is highly effective at preventing HPV in women who have not been exposed to the virus through sexual activity. It has therefore been recommended by a group of international experts that the vaccine be administered prior to commencement of sexual activity. It is further recommended that vaccinated women have regular Pap tests, because the vaccine does not protect against all types of HPV that cause cervical cancer.
While the vaccine has been added to the National Immunisation Program for girls and women aged 12-26, screening will need to continue for many decades to come. In the meantime, the vaccine’s impact on the screening program may be felt relatively quickly.

The Cancer Council Australia hosted the HPV roundtable in order to explore these complexities and make recommendations for Australian policy makers on the basis of latest evidence, expert opinion and stakeholder involvement.

**Objectives**

The key objectives of the HPV roundtable were to:

- Identify what information is currently available for health professionals and the community about the HPV vaccine;
- Lead discussion around the impact of HPV vaccination on the National Cervical Screening Program; and
- Generate outcomes and recommendations that can help inform policy and practice.

**Program**

**Presentations**

The following presentations were delivered at the roundtable (see appendix 1 for summaries of individual presentation):

<table>
<thead>
<tr>
<th>Presenter</th>
<th>Topic</th>
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| Prof Ian Frazer, Director, Centre for Immunology and Cancer Research, University of Queensland | HPV vaccination: an Australian perspective  
An overview of future HPV vaccine developments |
| Dr Marion Saville, Director, Victorian Cytology Service | Impact of HPV vaccination on the National Cervical Screening Program |
| Assoc Prof Dorota Gertig, Director, Victorian Cervical Cytology Service | A review of evidence for primary screening with HPV testing |
| Dr Karen Canfell, Research Fellow, The Cancer Council NSW | Modelling HPV vaccination and cervical screening in Australia |
| Dr Sophie Couzos, Public Health Officer, National Aboriginal Community Controlled Health Organisation | A focus on Aboriginal women for cervical cancer prevention |
| Andriana Koukari, Assistant Secretary, Population Health Programs Branch, Department of Health and Ageing | A review of materials available for health professionals and the community about the vaccine  
An Australian Government perspective on the rollout of the HPV immunisation program and its impact on the National Cervical Screening Program |
Discussion: barriers and research questions

A key component of the roundtable was a workshop facilitated by Professor Terry Nolan, Head of School, School of Population Health, University of Melbourne, which identified:

1. Potential barriers to the successful rollout of the HPV vaccination program;
2. Potential barriers to ensuring the National Cervical Screening Program delivers optimal results following the introduction of HPV immunisation; and
3. Research questions that need to be addressed in the short and long term.

All potential barriers and research questions documented here were considered important, with a ranking system ranging from + for 'significant' to +++ for 'most significant'. The workshop also recommended strategies for overcoming the barriers.

1. Potential barriers to the successful rollout of the HPV vaccination program

<table>
<thead>
<tr>
<th>Ranking</th>
<th>Barriers</th>
<th>Strategies</th>
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<tbody>
<tr>
<td>+++</td>
<td>Recognising the higher incidence and poorer outcomes in the ATSI community, a focus on equity in HPV vaccination service delivery is a high priority</td>
<td>Address in policy and provide appropriate funding</td>
</tr>
<tr>
<td>+++</td>
<td>Varying logistical needs – the program needs enhanced infrastructure, information systems and strong links with GPs and other health professionals</td>
<td>Develop national registry to address infrastructure and information system needs</td>
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<tr>
<td>+++</td>
<td>Coordination across professional boundaries is required</td>
<td>Identify stakeholders and changes needed to achieve</td>
</tr>
<tr>
<td>++</td>
<td>Communicating information about HPV and the vaccine – recognising that the way in which vaccination is presented to health professionals, parents, women and adolescents could impact vaccine uptake</td>
<td>Develop communications strategy to address issues of adolescent and parental consent</td>
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<tr>
<td>++</td>
<td>Introduction of GSK vaccine (Cervarix) could create confusion for health professionals and women</td>
<td>Develop communications strategy to address this issue</td>
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<tr>
<td>+</td>
<td>Reported vaccine “failures” leading to a loss of confidence in the vaccination program by providers and women</td>
<td>Develop communications strategy to provide explanations</td>
</tr>
<tr>
<td>+</td>
<td>Arguments put by anti-immunisation lobbyists have the potential to confuse or dissuade participation in immunisation</td>
<td>Develop communications strategy to provide responses</td>
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### 2. Potential barriers to ensuring the National Cervical Screening Program delivers optimal results following the introduction of HPV immunisation

