

Access to HPV vaccine widened

The human papillomavirus virus (HPV) vaccine reduces the incidence of HPV-related diseases, including genital warts and cervical cancer, as well as anogenital and oropharyngeal cancers. It is most effective if it is given before sexual activity begins. The quadrivalent HPV vaccine (Gardasil) has been part of the National Immunisation Schedule since 2008 and is currently subsidised for females aged under 20 years and additional groups at increased risk, e.g. transplant patients.¹

PHARMAC recently announced changes to subsidised access to the HPV vaccine in New Zealand.² From 1 January, 2017:

- A nonavalent vaccine (Gardasil 9) which protects against five additional HPV types will be subsidised
- Males will now be eligible for subsidised access
- The age range for subsidised access will be extended to 9–26 years
- The dosing schedule will change for children aged 9–14 years

HPV vaccination: how successful has the program been?

Coverage has remained low: The HPV vaccination program in New Zealand began in 2008 and has been subsidised for females up to age 20 years. Since 2010, approximately 50% of females in the eligible age range have received HPV vaccination.³ The Ministry of Health aims to increase coverage with a target of 75% of girls aged 12 years being vaccinated by the end of 2017.³

More time is required to evaluate the effect on rates of cervical cancer: Girls who were vaccinated in the first year of the school-based program will now be aged approximately 20 years. Females who were vaccinated outside of the school-based program at an older age will now be aged in their early to mid-20s, the youngest age at which cervical cancer is usually diagnosed.⁴ The effect of New Zealand's HPV vaccination programme is therefore likely to become apparent over the next decade. Rates of cervical cancer averaged 6.6 per 100,000 women in the five years prior to introduction of the HPV vaccine (2003–2007), with rates in recent years of 6.3 per 100,000 in 2012–2013, and 5.4 per 100,000 in 2014.^{4,5} In Australia, which has one of the highest rates of HPV vaccine uptake in the

world, the rate of high grade cervical abnormalities has fallen in women aged under 20 years, with a 46% reduction in 2011 compared to the years prior to introduction of the HPV vaccine. A smaller reduction of 12% was also observed in women aged 20–24 years.⁶

The incidence of genital warts has decreased: The majority of cases of genital warts are caused by HPV types 6 and 11, which are included in the HPV vaccine.⁷ The incidence of genital warts in New Zealand has reduced since the HPV vaccination program began, with the greatest reduction in incidence seen in females in their teens and those aged 20–24 years.⁸ ⁹ Dispensing rates of medicines indicated for the treatment of genital warts have also decreased.¹⁰ From 2009 to 2012, genital warts cases decreased by 32% at sexual health clinics and decreased by 52% at family planning clinics.⁸ In Australia, where a vaccine coverage of 70% has been achieved, a 93% reduction in the incidence of genital warts in eligible age groups has been recorded.¹¹

The new HPV vaccine will protect against five additional HPV types

The existing HPV vaccine provides immunity against four HPV types: 6, 11, 16 and 18. The new nonavalent HPV vaccine provides immunity against nine HPV types: 6, 11, 16, 18, 31, 33, 45, 52 and 58. Clinical trials of the nonavalent vaccine show that it generates an equivalent antibody response compared to the quadrivalent vaccine against HPV types 6, 11, 16, and 18.¹²

The new nonavalent vaccine may offer broader protection against cervical cancer and other HPV-related cancers. HPV types 16 and 18 are estimated to cause approximately 70% of cancers of the cervix, vagina and anus, and 30–40% of cancers of the vulva, penis and oropharynx.¹³ The HPV types 31, 33, 45, 52 and 58, covered by the nonavalent vaccine are thought to cause up to 20% of cervical cancers and to contribute up to approximately 20% of other HPV-related cancers.^{14, 15}

In a large clinical trial comparing the effectiveness of the quadrivalent and nonavalent vaccines in women aged 16 to 26 years, there were no overall differences in the rate of high-grade cervical, vulvar or vaginal pre-malignant lesions. However, among women who did not have HPV infection and had normal pap smear results at the start of the trial, the nonavalent vaccine reduced the incidence of high-grade cervical, vulvar or vaginal pre-malignant lesions attributable to HPV types 31, 33, 45, 52, 58 by more than 96% (95% confidence interval 81–100%); 30 women out of approximately 6000 women who received the quadrivalent HPV vaccine developed high-grade cervical, vulvar or vaginal pre-malignant lesions due to these HPV types compared to one out of approximately 6000 who received the nonavalent HPV vaccine.^{12, 16}

Eligibility criteria for the subsidised HPV vaccine will be widened

Females and males aged 9 to 26 years will be eligible for subsidised HPV vaccination from January, 2017:

- A maximum of two doses will be funded for males and females aged 14 years and under.
- A maximum of three doses will be funded for patients aged 15–26 years, transplant patients (including people receiving stem cell treatments) and those aged 26 years and under who have received chemotherapy.

