FactSheet

QUADRIVALENT HPV VACCINE

FREQUENTLY ASKED QUESTIONS

This fact sheet provides responses to common patient questions and concerns about human papillomavirus (HPV) and the quadrivalent HPV vaccine. Because there is misleading information about HPV vaccines on the Internet and social media, anyone with questions or concerns should be cautioned to check that they obtain information from reliable and trusted sources. More detailed information about HPV and the available vaccines can be found in the NCIRS fact sheet Human papillomavirus (HPV) vaccines for Australians: information for immunisation providers.

Questions about HPV vaccine safety

- Q1. How do we know the vaccine is safe?
- Q2. I've read that the ingredients in the HPV vaccine cause autoimmune diseases. Is that true?
- Q3. I've heard that the HPV vaccine triggers a range of rare but serious conditions, such as POF, POTS and CRPS. Is that true?
- Q4. Does the vaccine cause fainting?
- Q5. How do we know the vaccine won't cause cancer? Surely if HPV can, a vaccine based on it might too?
- Q6. I've heard the vaccine could cause infertility. Is that true?
- Q7. Is it safe to get the vaccine when pregnant?
- Q8. I've heard that it is a genetically modified vaccine. Is that true?

Questions about HPV and the HPV vaccine in general

- Q9. Is the vaccine really needed if only a small proportion of HPV infections lead to cancer?
- Q10. I've heard there are many HPV types that can infect people, but the vaccine only protects against four. Can I still get cancer caused by HPV even if I am vaccinated?
- Q11. Is it true that the risk of cervical cancer in Australia is really low, even without vaccination?
- Q12. I thought HPV vaccine prevents against cervical cancer. Why is it now being offered to boys too?
- Q13. How do we know that other HPV types won't replace those we vaccinate against?

Questions about HPV vaccine efficacy and impact

- Q14. I've heard the vaccine doesn't work if you get it after you've already become sexually active. Is that true?
- Q15. How do we know the vaccine will prevent cancers caused by HPV when cancer takes years to develop and the clinical trials ran for less than 5 years?
- Q16. Is it true that there are already reductions in HPV disease in Australia since vaccination was introduced in 2007?
- Q17. Isn't leading a healthy lifestyle enough to prevent cancer?

Other issues

- Q18. If all the trials were sponsored by the vaccine manufacturer, can we trust their data?
- Q19. Why is there information on the Internet and social media saying the vaccine is dangerous if it isn't?
- Q20. Could receiving HPV vaccine make my daughter or son promiscuous?

Questions about HPV vaccine safety

Q1. How do we know the vaccine is safe?

Overall, the vaccine has an excellent safety profile, similar to that for other vaccines routinely used in the National Immunisation Program. Population-based monitoring done around the world has found no evidence that there is any illness that occurs more frequently among people who have had HPV vaccine compared to those who have not. The HPV vaccine trials for Gardasil® which provided data for registration of the vaccine involved over 30,000 people worldwide. The trials have been evaluated by many expert groups, including the Food and Drug Administration (FDA) in the USA and the Therapeutic Goods Administration (TGA) in Australia, all of which have concluded that the vaccine is safe and effective. According to the World Health Organization (WHO), to date over 200 million doses of the vaccine have been distributed worldwide with many countries monitoring vaccine safety post-licensure (i.e. after the vaccine is in use).

The main side effects of the quadrivalent vaccine are reactions at the injection site (pain, redness and swelling) which occur in about 80% of recipients. However, these reactions generally resolve within a few days. In some people, fainting, or related symptoms such as dizziness, can be triggered in response to painful stimuli such as vaccination; however, this can be avoided with appropriate care (***see Q4***). The most common symptoms reported in the week after vaccination with Gardasil® are fever (slightly more frequently than in those who received a placebo injection), headache and fatigue (but these were no more common than in placebo recipients).