<table>
<thead>
<tr>
<th>Ranking</th>
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<th>Strategies</th>
</tr>
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<tbody>
<tr>
<td>+++</td>
<td>Sustainability (or non-sustainability) of the existing National Cervical Screening Program</td>
<td>Fund research including modelling studies</td>
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<tr>
<td>+++</td>
<td>The potential for reduced uptake of screening after vaccination – vaccinated girls may believe that they do not need to participate in the screening program, and; with an increased awareness of the role of HPV, women may (inaccurately) believe that they no longer need Pap tests. Confusion about screening has the potential to increase when the second vaccine (Cervarix) becomes available</td>
<td>Develop communications strategy to address lack of knowledge/confusion about screening, especially in under-screened women</td>
</tr>
<tr>
<td>+++</td>
<td>Resistance to changes to the National Cervical Screening Program by health professionals</td>
<td>Engage key health professionals and opinion leaders to lead change</td>
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<tr>
<td>+++</td>
<td>Appropriate time to plan</td>
<td>Commence planning</td>
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<td>+</td>
<td>Need to understand/map the success of the National Cervical Screening Program, with a particular focus on recruitment</td>
<td>Investigate programs (not exclusively screening) that are targeting the ATSI community well</td>
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<tr>
<td>+</td>
<td>Commercialisation of new technologies – can create confusion for women and health professionals</td>
<td>Develop communications strategy to address</td>
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### 3. Research questions that need to be addressed in the short and long term

<table>
<thead>
<tr>
<th>Ranking</th>
<th>Research questions/topic areas</th>
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<tbody>
<tr>
<td>+++</td>
<td>Compile the evidence on barriers to screening and the various experiences in different states</td>
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<td></td>
<td>How acceptable are different screening tests (ie, is self-sampling/or HPV DNA testing really more acceptable/culturally appropriate in underscreened communities)?</td>
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<td></td>
<td>Innovative strategies are required to ensure equity of access to the National Cervical Screening Program and National HPV Vaccination Program.</td>
</tr>
<tr>
<td>+++</td>
<td>Monitoring and evaluation of the National HPV Vaccination Program. Monitor full range of impacts (and set targets) including, effect on the screening program (rates of cervical cancer, incidence of LSIL and HSIL); population</td>
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</tbody>
</table>
### HPV vaccination in Australia – report/recommendations of a national policy roundtable

| Impact on genital warts; service delivery and uptake in ATSI community; before-and-after prevalence studies |
| What is the most effective way of screening for cervical cancer in a vaccinated population? |
| Genotype replacement over time |
| Duration of lifetime protection following natural infection, especially in older women |
| Evidence to support communication and implementation strategies |
| The feasibility of packaging HPV vaccination as part of a general adolescent health check - general need for investigation into how HPV vaccination can be embedded into more general aspects of adolescent healthcare. |
| An understanding of the natural history of HPV infection in older women – potential existence of second peak of prevalence of infection in older women in Australia. |
| Evidence for two versus three doses of the vaccine |
| Duration of vaccine efficacy and booster requirement |
| Epidemiology of HPV and vaccination in boys |
| Infant vaccination research – leading to possibility of earlier delivery |
| Knowledge about the acceptability of the HPV vaccine for NESB communities |

### Recommendations

Participants at the national HPV immunisation roundtable agreed on a set of recommendations to be adopted by national policy makers, built around five key areas of activity:

1. Review the National Cervical Screening Program;
2. ‘Central’ overseeing to monitor the HPV vaccine’s impact on the National Cervical Screening Program;
3. Develop an Indigenous ‘package’ for screening and vaccination;
4. Undertake post-implementation evaluation of the National HPV Vaccination Program; and
5. Address information systems issues.
The group proposed a range of specific initiatives and nominated organisations to take action, as follows:

1. **Review the National Cervical Screening Program**

   It should be recognised that the National Cervical Screening Program is essentially a program to prevent cervical cancer. A formal review of the National Cervical Screening Program is required – developing a framework and timeline for this is a priority.