Males will now be eligible for HPV vaccination

Since the HPV vaccine programme began more evidence has accumulated regarding potential benefits to males. Clinical trials have shown HPV vaccination in males can reduce the incidence of genital warts and anogenital cancer.^{17, 18} It is also expected to reduce the incidence of oropharyngeal cancer; the incidence of this cancer in males in New Zealand has doubled from 1995 to 2010.¹⁹

Modelling suggests that heterosexual males will benefit from vaccination as current uptake rates among eligible females are approximately 50%, and an uptake of 80% in females is required for maximal herd immunity for heterosexual males.²⁰ The current vaccination strategy also does not benefit men who have sex with men, as they do not benefit from herd immunity conferred by vaccinated female partners and are at higher risk for anogenital and oropharyngeal warts and cancers than heterosexual men.^{21, 22}

In Australia, both boys and girls have received school-based HPV vaccination since 2013.²³

People aged 9 to 26 years now eligible for free HPV vaccination

The HPV vaccine will not confer protection against previously acquired infection, however, it does protect against future infections of HPV types not yet acquired. First HPV infections typically occur within a few years of becoming sexually active, and data in New Zealand show that approximately 8% of adolescents are sexually active by age 13 years.⁸

The new nonavalent vaccine is indicated and subsidised from age 9 years: the same age as people included in clinical trials of the vaccine.^{12, 24} Vaccination will typically begin at age 11 years as part of the school-based HPV vaccination programme, which is consistent with international programmes which offer vaccination from ages 11–13 years.^{18, 23} This is expected to move from Year 8 to Year 7 in the future in order to align with the tetanus, diphtheria and acellular pertussis (Tdap) immunisations.^{2, 3, 20}

People in the eligible age range who are too old to receive school-based vaccination can be vaccinated in primary care.

Although the immune response to the nonavalent vaccine is highest in younger individuals aged 9 to 15 years, in clinical trials of nonavalent vaccine over 99% of males and females aged 16 to 26 years showed antibody responses to all nine HPV types.²⁴

The dosing schedule will change for children aged 9–14 years

The dosing schedule for HPV vaccines will change from January, 2015:^{2, 16}

- People aged 9–14 years: two doses at least six months apart**
- People aged 15–26 years: three doses, at zero, two and six months

* Transplant patients, those receiving stem cell treatments and people who have received chemotherapy require three doses at zero, two and six months, regardless of age, unless an alternative schedule is advised²⁸

** If females aged under 14 years have already had two doses of the quadrivalent HPV vaccine, a third dose will be required if the two doses were administered less than six months apart²⁸

The dosing schedule has been reduced for younger people because research has shown a two-dose course is as effective as the three-dose course in this age group.^{25–27} Reducing the number of vaccines in the schedule will decrease the cost of the vaccination programme and may increase patient compliance with the schedule.


Offer eligible patients HPV vaccination from 1 January 2017

Primary care clinicians are encouraged to discuss HPV vaccination with eligible patients, particularly with the following groups:

- Non-immunised school-aged males in Year 9 and above, as they will miss the school-based programme
- Non-immunised females and males aged under 27 years; those aged 26 years will have limited opportunity to receive free vaccination before turning 27 years*
- Non-immunised people aged 14 years, who might be eligible for a two-dose vaccine regimen before turning 15 years when they would require the three-dose regimen
- Non-immunised people aged between 9 and 26 years who declined their school vaccination programme

* Provided the first dose is given prior to turning 27 years, the subsidised course can still be completed

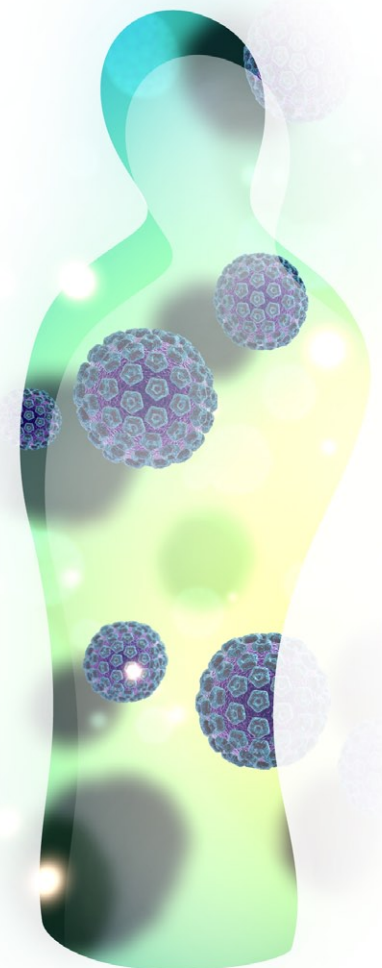
Updating recall processes ensures young males who do not complete their HPV vaccine dosing schedule in school are followed-up.²⁸

