The Royal Australian and New Zealand College of Obstetricians and Gynaecologists
Excellence in Women's Health

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: March 2019
Review Due: March 2022

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 March 2019.

Funding: The development and review of this statement was funded by RANZCOG.

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1. Plain language 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.

Further plain language information can be found at: https://www.ranzcog.edu.au/Womens-Health/Patient-Information-Guides/Patient-Information-Pamphlets

2. Summary of recommendations

Recommendation 1	Grade
Participation in the HPV Vaccination Program should be encouraged for all eligible boys and girls in the National programs in Australia and New Zealand.	Consensus-based recommendation
Recommendation 2	**Grade**
Current cervical screening recommendations in Australia and New Zealand should be followed regardless of vaccination status.	Consensus-based recommendation

3. The National HPV Vaccination Program

Cervical cancer remains a significant cause 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 vulva, vagina, anus, penis, as well as some head and neck cancers. Of the oncogenic HPVs, types 16 and 18 account for about 70% of cervical cancers[1]. Non-oncogenic HPV types 6 and 11 cause genital warts. HPV infection is common with an estimated 70-80% of sexually active women worldwide becoming infected at some stage in their life. [2-4]The use of HPV vaccines prevents infection with vaccine-related HPV types, and has been shown to reduce the incidence of precursor (pre-malignant) lesions and, potentially, malignant cervical cancer.[5]

In Australia, the National HPV Vaccination Program was established by legislation in 2007 and implemented in 2008. The Program now funds the routine school based vaccination of boys and girls in first year of high school (age 12 – 13)[6]. Girls and boys aged 9 years to under 27 years are eligible to participate in New Zealand's HPV immunisation programme.[7]

The National HPV Vaccination Program Register in Australia was established in early 2008 to support the National HPV Vaccination Program. The 2016 report on 3 dose vaccination coverage for all females turning 15 years was 79% nationally. For males turning 15 years of age in 2016, the coverage was 73% nationally.[8]

4. HPV Vaccines

The HPV vaccines are made from Virus Like Proteins (VLP) that do 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 the available HPV vaccines are therapeutic and therefore do not treat existing lesions.

The National programs in Australia and New Zealand use the Gardasil 9 vaccine (9 valent or containing 9 types of HPV).

Gardasil 9 contains HPV types 6,11,16,18,31,33,45,52,58 which potentially prevents 90% of the cervical cancers. Trials demonstrated 95-100% efficacy against HPV types in the vaccine and therefore increased potential for cancer prevention (cervix, vulva, vagina, anal, oropharynx, penile)[9].

4.1 Dosage

The National HPV Vaccination Programs recommend two doses given by intramuscular injection scheduled at 0 and 5-13 months. If immunocompromised or older than 15 years, 3 doses is recommended at 0, 2, 6 months.[10]

4.2 Safety and Clinical Efficacy

Breastfeeding women can be vaccinated without risk for the infant or mother.

Vaccination during pregnancy is not recommended. However monitoring of women who have inadvertently received Gardasil during pregnancy has not identified any risks for the fetus or mother.

Anaphylaxis after HPV vaccination occurs about 1–3 times in every one million vaccine doses. No other serious responses to the vaccine have been identified. Most adverse reactions after vaccination are minor (injection site reactions, fever, headaches, dizziness, muscle pain).

Gardasil 9 can be administered concurrently with other vaccines but separate syringes and different injection sites should be used.