   The review should recognise and address the following:

   - Screening interval and age of screening – reducing cancer through primary prevention will make the existing screening program much less cost-effective. Screening will still be required, albeit at reduced intervals for the vaccinated cohort. Modelling of screening pathways is required.
   - Capacity – there will be a reduction in the number of lesions as the vaccinated cohort enters the screening program. Fewer abnormalities seen by scientists may lead to reduced expertise. This has implications for laboratory measures, which will need to be adjusted as a consequence. Additionally, recruitment issues will become apparent as fewer scientists enter the field of cytology as a result of decreasing demand.
   - Primary screening – need formal review of primary screening with HPV testing.
   - Equity – the review should include an equity impact assessment to determine the screening program’s impact on reaching unscreened and under-screened women, and how this could be improved.

   Actions for implementing this recommendation should be the responsibility of the Screening Subcommittee of the Australian Population Health Development Principal Committee (APHDPC), which itself is a function of the Australian Health Ministers’ Advisory Committee. The APHDPC’s Screening Subcommittee should establish a working group to implement these measures in order to incorporate additional expertise as required.

2. **‘Central’ overseeing to monitor the HPV vaccine’s impact on the National Cervical Screening Program**

   It is important for systems and processes to be developed that monitor the HPV vaccine’s impact on the National Cervical Screening Program. These should encompass:

   - Data collection – identify the data required and ensure that it is captured in data collection processes;
   - Monitoring – develop a process to monitor data collected; and
   - Evaluation – analysis of data to measure any impact the vaccine may have on the National Cervical Screening Program.

   Responsibility for this recommendation should rest with the APHDPC’s Screening Subcommittee, again by acquiring additional specific expertise as required.
3. Develop an Indigenous ‘package’ for screening and vaccination

Aboriginal women are up to five times more likely to die from cervical cancer than non-Aboriginal Australian women, largely because they are less likely to participate as recommended in the National Cervical Screening Program. In order to reduce this inequity in cervical cancer outcomes, targeted efforts are required to expedite HPV immunisation of Aboriginal girls and women.

Recommended guiding principles for such targeted efforts, and ways to apply them, are:

- **Access** – Aboriginal people are more likely to be vaccinated attending an Aboriginal Community Controlled Health Organisation (ACCHO) than via private medical practice. ACCHOs and Aboriginal health workers should therefore be involved in the development of communication initiatives to promote the vaccine and measures to overcome structural/logistical barriers to the vaccine’s delivery. Additionally, any immunisation incentive programs should be designed to support ACCHOs;

- **Identification** – the National HPV Register and state-based cytology registers should include Aboriginal identifiers. For cytology registers to collect this data, the National Pathology Accreditation Advisory Council (NPAAC) standards could be amended to include recording of Aboriginal status as a standard. This would then need to be adhered to by all pathology laboratories reporting Pap test results; and

- **Uptake** – establish targets for the ongoing vaccination program and two catch-up programs. Determine what percentage of uptake in the Aboriginal community is considered successful? As Aboriginal girls are more likely to leave school at an earlier age and are more transient, targeted efforts to reach women in the catch-up programs is also required; relying on the school-based program alone is insufficient.

Responsibility for this recommendation rests with the Department of Health and Ageing Population Health Programs Branch, Targeted Prevention and Programs Branch and the Screening Subcommittee of APHDPC.

4. Undertake post-implementation evaluation of the National HPV Immunisation Program

An evaluation framework is required for the National HPV Immunisation Program. This should include targets for measurement, and cover important components such as:

- **Equity** – is the program reaching girls and women most at risk of cervical cancer (Aboriginal women, women from socially and economically disadvantaged background, women of culturally and linguistically diverse background etc.)?

- **Participation** – establish targets for the ongoing program and two catch-up programs. What percentage of participation is considered successful?

- **Impact** – direct effect on the number of cervical lesions, cervical cancer incidence and mortality, and screening participation rates (are vaccinated women less likely to participate in Pap testing?).

The Department of Health and Ageing’s Population Health Programs Branch and Targeted Prevention Programs Branch would take responsibility for these measures.
5. **Address information systems issues**

The way in which medical data is recorded and managed differs between states and territories. It is important that data linkages across states/territories and within sectors are streamlined and improved. Communicating across sectors will also need to improve.

Responsibility for this recommendation rests with the Department of Health and Ageing Population Health Programs Branch and Targeted Prevention and Programs Branch.
Appendix 1 - presentations

The six formal presentations delivered at the roundtable are summarised as follows.

