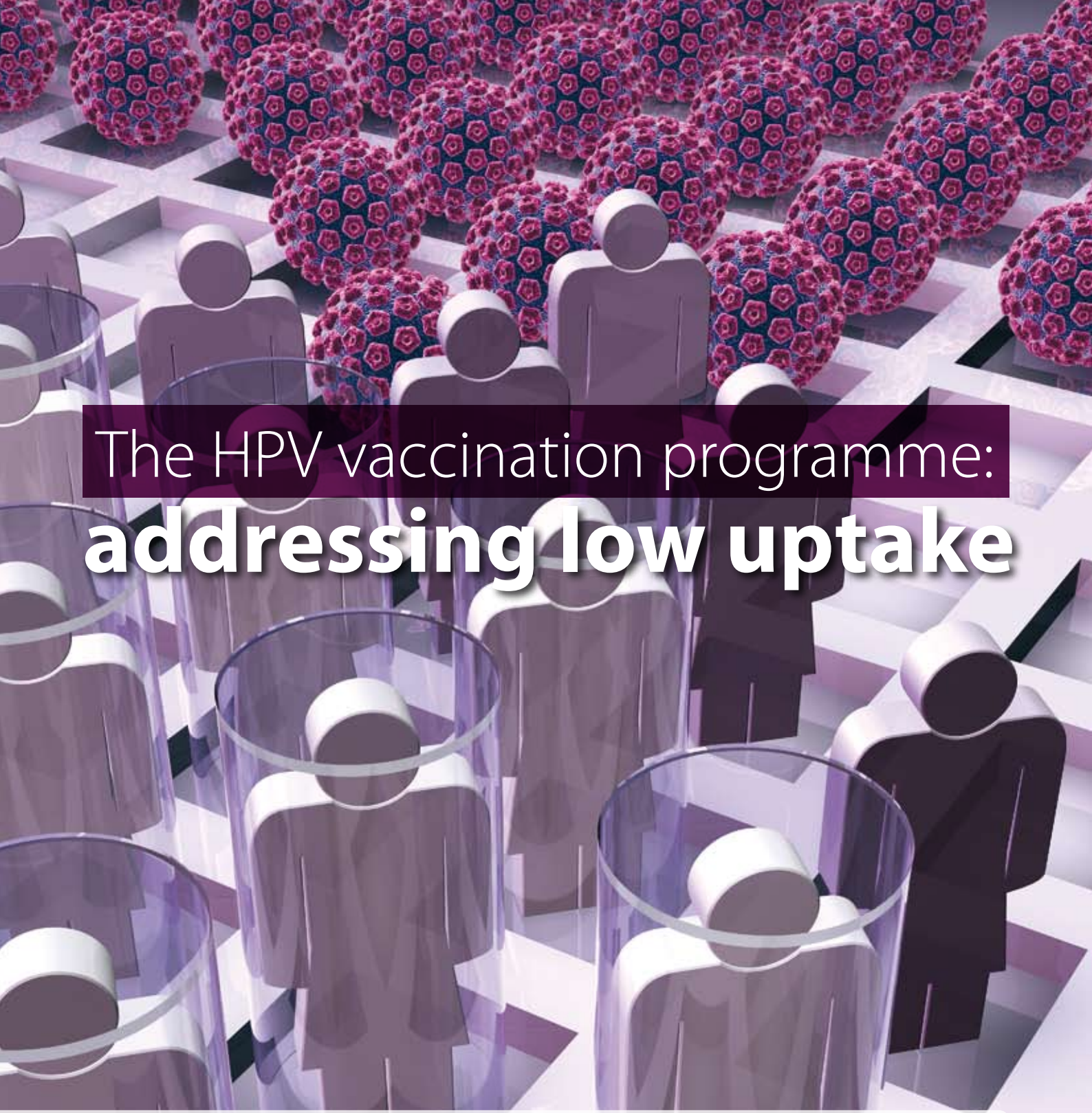


The HPV vaccination programme: addressing low uptake

Approximately 200 women develop cervical cancer in New Zealand each year. High-risk strains of human papillomavirus (HPV) is linked to more than 99% of the abnormalities that lead to cervical cancer.[1, 2] To help prevent these cancers the HPV vaccine (known as the cervical cancer vaccine) was added to the National Immunisation Schedule on 1 September, 2008 for girls aged 12 years. The cervical cancer vaccine used in New Zealand (Gardasil) protects against the two strains of HPV most commonly associated with cervical cancer (types 16 and 18) and two strains commonly associated with genital warts (types 6 and 11). Despite this, there has been a low uptake of the vaccine both in New Zealand and overseas.[3, 4] Primary health care providers are encouraged to offer information, address any fears and concerns, and promote uptake of the vaccine amongst young females in New Zealand.

The human papillomavirus

Human papillomavirus (HPV) is a common infection that is spread through skin and sexual contact. Epidemiological studies in the United States have shown that four out of five people will be infected with HPV between age 15 – 50 years.[5]

Risk factors for contracting HPV include:[6–8]

- Age < 25 years
- Multiple sexual partners
- Younger age at first sexual activity
- Long-term oral contraceptive use

The majority of HPV infections are transient and asymptomatic with an average duration of six months.[4, 9] However, approximately 10% of infections in females become persistent and can lead to atypical cell growth, resulting in pre-malignant lesions in the genital tract, particularly the cervix.[7] The likelihood of an infection becoming persistent increases with age, due to increased exposure time, reduced level of cells returning to normal and reduced immune response to HPV.[7, 8]

Of the more than 100 strains of HPV, approximately one-third affect the genital tract – 15 of which are referred to as high-risk strains.[10] HPV types 16 and 18 are high-risk strains that are associated with approximately 70% of cervical cancer cases.[8] Low-risk HPV strains are either asymptomatic or cause benign abnormalities; such as HPV types 6 and 11, which cause 90% of genital warts.

The role of HPV in cervical cancer

