Guidelines for HPV vaccine

This statement has been developed and reviewed by the Women’s Health Committee and approved by the RANZCOG Board and Council.

A list of Women’s Health Committee Members can be found in Appendix A.

Disclosure statements have been received from all members of this committee.

**Disclaimer** This information is intended to provide general advice to practitioners. This information should not be relied on as a substitute for proper assessment with respect to the particular circumstances of each case and the needs of any patient. This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The document has been prepared having regard to general circumstances.

First endorsed by RANZCOG: November 2006
Current: July 2015
Review due: July 2018

**Values:** The evidence was reviewed by the Women’s Health Committee (RANZCOG), and applied to local factors relating to Australia and New Zealand.

**Background:** This statement was first developed by Women’s Health Committee in November 2006 and reviewed in July 2015.

**Funding:** The development and review of this statement was funded by RANZCOG.
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1. **Patient Summary**

Vaccination against the human papillomavirus (HPV) is available in Australia and New Zealand. Infection with high-risk types of HPV has been linked to a number of adverse health outcomes for both women and men, including cervical cancer. HPV vaccination has been shown to be safe and effective, and is recommended for all eligible young women and men.

2. **Summary of recommendations**

<table>
<thead>
<tr>
<th>Recommendation 1</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participation in the HPV Vaccination Program should be encouraged in all eligible boys and girls in the first year of high school.</td>
<td>Consensus-based recommendation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommendation 2</th>
<th>Grade</th>
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</thead>
<tbody>
<tr>
<td>Current cervical cytology screening recommendations remain unchanged and should be followed regardless of vaccination status.</td>
<td>Consensus-based recommendation</td>
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</tbody>
</table>

3. **The National HPV Vaccination Program**

Cervical cancer is one of the leading causes of cancer morbidity and mortality in women throughout the world. Persistent infection with oncogenic Human Papilloma Virus (HPV) is associated with the development of cervical cancer. Infection with oncogenic HPV types is also implicated in the development of other cancers, including neoplasms of the vulva, vagina, anus, penis and also some head and neck cancers. Of the oncogenic HPVs, types 16 and 18 account for some 70% of cervical cancers. Some non-oncogenic HPV types cause genital warts. HPV infection is common with an estimated 70% of sexually active women becoming infected.\(^1\)\(^-\)\(^3\) The use of HPV vaccines prevents infection with vaccine-related HPV types and has the potential to reduce the incidence of precursor lesions and cervical cancer.\(^4\)

In Australia the National HPV Vaccination Program was established by legislation in 2007 and implemented in 2008. The Program now funds routine school based vaccination of boys and girls in first year high school (age 12 – 13). Girls and young women up to their 20th birthday are eligible to participate in New Zealand’s HPV immunisation programme free of charge.\(^5\)

The National HPV Vaccination Program Register December 2014 report on 3 dose vaccination coverage for all females turning 15 years of age in 2012 – 2013 was 71.0% – 71.1% nationally.\(^6\) The school-based program ensures the National HPV Vaccination Program is accessible to all 12 – 13 year old females regardless of socio-economic status (SES). In the High SES Quintile, 75.6% received the 3 doses compared to the Low SES Quintile where 71.5% received the three doses.\(^7\)

4. **HPV Vaccines**

The HPV Vaccines are made from Virus Like Proteins (VLP) that does not contain live, attenuated or killed virus. Given by intramuscular injection the VLP induces an antibody response. If the vaccinated individual is exposed to live HPV, the antibody response protects that individual from infection.
None of these vaccines are therapeutic and therefore do not treat existing lesions.

There are three commercially available HPV vaccines.

- 2v HPV vaccine (Cervarix®) is licensed for use in females from 10 to 45 years of age for the prevention of cervical cancer and its precursor lesions due to HPV types 16 and 18. These types account for over 78% of cervical cancers.

- 4v HPV vaccine (Gardasil®) is licensed for use in females aged 9 to 45 years, and in males age 9 to 26 years. It provides protection against persistent infection and cervical/genital disease due to HPV types 16 and 18 and HPV types 6 and 11, the latter two which cause 90% of genital warts. Gardasil® has also been registered for the prevention of vulvar and vaginal cancer, and their precancerous or dysplastic lesions.

Both vaccines have been shown to demonstrate limited cross-protection against other non-vaccine types, although the clinical significance of this remains to be demonstrated.

9v HPV (types 6, 11, 16, 18, 31, 33, 45, 52, 28) will cover 90% of the cervical cancers worldwide. Demonstrated 95% efficacy against all types in vaccine and therefore additional potential for cancer prevention (cervix, vulva, vagina, anal, oropharynx, penile).