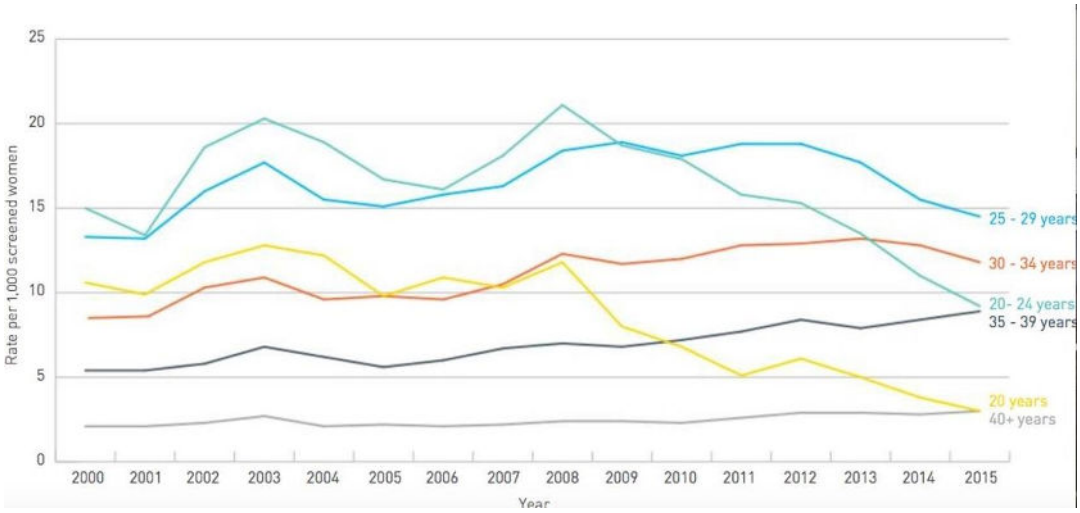
In clinical trials Gardasil vaccine demonstrated high efficacy against all included HPV types in both males and females. Efficacy was initially assessed in 14,215 women aged 16 to 26 years in a double-blind, phase IIb/III trial. Three doses of either Gardasil (4 valent) or Gardasil 9 (9 valent) were administered at 0, 2 and 6 months. HPV 9 efficacy was 97%. Many studies have now been completed confirming the high efficacy of Gardasil 9. [11-13]

Effectiveness is optimal when the vaccine is given under 15 years of age, and prior to onset of sexual intercourse.

In countries with high HPV vaccine coverage, such as Australia and Denmark, there has been a profound reduction in the number of genital wart cases. Data from Australia suggest elimination of genital warts is possible.[14]

Data collected by the Victorian Cervical Screening Register indicates a reduction in the incidence histologically confirmed high-grade cervical abnormalities since the introduction of the HPV vaccine in women aged under 20, and 20-24, and that this decrease is now becoming manifest in the 25-29 age group. In young women, there has been a decline in incidence of almost 75%.[15]

Table: Trends in high-grade cervical abnormalities (histologically confirmed) by age, 2000-2015, as recorded on the VCCR.[15]



4.3 Target populations

- Females aged 9 to 45 years and males aged 9 to of 26 years can receive the HPV vaccine.[14]
- 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 the benefits will be limited to future HPV exposure. Cervical screening and corresponding management based on National guidelines and RANZCOG recommendations must continue.
- Gardasil 9 is classified as pregnancy category B2. The vaccine is not recommended for use in pregnancy. No adverse effects have been identified, but caution is advised.[14]
- 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[14].
- The presence of immunosuppression, either medically or in patients with HIV infection, is not a contraindication for Gardasil 9. However, the immune response may be smaller in the immunocompromised patient than in immunocompetent patients.[14]

4.4 Ongoing screening

- Current cervical screening recommendations should be followed regardless of vaccination status.
- The need for continued cervical screening according to recommended national policies should be emphasised.

4.5 Other considerations

Participation in the cervical screening program has declined among young women since the introduction of the National HPV Vaccination program. The need for continued cervical screening according to recommended national policies should be emphasised.