HPV DNA is detected in 95 – 100% of all cervical cancers (HPV types 16 and 18 account for 70%), as well as in 50% of anal cancers and in some rarer penile, vaginal and oropharyngeal cancers.[11]

Cervical cancer develops from HPV infection, via the following pathway:[10]

1. Exposure to a high-risk strain of HPV
2. HPV infection occurs
3. HPV infection is not cleared and becomes persistent
4. Detectable, pre-malignant changes occur in cells on or around the cervix
5. Cervical cancer develops from these pre-malignant lesions

Squamous epithelial cell abnormalities are predominantly found in younger females, while cancers are more prevalent in older females, suggesting a slow development from HPV infection through to cancer.[9, 12, 13]

The New Zealand cervical cancer vaccine programme

The cervical cancer vaccination programme, using the HPV vaccine, began in New Zealand in September, 2008 with the aim of reducing the incidence of cervical cancer.

HPV vaccination is currently funded for females aged 12 – 20 years:

- Females born between 1 January and 31 December, 1992 have until 31 December, 2012 to receive their first vaccination dose
- Females born after 1 January 1993 have until their 20th birthday (not the end of their twentieth year) to receive their first vaccine dose

School-based vaccination programmes for females in Year Eight (age 12 years) are available nationwide, with the exception of the Canterbury DHB region, where the vaccine is only available through primary care providers.

Girls who decline (or if aged under 16 years, girl's parents who decline) to participate in the school programme can still have the funded vaccine through primary care.

The vaccine

Gardasil is the funded vaccine for cervical cancer in New Zealand. It is made from protein sub-units and contains no live or whole viruses. It protects against four strains of the HPV virus: high-risk strains 16 and 18, and low-risk strains 6 and 11.

The vaccine is given in three doses over six months, at months zero, two and six. This schedule is designed to provide maximum immune response, however, people who have missed a scheduled dose should still be strongly encouraged to continue the vaccination programme. Previous doses do not need to be repeated and immunity is still likely to be achieved as long as the course is completed.

HPV testing should not be requested prior to, or post, vaccination.