There were very few serious adverse events reported after vaccination in clinical trials and they were no more frequent in participants who received the vaccine than in participants who received a placebo. Similarly, the overall proportion of people reporting new onset autoimmune conditions was similar between the vaccine and placebo groups in the trials (***see Q2***).

Ongoing, in-depth follow-up in women and men vaccinated in the clinical trials is continuing, to monitor the duration of vaccine effectiveness and to confirm safety over longer periods of time. In particular, Scandinavian women originally enrolled in the Gardasil® trials decades ago are being followed using systems that can link to health registers of cancer, Pap tests and other conditions.

Post-licensure safety monitoring is ongoing, particularly through passive reporting systems which rely on healthcare professionals and members of the public to report any suspected adverse events following vaccination. In Australia, such reports are collected by the TGA and summaries are publicly available through the Database of Adverse Event Notifications (DAEN) (www.tga.gov.au/database-adverse-event-notifications-daen). However, it is important to remember that an assessment of the safety of a vaccine (or medicine) cannot be made by looking at reports on the DAEN, as they do not contain information on whether the reactions are likely to have been caused by the vaccine or whether other causes have been considered. National and international analyses by expert groups of all reports of adverse events following HPV vaccine, together with many well-conducted epidemiological studies, have shown the vaccine to be very safe (***see also Q2 and Q3***). More detailed information of reported reaction rates are published each year by the National Centre for Immunisation Research and Surveillance (NCIRS) and TGA (www.health.gov.au/internet/main/publishing.nsf/Content/cda-aefi-anrep.htm).

The only contraindication to vaccination with Gardasil® is known anaphylaxis (severe allergy) to yeast or severe allergy to any other vaccine ingredient(s). As with any medication, there is always a small risk of an allergic reaction (anaphylaxis) following administration. Although these events are rare, all patients should be observed for 15 minutes after vaccination.

References

Block SL, Brown DR, Chatterjee A, et al. Clinical trial and post-licensure safety profile of a prophylactic human papillomavirus (types 6, 11, 16, and 18) L1 virus-like particle vaccine. *Pediatric Infectious Disease Journal* 2010;29:95-101.

Ferris D, Samakoses R, Block SL, et al. Long-term study of a quadrivalent human papillomavirus vaccine. *Pediatrics* 2014;134:e657-65.

Gee J, Naleway A, Shui I, et al. Monitoring the safety of quadrivalent human papillomavirus vaccine: findings from the Vaccine Safety Datalink. *Vaccine* 2011;29:8279-84.

Macartney K, Chiu C, Georgousakis M, Brotherton JM. Safety of human papillomavirus vaccines: a review. *Drug Safety* 2013;36:393-412.

Slade BA, Leidel L, Vellozzi C, et al. Postlicensure safety surveillance for quadrivalent human papillomavirus recombinant vaccine. *JAMA* 2009;302:750-7.

World Health Organization (WHO). Global Advisory Committee on Vaccine Safety, 2–3 December 2015. *Weekly Epidemiological Record* 2016;91:21-31. Available from: www.who.int/wer/2016/wer9103.pdf?ua=1 (Accessed 4 March 2016)

Q2. I've read that the ingredients in the HPV vaccine cause autoimmune diseases. Is that true?

Like many other vaccines, HPV vaccines contain an adjuvant. Adjuvants are substances added to vaccines to improve the immune response to the part of the vaccine that mimics the pathogen.

The adjuvant in the quadrivalent HPV vaccine is an aluminium adjuvant. Aluminium-containing adjuvants have been around for more than 50 years and are widely used in human vaccines. Much larger amounts of aluminium are taken into the body through other means, such as food, than through vaccines. There is no evidence that aluminium in vaccines results in any serious or long-term adverse events, including autoimmune diseases.