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**HPV vaccination: an Australian perspective**  
**An overview of future HPV vaccine developments**

- Professor Ian Frazer*, Director, Centre for Immunology and Cancer Research, University of Queensland

**Key points**

- Infections, including HPV, hepatitis B & C, H. Pylori and Epstein Barr cause more than 23% of cancers, of which more than a fifth are causes by HPV
- HPV is the second most common cause of cancer in women worldwide
- There’s an average 15-year delay between HPV infection and cancer
- Immunity has been shown to control many HPV infections
- Role of adaptive (specific) immunity is uncertain
- Innate (non-specific) immunity is important
- Protection post-immunisation is by serum antibody to virus-like particle conformation
- Prophylactic HPV vaccines are:
  - conventional vaccines
  - made using rDNA technology (HPV can’t be grown in tissue culture)
  - based on technology for production of L1 virus like particles
  - produced by expressing the papillomavirus capsid protein in cells using gene technology
  - resemble the virus physically and immunologically
- Using the same technology, there are two vaccines – Gardasil, which immunises against HPV strains 6,11,16,18, and Cervarix, which protects against strains 16 and 18
- Laboratory work on the vaccine began in 1980, with licensing of the first product in 2006; the first clinical trials of the virus-like particle was 1995

* Professor Frazer disclosed that he and the University of Queensland, which developed HPV immunisation under his leadership, may gain financially from the commercial sale of the vaccine.
Clinical trials showed the vaccine to be 100% efficacious against HPV strains 6,11,16,18

Evidence shows best antibody response is in prepubescent youths

The vaccine is not therapeutic – it has no effect on pre-existing HPV infection

The vaccine is most efficacious before the risk of HPV infection is high (it is not possible to screen for a past infection)

Clinical trials showed no vaccine side effects; identical ratio (3.6%) of pregnant women in both the vaccine and the placebo group reported adverse congenital abnormalities

2 million doses administered over six months, with 750 possibly associated events reported - mostly fainting after vaccination (one broken nose). Three related cases of Guillain Barre syndrome were reported

Next steps include longer term research to demonstrate duration of vaccine protection, studies of vaccine efficacy in men and the development of broader spectrum vaccines

HPV vaccine licensed for use in more than 50 countries, with government immunisation programs in Australia, Germany and Italy

Conclusion

- If administered before sexual activity, HPV immunisation will prevent: up to 70% of cervical cancer in an unscreened population; the majority of abnormal Pap smears in screened populations; and more than 90% of genital warts (no data for males yet)
- HPV immunisation should not be seen as a replacement for cervical cancer screening
- HPV vaccines provide no therapeutic benefit for existing infection

Impact of HPV vaccination on the National Cervical Screening Program

Dr Marion Saville, Director, Victorian Cytology Service

Key points

There are three main impacts of cervical cancer immunisation in Australia: 1) confusion about the need to continue screening; 2) reduction in the numbers of abnormalities detected; and 3) reduction in the number of cancers
Confusion about the need to continue screening

- Any change to screening recommendations will not affect women already being screened, so our existing programme will need to continue in some form until the youngest of these women reaches the age of stopping screening, presently 69 years.
- The vaccine only protects against HPV 16- and 18-related cancers, so some form of screening will still be required by the vaccinated cohort.
- Workforce implications in cytology – anecdotal reports of student reluctance to select cytology as a major subject, potentially leading to decline in capacity to screen before commensurate decline in demand.

Reduction in the number of abnormalities detected in Pap tests

- When the vaccinated cohort enters the screening program, low-grade squamous intraepithelial lesions are expected to decline by around 20%, high-grade SIL by 40% for those vaccinated against HPV 16/18 and 50% for those vaccinated against 6/11/16/18.
- Reduced LSIL and HSIL may lead to a reduction in the positive predictive value (PPV) of diagnoses and reduced scientific expertise in treating such abnormalities.
- The National Pathology Accreditation Advisory Committee will need to review the screening program’s laboratory performance standards in view of the decline in abnormalities.
- Image-assisted liquid-based cytology may have two strategic advantages not captured by cost-effectiveness analyses:
  - delivering the increased productivity that may be needed if our capacity to report cytology falls below demand in the next five to 10 years.
  - increased productivity could also compensate for the reduced prevalence of abnormalities, maintaining the absolute number of abnormalities seen by scientists.

Reduction in the number of cancers

- Australian-specific data suggests that HPV 16/18 may account for closer to 80% of cervical cancers – 10% higher than global average.
- It will take decades for immunisation to reduce cervical cancer incidence in Australia.
- Reduction in cervical cancer burden through primary prevention will eventually make the screening program much less cost-effective.