Gardasil is approved for males aged 9 – 26 years and females aged 9 – 45 years. If females outside the funded age range or males wish to be vaccinated they can, at a cost of approximately $450.00 for the three doses (see Page 36 for further discussion of vaccination in men and in women aged over 20 years).

Safety

The HPV vaccine has a strong safety profile.[14] A report of the most recent adverse event data in New Zealand, to the end of 2009, indicated that 236, 299 doses had been given, resulting in 236 adverse reactions.[15] The majority of these were common immunisation adverse reactions (see below). Ten reports were categorised as serious, including one death, however, there is no evidence that this was related to the vaccine. The Centre for Adverse Reactions Monitoring (CARM) noted that the pattern of events was typical of post-immunisation symptoms and does not raise any particular safety concerns.[15] The World Health Organisation has reported few significant adverse effects linked with the vaccination, after over 54 million doses administered in the previous six years.[9]

The most common adverse effects associated with HPV vaccination include:

- Mild pain at the injection site
- Mild swelling/redness at the injection site
- Nausea or headaches
- Dizziness/fainting

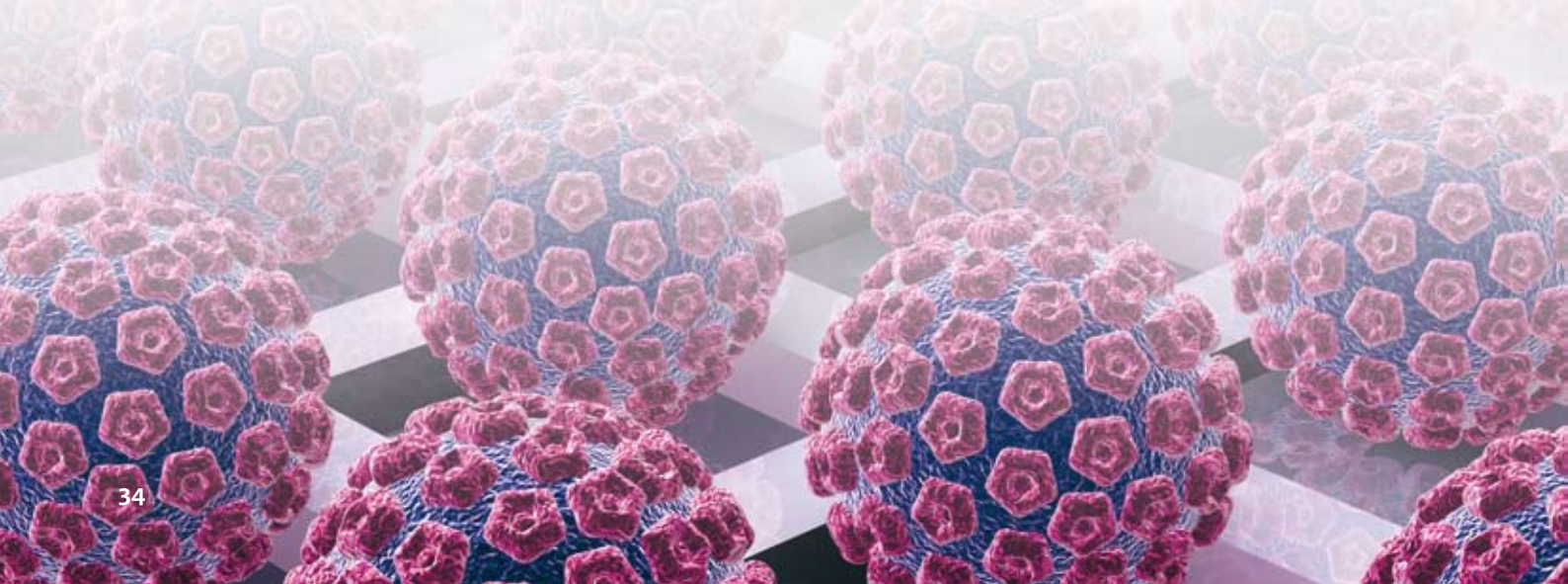
A 20 minute post-vaccination observation period is recommended to monitor for fainting or anaphylactic reactions.