### 4.1 Dosage

The National HPV Vaccination Program recommends three doses given by intramuscular injection at 0, 2 and 6 months for long lasting immunity. Antibody persistence has been demonstrated up to 9 years post vaccination.

### 4.2 Safety and Clinical Efficacy

The Therapeutic Goods Administration 2013 report on acute adverse events following immunisation (AEFI) did not note any safety concerns.

Meta-analysis on clinical trials on HPV vaccines do not show any increased risk of serious adverse events among those who receive the vaccine compared to placebo. The main side effect is mild local reaction at the injection site. Reporting rates of serious AEFI include urticaria (0.1 per 100,000 doses), pruritis (0.14 per 100,000 doses), anaphylaxis (0.06 per 100,000 doses), syncope (0.14 per 100,000 doses), seizure (0.21 per 100,000 doses), Guillain-Barre syndrome (0.04 per 100,000 doses), encephalitis (0.02 per 100,000 doses).

Australian Institute of Health and Welfare 2011 – 2012 report documents a significant reduction in histological high grade cervical abnormalities in Australia amongst <20 year old (53% reduction) and 20 – 24 year olds (21% reduction) from 2004 – 2012. The 4v HPV vaccine has resulted in a significant decline in proportion of genital warts in Australian women and men under the age of 21 (92.6% and 81.8% reduction respectively). No significant changes in genital wart diagnosis was observed in women and men over the age of 30.

### 4.3 Target populations

- Sexually active women up to the age of 45 and men up to the age of 26 can receive the HPV vaccine.
- Women with a history of previous HPV infection will most likely benefit from protection against disease caused by the other HPV vaccine genotypes with which they have not been infected.
- The vaccine can be given to patients with previous cervical intraepithelial neoplasia, but practitioners need to emphasise that the benefits will be limited to future HPV exposure. Cervical cytology screening and corresponding management based on NHMRC and RANZCOG recommendations must continue.
- Gardasil® and Cervarix® have been classified as pregnancy category B2. The vaccine is not recommended for use in pregnancy. There is no evidence to suggest that administration of Gardasil® or Cervarix® adversely affects fertility, pregnancy or infant outcomes.
• Women who become pregnant during the course of vaccination should defer the subsequent doses until the completion of pregnancy, regardless of timing. Vaccination should resume at the appropriate dose interval. There is no need to recommence the complete vaccination program. For example, women who have received one or two doses should receive the second and/or third dose at the completion of the pregnancy.
• The presence of immunosuppression, either medically or in patients with HIV infection, is not a contraindication for Gardasil® or Cervarix®. However, the immune response may be smaller in the immunocompromised patient than in immunocompetent patients.\textsuperscript{10, 16}
• While it is impossible to give women older than 26 years an exact assessment of their individual potential for benefit, women can be provided with information to make a balanced decision about the costs and benefits of vaccination\textsuperscript{17}. It should be emphasised however that vaccination is about prevention of future HPV infections, whilst continuation of cervical screening is vital to detect pre-neoplastic changes related to past infections.

4.4 Ongoing screening
• Current cervical cytology screening recommendations remain unchanged and should be followed regardless of vaccination status.
• The need for continued cervical cytology screening according to recommended national policies should be emphasised.
• There is no practical or reliable method for screening for HPV susceptibility prior to consideration of vaccination.

4.5 Other considerations
The national coverage rate of 71\% in the school-based vaccination program in Australia is lower than similar programs in England (86\%) and Scotland (91\%).\textsuperscript{18}
Participation in the cervical cytology screening program has declined among young women since the introduction of the National HPV Vaccination program.\textsuperscript{13} The need for continued cervical cytology screening according to recommended national policies should be emphasised.

5. References


6. Other suggested reading

7. Useful Links

8. Links to other College statements
Cervical Cancer Screening in Australia (C-Gyn 19)
Evidence-based Medicine, Obstetrics and Gynaecology (C-Gen 15)

9. Patient information
A range of RANZCOG Patient Information Pamphlets can be ordered via: https://www.ranzcog.edu.au/Womens-Health/Patient-Information-Guides/Patient-Information-Pamphlets