Cervical screening in the era of HPV vaccination – key questions

- Do we have different programmes for screened and unscreened women?
Will practitioners contact an immunisation register on a woman-by-woman basis before conducting a Pap test?

Will practitioners rely on women’s recall?

Do we screen all women less intensively?

Equity issues

Immunisation could benefit some population groups over others

Women in apparently vaccinated cohorts may still develop cervical cancer because: they were not vaccinated; missed some doses; the vaccine did not work

HPV testing as part of cervical cancer screening – barriers

HPV testing is more expensive than conventional cytology

HPV screening would depend on commercial interests

There are complex public health education issues

The IARC Cervix Cancer Screening Meeting in April 2004 concluded:
- There is sufficient evidence that: screening by conventional cytology has reduced cervical cancer incidence and mortality rates
- Screening by liquid-based or automated cytology can reduce cervical cancer incidence and mortality rates
- Testing for human papillomavirus infection as the primary screening modality can reduce cervical cancer incidence and mortality rates

Conclusion - how will cervical screening work in the HPV immunisation era?

Screening must be reformulated to operate in conjunction with immunisation

We must recognise there are two prevention strategies: one new and the other in transition

Decisions about screening the vaccinated cohort will need to be made without the benefit of empirical data

Modelling will be needed to assist decision making

Detailed post-vaccination surveillance is essential to providing evidence

HPV Register

A national HPV vaccination register is being developed to collect information about the HPV immunisation program
• The immunisation program’s impact on cervical abnormality and cancer rates must be evaluated and matched with Pap test registers

Next steps

• Formal review of evidence on cervical cancer screening in the immunisation era
• Model proposed new screening pathways
• Implement modified screening for immunised age cohort
• Assess the outcomes through post-vaccination surveillance, using immunisation and Pap test registers.

A review of evidence for primary screening with HPV testing

- Associate Professor Dorota Gertig, Director, Victorian Cervical Cytology Service

Key points about HPV testing

• Test is for high-risk HPV DNA from cervical specimens:
  o i) Hybrid capture II (13 high-risk and five low-risk subtypes) of HPV
  o ii) Polymerase chain reaction

• Test does not refer to HPV serology, due to low sensitivity (<50%)

• NHMRC guidelines released in 2006 recommend “test for cure” following treatment of a histologically proven high-grade cervical abnormality

• Under these circumstances, Medicare rebate applies

• Insufficient evidence of cost-effectiveness for use following LSIL.

Case for HPV testing in cervical screening

• Higher sensitivity than cytology

• More “upstream” in carcinogenic process meaning there is potential for longer safety margin for screening intervals

• Can be automated, centralised, quality-controlled for high specimen throughput

• High-volume testing may be more cost-effective

• A more intuitive choice for screening vaccinated women.
HPV as a primary screening test

- HPV testing has a higher sensitivity and negative predictive value for cervical abnormalities but the trade-off is lower specificity and positive predictive value than cytology
- Low specificity means more false positives and consequently greater number of unnecessary investigations especially colposcopy

Study results: HPV testing v. cytology in population-based screening

- Sensitivity for HPV testing substantially higher than for Pap testing, ranging from around 75% to 95-97%.
- Pap testing had higher specificity than HPV testing which is particularly important in the context of population screening, because as the specificity goes down the false-positive rate goes up resulting in a higher number of unnecessary investigations and a more costly program.
- Methodological limitations
  - all studies were based on cross-sectional design with double testing of all women
  - single HPV test compared with single Pap test
  - Outcome >=CIN2, but much of CIN2 regresses

How can specificity be increased?

- Cytology triage, i.e. conducting Pap tests on women who are found to be HPV positive
- Role of HPV genotyping
- Other novel markers of persistence:
  - viral load analysis
  - High-risk HPV mRNA analysis
  - p16
  - Microarray analyses.
- An important research question is, What factors increase the risk of persistent infection or progression to cancer?
- Specificity of HPV testing by age
  - Koliopoulos (2007): suggested similar specificity for women over 30 years
  - Cuzick (2006): specificity 7% higher in women aged 35 years and older compared to younger women
Psychological consequences of HPV testing

- Low awareness of link between HPV and cancer, though this is increasing with publicity around the vaccine
- Information about HPV tests can result in anxiety, concern about health and relationships
- More health education is necessary

Randomised controlled trials of HPV as a primary screening test

- Seven ongoing RCTs of HPV as a primary screening test
- Involve collection of samples for HPV and Pap test, randomised to reveal or conceal the HPV result
- Main postulated outcome is a reduction in cumulative incidence of CIN3, three to five years after screening among baseline HPV negative women compared to baseline cytology negative women.