Efficacy

Gardasil is effective at creating antibody-resistance against the four HPV strains.[9] Randomised, post-marketing trials have found a seropositive response (i.e. antibodies to HPV were at detectable levels) in 100% of females aged 15 – 55 years who received the vaccine.[16]

There are early signs that the vaccine has begun to have an effect on the incidence of genital warts in New Zealand, which has dropped among sexually active females aged under 20 years by approximately 63% since the vaccination programme began.[17] A similar decline in genital warts is being seen for males aged under 20 years.[17] Large-scale studies in Australia have shown that the incidence of genital warts has declined almost completely in young, heterosexual males and females, four years after the HPV vaccine was introduced.[18]

It is yet unclear how effective the vaccine will be at protecting against cervical cancer, as the first trial populations vaccinated have not reached an age where they are at an increased risk of cervical cancer. The significant increase in antibodies following immunisation is strongly suggestive of protection.[19] Analysis of international studies (FUTURE I and II) has shown that the



HPV vaccine has significantly reduced the incidence of high grade disease of the cervix by 65%.[20] This is expected to be indicative of a lower rate of progression to cervical cancer.

HPV immunisation is still beneficial in people who are sexually active. Sexually active people may not have been exposed to all four types of HPV and in addition, immunisation has been shown to significantly increase antibodies, which may help to prevent re-infection.[21]

Duration

Immunity gained from the HPV vaccine is predicted to be long-term. Ongoing studies indicate that the vaccine provides at least six years protection with limited antibody decline.[19] Protection against the four HPV types included in the vaccine remains at 100% at six years post-vaccination.[16] These studies will continue to monitor both the duration of immunity and safety of the vaccine.

The continuing role of cervical screening

Regular cervical screening, as part of the national screening programme, is still required for females who have received the HPV vaccine.

The vaccine protects against the two HPV strains that cause approximately 70% of cervical cancers. The remaining 30% of cancers are caused by other HPV strains and cervical screening will still be required to detect abnormalities arising from them.

Current coverage of the vaccination programme in New Zealand

The current immunisation goal, set out initially by the World Health Organisation, was for a minimum of 70% of young females to receive the HPV vaccine.[14] This level was recommended as it was thought to be the most cost-effective way in which to reach herd immunity and reduce cervical cancer. International debate is ongoing as to the advantage of now including young males in vaccination programmes, to improve herd immunity.

In 2010, the national uptake of the first dose of HPV vaccine for all females born between 1992 and 1997 was 52%.[3, 4] Vaccination was highest amongst Pacific females (70%), followed by Māori females (57%).[3] Almost all went on to complete the course, with national uptake of the third dose at 50%.[22]

Although overall figures are well below the immunisation target, uptake and completion of doses is higher in New Zealand than in many other countries. In the United States uptake of the vaccine was 44% for the first dose, but decreased to 27% for the final dose.[23]

Addressing low uptake of the school-based vaccination programme

With current uptake of school-based vaccination low, general practice can help to ensure that target levels of immunisation are reached.

All females aged 12 to 20 should be asked whether they have received the cervical cancer vaccine (and completed the course), whenever they present for a consultation. The National Immunisation Register will contain this information for some people, but only if they have agreed for the information to be collected and have provided contact details of their General Practitioner.

Those that have not received the HPV vaccine should be given information about the vaccine and vaccination should be offered. Providing education about the vaccine may help to increase uptake. If girls or their parents feel that they are still not ready or do not wish to receive the vaccine, a reminder can be set in the patient management system to ask again at a subsequent consultation.