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Appendices

Appendix A Women’s Health Committee Membership

<table>
<thead>
<tr>
<th>Name</th>
<th>Position on Committee</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associate Professor Stephen Robson</td>
<td>Chair and Board Member</td>
</tr>
<tr>
<td>Dr James Harvey</td>
<td>Deputy Chair and Councillor</td>
</tr>
<tr>
<td>Associate Professor Anusch Yazdani</td>
<td>Member and Councillor</td>
</tr>
<tr>
<td>Associate Professor Ian Pettigrew</td>
<td>Member and Councillor</td>
</tr>
<tr>
<td>Dr Ian Page</td>
<td>Member and Councillor</td>
</tr>
<tr>
<td>Professor Yee Leung</td>
<td>Member of EAC Committee</td>
</tr>
<tr>
<td>Professor Sue Walker</td>
<td>General Member</td>
</tr>
<tr>
<td>Dr Lisa Hui</td>
<td>General Member</td>
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<tr>
<td>Dr Joseph Sgroi</td>
<td>General Member</td>
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<tr>
<td>Dr Marilyn Clarke</td>
<td>General Member</td>
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<tr>
<td>Dr Donald Clark</td>
<td>General Member</td>
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<tr>
<td>Associate Professor Janet Vaughan</td>
<td>General Member</td>
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<tr>
<td>Dr Benjamin Bopp</td>
<td>General Member</td>
</tr>
<tr>
<td>Associate Professor Kirsten Black</td>
<td>General Member</td>
</tr>
<tr>
<td>Dr Jacqueline Boyle</td>
<td>Chair of the ATSIWHC</td>
</tr>
<tr>
<td>Dr Martin Byrne</td>
<td>GPOAC representative</td>
</tr>
<tr>
<td>Ms Catherine Whitby</td>
<td>Community representative</td>
</tr>
<tr>
<td>Ms Sherryn Elworthy</td>
<td>Midwifery representative</td>
</tr>
<tr>
<td>Dr Nicola Quirk</td>
<td>Trainee representative</td>
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</tbody>
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Appendix B Overview of the development and review process for this statement

i. Steps in developing and updating this statement

This statement was originally developed in November 2006 and was most recently reviewed in July 2015. The Women’s Health Committee carried out the following steps in reviewing this statement:

- Declarations of interest were sought from all members prior to reviewing this statement.
- Structured clinical questions were developed and agreed upon.
- An updated literature search to answer the clinical questions was undertaken.
- At the July 2015 face-to-face committee meeting, the existing consensus-based recommendations were reviewed and updated (where appropriate) based on the available body of evidence and clinical expertise. Recommendations were graded as set out below in Appendix B part iii)

ii. Declaration of interest process and management

Declaring interests is essential in order to prevent any potential conflict between the private interests of members, and their duties as part of the Women’s Health Committee.

A declaration of interest form specific to guidelines and statements was developed by RANZCOG and approved by the RANZCOG Board in September 2012. The Women’s Health Committee members were required to declare their relevant interests in writing on this form prior to participating in the review of this statement.
Members were required to update their information as soon as they become aware of any changes to their interests and there was also a standing agenda item at each meeting where declarations of interest were called for and recorded as part of the meeting minutes.

There were no significant real or perceived conflicts of interest that required management during the process of updating this statement.

### iii. Grading of recommendations

Each recommendation in this College statement is given an overall grade as per the table below, based on the National Health and Medical Research Council (NHMRC) Levels of Evidence and Grades of Recommendations for Developers of Guidelines. Where no robust evidence was available but there was sufficient consensus within the Women’s Health Committee, consensus-based recommendations were developed or existing ones updated and are identifiable as such. Consensus-based recommendations were agreed to by the entire committee. Good Practice Notes are highlighted throughout and provide practical guidance to facilitate implementation. These were also developed through consensus of the entire committee.

<table>
<thead>
<tr>
<th>Recommendation category</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>Evidence-based</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>Body of evidence can be trusted to guide practice</td>
</tr>
<tr>
<td>B</td>
<td>Body of evidence can be trusted to guide practice in most situations</td>
</tr>
<tr>
<td>C</td>
<td>Body of evidence provides some support for recommendation(s) but care should be taken in its application</td>
</tr>
<tr>
<td>D</td>
<td>The body of evidence is weak and the recommendation must be applied with caution</td>
</tr>
<tr>
<td>Consensus-based</td>
<td>Recommendation based on clinical opinion and expertise as insufficient evidence available</td>
</tr>
<tr>
<td>Good Practice Note</td>
<td>Practical advice and information based on clinical opinion and expertise</td>
</tr>
</tbody>
</table>
Appendix C Full Disclaimer

This information is intended to provide general advice to practitioners, and should not be relied on as a substitute for proper assessment with respect to the particular circumstances of each case and the needs of any patient.

This information has been prepared having regard to general circumstances. It is the responsibility of each practitioner to have regard to the particular circumstances of each case. Clinical management should be responsive to the needs of the individual patient and the particular circumstances of each case.

This information has been prepared having regard to the information available at the time of its preparation, and each practitioner should have regard to relevant information, research or material which may have been published or become available subsequently.

Whilst the College endeavours to ensure that information is accurate and current at the time of preparation, it takes no responsibility for matters arising from changed circumstances or information or material that may have become subsequently available.