General methodological issues

- Most trials based within population-based screening programs
- Target age groups and screening intervals differ
- Management of HPV positive women, comparing either immediate colposcopy to a repeat test in six to 12 months which may impact on the sensitivity
- Outcome >=CIN2 or >=CIN3
- Issues around verification bias.

Issues in adopting HPV testing in the cervical screening program

- Changes to existing screening programs will be costly and require extensive changes in workforce
- At present, HPV testing is more expensive than cervical cytology
- Health education issues
- Possible adverse psychological consequences
- Characteristics of Pap tests will differ post-vaccination.

Where to next?

- Proper evaluation of proposed changes to existing screening program
- Await longitudinal data from ongoing RCTs (2007-08), however none of the studies are being conducted in the context of the national vaccination program
Further research on triage of HPV positive women
Further research on risk factors for persistence
Role of modeling v. trial results.

Modelling HPV vaccination and cervical cancer screening in Australia

- Dr Karen Canfell, Cancer Epidemiology Research Unit, The Cancer Council NSW

Note that Dr Canfell’s presentation was largely graphic and diagramatic in nature and could not be fully reproduced in this text-based summary. Dr Canfell provided an overview of a project modelling HPV vaccination and cervical cancer screening in Australia, the key points of which follow.

The overall aims of the modelling project are to perform epidemiologic and health economic evaluations of potential changes to cervical screening in the context of HPV vaccination. Some of the outcomes from the project include: (1) Effectiveness - cancer incidence and mortality, life years saved; (2) Health resources utilisation – number of smears, colposcopies and treatments by age and over time; and (3) Costs – discounted lifetime costs, and annual costs of screening and vaccination.

The approach involves a group of interlinked models – including a model of sexual behaviour and HPV transmission in Australia, a model of the natural history of CIN, a model of invasive cancer survival, and a model of screening, diagnosis and treatment. The dynamic model of HPV transmission was adapted from a model originally developed for Finland. It was parameterised for Australia using local data on the age of sexual debut, rates of partner change and hysterectomy, fertility and mortality rates. The model of screening, diagnosis and treatment was developed as a flexible platform and makes use of registry data to ensure that compliance with recommended re-screening and follow-up intervals are taken into account in the evaluations.

The validation and initial application of the models were described and the results discussed. The HPV transmission model was used to estimate the impact of the current vaccination program on HPV incidence in Australia, and was also used to estimate the impact of vaccination of additional groups including males and older women. An initial application of the screening model - to perform an economic evaluation of proposed changes to cervical screening in New Zealand - was also described.

Future work will focus upon evaluating the role of primary HPV testing in the context of HPV vaccination.
A focus on Aboriginal women for cervical cancer prevention

- Dr Sophie Couzos, Public Health Officer, National Aboriginal Community Controlled Health Organisation

Aboriginal Community Controlled Health Services

- Over 130 services deliver comprehensive primary health care
- Over 1.4 million episodes of care (2003-04) recorded by ACCHSs to Aboriginal and Torres Strait Islander peoples (vastly greater than private GP contacts (BEACH data)
- 70% employees are Aboriginal
- Significant source of training for all health professionals (e.g. KAMSC has provided training to over 600 Aboriginal Health Workers since its establishment)
- Deliver more expansive programs and clinic services than general practice:
  - Provide clinical and preventive services
  - Advocacy and policy development
  - Support services.

Cervical cancer

- The most common cause of cancer death among Aboriginal women
- Overall age standardised mortality rate is ~5 times greater than that of non-Aboriginal women (in NT= 9 times higher)
- Higher risk for Aboriginal women in rural and remote areas than those in metropolitan areas (probably reflects poor access to screening services)
- Aboriginal women are younger: mean age of death= 53 years
- Incidence ICC (AS): 11.4/100,000 Aboriginal cf 2.5/100,000 (Qld, WA, NT,SA, 1998-2001) (also higher in NSW).