Evidence from clinical trials and post-licensure studies of the quadrivalent HPV vaccine shows no link between the vaccine and autoimmune diseases. An analysis of several early and pivotal trials, involving a total of more than 20,000 girls and women aged 9–26 years and about 1,350 boys aged 9–16 years, found that the overall proportion of participants who reported new onset autoimmune conditions was similar among those who got the vaccine and those who got a placebo (2.4% of people in each group). Post-licensure epidemiological studies have not identified any association between HPV vaccination and autoimmune conditions including multiple sclerosis and type 1 diabetes.

One recent French study in over 2 million girls also showed no link with many of these conditions, but suggested a possible very small risk (approximately 1 in 1 million girls vaccinated) of Guillain-Barré syndrome (GBS), a disease that causes inflammation of nerves and results in generalised muscle weakness, and for which the cause is usually unknown. However, a relationship between HPV vaccination and GBS has not been observed in any other well-conducted studies. Publication of this study in the peer-reviewed literature and more research to understand if there is any increased risk of GBS after HPV vaccine is awaited. Providers and the public should remember that the benefits of vaccination far outweigh any small theoretical risk.

The other HPV vaccine available in Australia, the bivalent HPV vaccine (Cervarix®), has a unique adjuvant, ASO4, which contains aluminium, in the form of aluminium hydroxide, combined with another compound called monophosphoryl lipid A. No association has been found between ASO4-containing vaccines (including Cervarix®) and autoimmune conditions.

References

Block SL, Brown DR, Chatterjee A, et al. Clinical trial and post-licensure safety profile of a prophylactic human papillomavirus (types 6, 11, 16, and 18) l1 virus-like particle vaccine. *Pediatric Infectious Disease Journal* 2010;29:95-101.

Chao C, Klein NP, Velicer CM, et al. Surveillance of autoimmune conditions following routine use of quadrivalent human papillomavirus vaccine. *Journal of Internal Medicine* 2012;271:193-203.

Jefferson T, Rudin M, Di Pietrantonj C. Adverse events after immunisation with aluminium-containing DTP vaccines: systematic review of the evidence. *The Lancet Infectious Diseases* 2004;4:84-90.

World Health Organization (WHO). Global Advisory Committee on Vaccine Safety, 2–3 December 2015. *Weekly Epidemiological Record* 2016;91:21-31. Available from: www.who.int/wer/2016/wer9103.pdf?ua=1 (Accessed 4 March 2016)

Q3. I've heard that the HPV vaccine triggers a range of rare but serious conditions, such as POF, POTS and CRPS. Is that true?

Many organisations, including the Global Advisory Committee on Vaccine Safety (GACVS), established by the WHO, have systematically investigated all HPV vaccine safety concerns that have been raised and continue to recommend the vaccine as safe and effective. Recent case reports have been put forward that hypothesise that a range of rare and poorly understood conditions, such as premature ovarian failure (POF), postural orthostatic tachycardia Syndrome (POTS) and complex regional pain syndrome (CRPS) could be induced by the quadrivalent HPV vaccine. These reports lack scientific and epidemiological credibility and do not

provide sufficient evidence to suggest a causal link between the vaccine and these illnesses. One country, Japan, has suspended promotion of the use of HPV vaccine, despite an expert Japanese committee and all respected scientific groups worldwide finding no evidence that the vaccine is responsible for causing these conditions.

POF, also known as premature menopause, occurs when the menstruation cycle ceases before the age of 40, and in up to 90% of cases, the cause is unknown. It has recently been suggested that the HPV vaccine may be a cause, based on some reports of teenage girls in Australia and America presenting with POF-like symptoms after receiving the HPV vaccine. However, because many girls have received HPV vaccine and POF has long been known to occur in females who have not been vaccinated, these few cases do not show an increase in POF or prove a link to the vaccine.