Patient leaflets are available from:
www.cervicalcancervaccine.govt.nz

Barriers to vaccination – concerns, fears and misconceptions

The role of the health-care provider should be to offer unbiased, evidence-based information about the HPV vaccine and to address any fears or concerns. Research shows that the strongest indicator for acceptance and uptake of the HPV vaccine is a recommendation from a general practitioner.[24]

"My daughter is too young"

Evidence indicates that many parents prefer to have their child vaccinated later than the recommended age 12 years.[25] However, this age-based recommendation has been formed for two reasons; firstly, females in this age group have a stronger antibody response to the vaccine than older females and secondly, it allows for the majority of females to be vaccinated prior to commencing sexual activity.[9] The period with the highest risk of HPV infection is within two to three years after commencing sexual activity.[2] If sexual activity does not commence until adulthood there is unlikely to be

any disadvantage in early vaccination as immunity does not appear to decline over time.[19]

"Why bother with the vaccine if I'm already sexually active"
There is still benefit in immunising young people who are sexually active. Even after sexual activity has begun most people are very unlikely to have contracted all four of the strains in the vaccine and, even if they have, the vaccine increases antibody levels, which may prevent re-infection.[21]

"Vaccines are unsafe /I don't believe in them"
The HPV vaccine has a strong safety profile and has been extensively used world-wide without serious complications.[10, 16]

Patient education has been shown to increase acceptance and uptake of vaccines in people who are "anti-vaccine" or concerned about the consequences of vaccination.[24, 25] The considerable benefit of an effective vaccine against cervical cancer should be carefully weighed against the small risk of adverse effects.

"The vaccine will promote unsafe sex/promiscuity"
The HPV vaccine is an important part of practicing "safe sex". There is no evidence to suggest that immunisation against HPV leads to unsafe sex, lower rates of condom usage, a younger age of commencing sexual activity or an increased number of partners.[26, 27] Having the HPV vaccine has been shown to lead to increased communication about sex between mothers and daughters.[27]

"Why bother, that's what condoms are for"
Being vaccinated is not a reason to stop using condoms, nor is the regular use of condoms a reason not to be vaccinated. Condoms provide modest protection against most genital HPV strains, however, skin-to-skin contact is sufficient to spread the virus so protection is not guaranteed.[28] Co-infection with chlamydia or gonorrhoea significantly increases HPV infection rate and condoms reduce the infection rate of these sexually transmitted infections (STIs).[28] Condoms also reduce the likelihood of persistent HPV infection in women due to reduced viral load and reduced co-infection with other STIs.[28]

Best Practice tip: using the term "cervical cancer vaccine" rather than "HPV vaccine" may increase acceptance of the vaccine among younger females and their parents. Anecdotal evidence suggests that some people mistake "HPV" for "HIV".

The potential benefit of immunising males and older females

What about males?

Gardasil is approved for males aged 9 – 26 years.[29] In males the vaccine will directly protect against genital warts, some anal and penile cancers, and provide indirect protection to future female partners against cervical cancer.

There is currently no recommendation to routinely vaccinate males in New Zealand, however, those who wish to be vaccinated can be encouraged to do so. Vaccination is not funded for males.

In response to the low uptake of the HPV vaccine in the United States, the Centre for Disease Control and the American Academy of Paediatrics have recently issued a recommendation that all males aged 11 – 12 years be routinely offered the vaccine, and that all males age 13 – 21 be included in a catch-up programme.[30]

HPV vaccine can be beneficial in females aged over 20 years

Gardasil is approved for females aged 9 – 45 years,[29] but only funded for those aged 12 – 20 years. There is no recommendation to routinely vaccinate females aged over 20 years, however, it may provide protection for people in this age group, particularly those with risk factors for HPV infection, e.g. multiple partners.

The prevalence of HPV has two peaks in females: one between age 15 – 24 years and a second between aged 45 – 50 years.[16] The reason for this second peak is not well understood, but is likely to be due to either an age-related reduction in resistance to HPV, or an increase in sexual activity with new partners at that age. Vaccination may offer benefit in preventing this second peak.

Initially it was thought that immunising females after the commencement of sexual activity would not be beneficial due to the increasing likelihood that they will already have been exposed to the HPV strains in the vaccine. However, a study of females aged 26 years found that while many had some form of HPV infection very few had both strains 16 and 18.[16] In addition, those who had HPV prior to vaccination had a greater antibody response to the vaccine, suggesting that even if a person is already infected, or was infected in the past, they may still benefit from vaccination.[16]

More information on the HPV vaccine can be found at **www.cervicalcancervaccine.govt.nz** and **www.immune.org.nz**

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