Cervical screening coverage

- Overall for all Australian women: 62-68% participation rates (PHOFA reports), but cervical screening participation rates not required to be reported/colllected for Aboriginal women under the PHOFAs
- Cross sectional survey: biennial participation rate for Aboriginal women in rural and remote areas was 41% (Qld), 30% lower than the rest of Queensland.
• In NT, 42% coverage (2003-04)
• Pap smear participation rates overall are lower for Aboriginal women

**Human papilloma virus**

• Limited data, but rates of HPV infection for Aboriginal women appear about the same as for non-Indigenous population: 42% (NT), suggesting that high cancer rates are due to poor access to primary health care

• There is limited data on the prevalence of different HPV types among populations of Aboriginal women. The prevalence of HPV and serotypes among Aboriginal women is being examined as in the WHINURS study (Women's HPV prevalence Indigenous Non-indigenous Urban Rural Study) that will help to inform future immunisation strategies

• Pap smear is the main test for detection of cervical HPV infection.

**Poor primary health care access**

• Access to primary health care services can be ascertained by proportionate expenditure

• Non-hospital spending:
  
  o MBS 34% of that for other Australians (per person) (including S100)
  
  o PBS 30%
  
  o Dental 24%

• Primary health care spending from federal and state sources for Aboriginal people is only 1.2 times that for non-Aboriginal peoples (2001-02), when it should be at least three times higher.

**Immunisation coverage in general**

• Vaccine coverage for pre-school children: suboptimal (9-17% lower for Aboriginal children aged 2-6 years)*

• Vaccine coverage for adults: not optimal and not directly comparable between populations. Influenza coverage for over 50 years of age 51% for Aboriginal and 47% for non-Aboriginal. Aboriginal people are a specific target group – whereas the over 65 year old population is targeted for non-Aboriginal people

• Aboriginal and Torres Strait Islander people are more likely to be vaccinated if attending ACCHSs than if attending private general practice

• HPV vaccination through GPs must target ACCHSs.

**Enhancing Pap screening coverage**

• 84% of ACCHSs deliver women’s health programs (SAR 2000-01)
• 79% of ACCHSs provide Pap smears (not all ACCHSs are large enough to employ GPs)

• Plus additional specific Pap programs

• Context is important:
  o an accessible and appropriate environment (gender and culture)
  o choice of provider eg. many Pap smears are taken by Aboriginal Health Workers (AHWs)
  o holistic: women’s health is seen as part of overall wellbeing and is linked to the health of their families.

STI control in general

• Up to 70% of ACCHSs provide routine STI screening (as part of preventive health checks), treatment and contact tracing

• Pap smears are part of that health check

• Condoms may have a role in preventing HPV transmission (study findings are conflicting)

• ACCHSs promote risk reduction and health seeking behaviour in innovative ways eg. “condom trees”.

National Cervical Screening Program

• Cervical cytology registers across Australia are not required to record Aboriginality (WA is taking some steps)

• Funding agreements with the states don’t require reporting on Pap coverage for Aboriginal women

• It is not possible to ascertain percentage of program expenditure reaching Aboriginal women

• Grants to the states are untied.

Practice Incentive Program (PIP) Cervical Screening Incentive

• ACCHSs ‘locked out’ by PIP ineligibility, expenditure did not reach ACCHSs

• Program poorly targeted to under-screened Aboriginal women

• Evaluation findings withheld from the public

• For example (information was obtained through Senate Estimates):
  o In 2004–05, there were only 279 claims under the cervical prevention PIP from Aboriginal medical services across Australia
  o Claims from 33 services totalled $9765 or $296 each
Services reaching the screening target numbered 16 with payment of $1666 each.

**MBS rebates for Pap smears**

- Rebates not accessible to AHWs
- AHWs are important in taking Pap smears
- AHWs outnumber practice nurses 2:1 and 90% of nurses are non-Indigenous (within ACCHSs).

**Aboriginal women**

- Mainstream policies don’t always work for the Aboriginal population, that’s why government supports supplementary population programs for this population (NSFATSIH)
- Increased access to both core primary health care and supplementary population programs are needed to reduce cervical cancer
- Any ‘cost-effectiveness-driven’ reductions in cervical cancer screening (now that we have HPV vaccine) should not apply to the population of Aboriginal women (there is an underspend for their health care)

**Making existing policies relevant**

- There are number of ways to make existing cancer prevention policies more relevant to this population:
  - Incentive programs must be designed to support Indigenous-specific service providers like ACCHSs instead of ‘locking them out’
  - Include provider incentives for Pap smears from Aboriginal women
  - Introduce AHW MBS rebates
  - Public Health Outcomes Funding Agreements must require disaggregated Pap participation rates (for Aboriginal women)
  - Registers must include Aboriginal identifiers nationally
  - Establish PHOFA targets for Aboriginal women’s Pap coverage
  - Implementation strategies needed for item 710 adult health check Medicare rebate; and for incentives MBS items targeted for ACCHSs
  - Promote case studies/exemplar sites for Pap coverage.