 For further information on the HPV vaccine programme, see: www.immune.org.nz/education-and-training/hpv-vaccination-module

Transitioning between subsidised vaccines

A transition period will occur while stocks of the quadrivalent HPV vaccine are used up. Once this occurs in early 2017, practices can then administer the new nonavalent vaccine. Females who have started the quadrivalent vaccine course will be able to complete this in early 2017. If patients seek HPV vaccination in early 2017, it is recommended that the quadrivalent vaccine is administered if it is still available.²⁸ If stocks of the quadrivalent vaccine are used up prior to patients finishing their dosing schedule, they will be able to switch to the new nonavalent HPV vaccine.²⁸ The school-based vaccination programme will administer the nonavalent HPV vaccine from 2017, and the quadrivalent vaccine will be delisted from 1 October, 2017.^{2, 28}

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HPV vaccination information for parents and patients

Questions which clinicians may be asked during discussion with parents or patients include:

What are the benefits of the new vaccine? The new vaccine and wider subsidised access is likely to result in a greater reduction in the incidence of cervical cancer and other HPV-related diseases in both males and females.

If HPV is a sexually transmitted infection, why does my child need this now? HPV vaccination is most effective when it is given before sexual activity begins. Vaccination is recommended between the ages of 11 to 13 years as the vast majority of New Zealand adolescents of this age will not have been exposed to HPV.⁸ Vaccinating at this age should not be interpreted as an expectation that the child is about to engage in sexual activity or that permission is given for sexual activity to begin. Research shows that HPV vaccination does not influence the age of onset of sexual activity, condom usage, number of sexual partners, or rates of STI diagnosis, pregnancy or termination of pregnancy.²⁹

Does the vaccine contain the HPV virus? The vaccine contains virus-like particles which are made with recombinant DNA, as is the case with previous HPV vaccines.^{8, 30} These are recognised by the immune system and allow the body to generate antibodies, but are not capable of causing infection.³⁰

Will it hurt? The most frequent adverse effects in females are local injection site reactions such as pain (90%), swelling (40%) and erythema (34%).²⁴ Rates of injection site reactions are lower in males, and tend to increase with subsequent doses.²⁴ Injection site reactions may be more painful and with greater swelling after the nonavalent vaccine than the current quadrivalent vaccine.¹² Approximately 55% of patients can be expected to experience some form of systemic symptom, such as

headache, pyrexia, nausea, dizziness or fatigue following administration; these rates are similar to the current quadrivalent vaccine.¹²

I heard that the vaccine isn't safe. HPV vaccination has been subject to intense scrutiny by members of the public, news media and some academics raising concerns over adverse effects.³¹⁻³⁵ These have tended to focus on the development of rare conditions in a small number of people, such as complex regional pain syndrome (CRPS), postural orthostatic tachycardia syndrome (POTS), autoimmune diseases and primary ovarian failure, which have featured in some case reports.³⁵⁻³⁹ A highly publicised Coroner's court case in New Zealand involved an investigation into the death of a young woman a few months after receiving the final dose of the quadrivalent HPV vaccine. In all of these cases, assessments by regulatory agencies, the Coroner's court verdict or monitoring of adverse event rates have not supported the conclusion that HPV vaccination was the cause of these events.³⁶⁻³⁹

The new nonavalent vaccine has been approved by Medsafe as well as authorities overseas, including in the United States and Europe, and is subject to ongoing monitoring. If patients develop unexpected signs or symptoms following vaccine administration, clinicians can submit a Medicines Adverse Reaction Report (<https://nzphvc.otago.ac.nz/report/>).

Clinicians should encourage parents to obtain information regarding the HPV vaccine from reliable sources, such as the Ministry of Health and Immunisation Advisory Centre:

- www.immune.org.nz/diseases/human-papillomavirus
- www.health.govt.nz/your-health/conditions-and-treatments/diseases-and-illnesses/cervical-cancer/hpv-immunisation/

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