5. References

1. Brotherton J GD, May C, Chappell G, Saville M. HPV vaccine impact in Australian women: ready for an HPV-based screening program, Med J Aust. 2016;204(5):184.
2. Villa LL CR, Petta CA, Andrade RP, Ault KA, Giuliano AR, et al. Prophylactic quadrivalent human papillomavirus (types 6, 11, 16, and 18) L1 virus-like particle vaccine in young women: a randomised double-blind placebo-controlled multicentre phase II efficacy trial., Lancet Oncol. 2005;6(5):271-8.
3. Stevens MP TS, Quinn MA, Garland SM. Human papillomavirus genotype prevalence in cervical biopsies from women diagnosed with cervical intraepithelial neoplasia or cervical cancer in Melbourne, Australia., int j gynaecol cancer. 2006;16(3):1017-24.
4. Brestovac B HG, Smith DW, Shellam GR, Frost FA. . Human papillomavirus genotypes and their association with cervical neoplasia in a cohort of Western Australian women, J Med Virol 2005;76(1):106-10.
5. Frazer IH. Prevention of cervical cancer through papillomavirus vaccination, Nat Rev Immunol. 2004;4(1):46-54.
6. Australian Government Department of Health. Preventing human papillomavirus (HPV) cancers and diseases by vaccination. 2018.
7. New Zealand Ministry of Health. About the HPV Vaccine. 2015.
8. Brotherton J CG, Brosi J, Bicknell L, Winch K, Barbaro B, Saville M. Human Papillomavirus control. How are we going with vaccination coverage seven years in? Poster presentation Communicable Disease Control Conference: 2015.
9. NCIRS. Human papillomavirus (HPV) vaccines for Australians. 2018.
10. Health AGDo. HPV vaccine – Gardasil®9 – Clinical advice fact sheet for GPs. 21 February 2018.
11. Osborne SL, Tabrizi SN, Brotherton JM, Cornall AM, Wark JD, Wrede CD, et al. Assessing genital human papillomavirus genoprevalence in young Australian women following the introduction of a national vaccination program, Vaccine. 2015;33(1):201-8.
12. Tabrizi SN, Brotherton JM, Kaldor JM, Skinner SR, Liu B, Bateson D, et al. Assessment of herd immunity and cross-protection after a human papillomavirus vaccination programme in Australia: a repeat cross-sectional study, Lancet Infect Dis. 2014;14(10):958-66.
13. Medical Services Advisory Committee. National Cervical Screening Program renewal: effectiveness modelling and economic evaluation in the Australian setting (MSAC application no. 1276.) 2013.
14. Gardasil 9 Product Information. 2017.
15. Statistical Report 2015 [Internet]. 2015. Available from: https://www.vccr.org/site/VCCR/filesystem/documents/dataandresearch/StatisticalReports/17030_VCS_StatsReport15_ART.3.pdf.

6. Other suggested reading

Munoz et al. Safety, immunogenicity and efficacy of quadrivalent HPV (types 6, 11, 16, 18) recombinant vaccine in women aged 24-45 years. Lancet 2009; 373 (9679): 1949-1957.

Casey GM, Morris B, Burnell M, et al. Celebrities and screening: a measurable impact on high-grade cervical neoplasia diagnosis from the "Jade Goody effect" in the UK. Br J Cancer 2013; 109: 1192-1197.

7. Useful Links

Human Papillomavirus (HPV) Immunise Australia Program, Department of Health
http://www.health.gov.au/internet/immunise/publishing.nsf/Content/immunise-hpv

Cervical Cancer Vaccine, Ministry of Health, New Zealand

https://www.health.govt.nz/our-work/preventative-health-wellness/immunisation/hpv-immunisation-programme/hpv-vaccine

National Cervical Screening Program: Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding (Australia)
Primary HPV screening from 1st December 2017
http://wiki.cancer.org.au/australia/Guidelines:Cervical_cancer/Screening

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

Appendices

Appendix A Women's Health Committee Membership

Name	Position on Committee
Professor Yee Leung	Chair and Board Member
Dr Gillian Gibson	Deputy Chair, Gynaecology
Dr Scott White	Deputy Chair, Obstetrics and Subspecialties Representative
Associate Professor Ian Pettigrew	Member and EAC Representative
Dr Kristy Milward	Member and Councillor
Dr Will Milford	Member and Councillor
Dr Frank O'Keeffe	Member and Councillor
Professor Sue Walker	Member
Dr Roy Watson	Member and Councillor
Dr Susan Fleming	Member and Councillor
Dr Sue Belgrave	Member and Councillor
Dr Marilyn Clarke	ATSI Representative
Associate Professor Kirsten Black	Member
Dr Thangeswaran Rudra	Member
Dr Nisha Khot	Member and SIMG Representative
Dr Judith Gardiner	Diplomate Representative
Dr Angela Brown	Midwifery Representative
Ms Ann Jorgensen	Community Representative
Dr Rebecca Mackenzie-Proctor	Trainee Representative
Prof Caroline De Costa	Co-opted member (ANZJOG member)
Dr Christine Sammartino	Observer

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 March 2019. 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 November 2018 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 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.

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

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.