**Conclusion**

- HPV vaccine wont stop the need for Pap smears for Aboriginal women [in the short-term] because:
  - access to vaccine wont be optimal
  - vaccine won’t affect those already affected by HPV
  - we don’t know about non-vaccine-type HPV infections
• Pap smear coverage won’t improve unless Indigenous specific primary health care is enhanced and supplementary population programs for cervical cancer prevention are funded

• Pap smear coverage won’t improve unless existing policies are made relevant to Aboriginal women and their service providers

• Support ACCHSs to distribute HPV vaccine (eg. communication strategy for services and Aboriginal women)

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National HPV Vaccination Program: Information for parents, young women and immunisation providers

- Andriana Koukari, Assistant Secretary, Targeted Prevention Programs Branch, Population Health Division, Department of Health and Ageing

**Background**

• Vaccination program announced 29 November 2006

• Eligible cohorts:
  - ongoing school program
  - school and community-based catch up program

• To be implemented from April 2007, with materials in place by March 2007.

**Testing messages**

• HPV and the link to cervical cancer (and genital warts)

• There is a vaccine available that prevents the HPV types that cause 70% of cervical cancer

• HPV vaccine is most effective prior to commencement of sexual activity

• Women will still need to have regular Pap smears – the vaccine doesn’t prevent all types of cervical cancer causing HPV types.

**Campaign development**

Formative research:

• Conducted in January and February 2007
HPV vaccination in Australia – report/recommendations of a national policy roundtable

• Key findings:
  o Questioners/accepters
  o Knowledge deficit about HPV
  o Anxiety about ‘cancer’
  o Concern about lack of information

Target markets:
• 14-17 year olds
• 18-26 year olds
• Parents
• GPs.

Campaign resources
• Print advertisements
• Pamphlets
• Translated fact sheets
• GP booklet
• GP cheat sheet.

Implementation
Two phases in 2007
• Phase 1: Mainstream target audiences
  o Print ads
  o Radio ads
  o Pamphlet
  o Website

• Phase 2: People from culturally and linguistically diverse backgrounds and Aboriginal and Torres Strait Islander peoples

Evaluation
• Benchmark research has been conducted
• Tracking research will be conducted over the next two years
Communications/education strategy will be adjusted according to research findings

National HPV Vaccination Program: Rolling out the vaccine program – impact on the National Cervical Screening Program

- Andriana Koukari, Assistant Secretary, Targeted Prevention Programs Branch, Population Health Division, Department of Health and Ageing (This the second of two presentations by Ms Koukari)

New HPV vaccination program

Funding

- Vaccine - $436 million
- Support - $101 million
  - States and territories – service delivery
  - Communication campaign
  - Register.

Eligible cohorts

Ongoing

- 12-13 year old girls (school based)

Catch-up

- 14-18 year old girls (school based)
- 18-26 year olds (community based)

Rollout schedule

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<th>Calendar Year 2008</th>
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<td>From 11 April 2007</td>
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HPV vaccination in Australia – report/recommendations of a national policy roundtable

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*In some (smaller) areas the whole school will be vaccinated

**Country and remote schools may be earlier.

Consultation and collaboration

- Expert group to develop and review materials
- Jurisdictional immunisation coordinators
- State and territory cervical screening program managers
- Building connections between immunisation and cervical screening.

National HPV Vaccination Program register

- Collecting data beyond 7 year olds
- Establishing a register for now and the future
- Ensuring capacity to link between HPV vaccine register and Pap test registers.
References


2 ibid.

3 J. Ferlay, F. Bray, P. Pisani and D.M. Parkin. GLOBOCAN 2002: Cancer Incidence, Mortality and Prevalence Worldwide IARC CancerBase No. 5. version 2.0. IARCPress, Lyon, 2004


6 Wright TC, Bosch FX, Franco EL, Cuzick J, Schiller JT, Garnett GP & Meheus A 2006. HPV vaccines and screening in the prevention of cervical cancer; conclusions from a 2006 workshop of international experts.