POTS is a persistent condition where dizziness, light-headedness and heart palpitations occur when an individual stands up, and the condition usually persists for about1 year. It occurs mostly in women between the ages of 15 and 50, and is thought to be caused by a variety of known and unknown factors. Again, based on 6 cases who presented with POTS-like symptoms between 1 week and 4 months after receiving a dose of the quadrivalent vaccine, it was hypothesised that the HPV vaccine may be the cause. However, POTS occurs irrespective of vaccination, and pre-clinical and clinical studies have found no evidence or basis to suggest a causative relationship between POTS and HPV vaccination. In 2015, the European Medicines Agency reviewed all evidence regarding the hypothesised association between HPV vaccine and both POTS and CRPS (see below) and concluded there was no evidence to support a causal association between HPV vaccination and these conditions.

CRPS is a painful condition characterised by spontaneous pain, sensitivity, weakness and swelling, usually in one limb. It is usually triggered following trauma to the site. There have been four reported cases of teenage girls in Australia developing CRPS after receiving a dose of Gardasil® and a few cases have been reported after other types of vaccines. However, any painful trigger (for example, a needle, scratch or insect bite) can, very rarely, lead to development of CRPS. There is no evidence to support HPV vaccine being a particular trigger of CRPS over and above that rarely seen for any other painful stimuli. Any person experiencing pain at the injection site following immunisation should be encouraged to use that limb as normally as possible.

Over 200 million HPV vaccine doses have been administered worldwide and the vaccine has been shown to have an excellent safety profile. Cases of POF, POTS and CRPS have not been shown to be increased or have a clear biological or epidemiological causal association to the HPV vaccine. Evidence from surveillance systems and follow-up studies have not indicated that these illnesses are occurring more frequently in vaccinated people than in unvaccinated people. The WHO, the Centers for Disease Control and Prevention (CDC) in the USA, The Australian Technical Advisory Group on Immunisation (ATAGI), and many other experts continue to recommend that HPV vaccine be administered and promoted to prevent HPV-related disease and deaths.

References

European Medicines Agency. Review concludes evidence does not support that HPV vaccines cause CRPS or POTS [press release]. 5 November 2015. Available from: www.ema.europa.eu/docs/en_GB/document_library/Press_release/2015/11/WC500196352.pdf (Accessed 4 March 2016)

Hawkes D, Buttery JP. Human papillomavirus vaccination and primary ovarian insufficiency: an association based on ideology rather than evidence [editorial]. *Current Opinion in Obstetrics and Gynecology* 2016;28:70-2.

Macartney KK, Chiu C, Georgousakis M, Brotherton JM. Safety of human papillomavirus vaccines: a review. *Drug Safety* 2013;36:393-412.

Vichnin M, Bonanni P, Klein NP, et al. An overview of quadrivalent human papillomavirus vaccine safety: 2006 to 2015. *Pediatric Infectious Disease Journal*. 2015;34:983-91.

World Health Organization (WHO). Global Advisory Committee on Vaccine Safety, 2–3 December 2015. *Weekly Epidemiological Record* 2016;91:21-31. Available from: www.who.int/wer/2016/wer9103.pdf?ua=1 (Accessed 4 March 2016)

World Health Organization (WHO). Global Advisory Committee on Vaccine Safety statement on safety of HPV vaccines. 17 December 2015. Available from: www.who.int/vaccine_safety/committee/GACVS_HPV_statement_17Dec2015.pdf?ua=1 (Accessed 4 March 2016)

Q4. Does the vaccine cause fainting?

Some people who receive an injection of any kind do faint or have other symptoms associated with fainting, such as headache or feeling weak, nauseous and/or dizzy. Others may become very anxious due to fear of needles and/or the responses of others around them who are being vaccinated (e.g. in school-based clinics). These reactions are more common in adolescents and young people, independent of whether a vaccine is being given. Although sometimes distressing, these symptoms usually resolve with simple treatment such as lying down, adequate food and drink intake, and reassurance. When administering the vaccine, it is important to make sure patients have eaten properly before vaccination and are observed for 15 minutes afterwards.

Adverse events occurring around the time of vaccination in the school setting are reported and investigated as appropriate.

In May 2007, media reports publicised that a group of school girls in Melbourne became unwell after being vaccinated. All of these episodes fully resolved and were attributed by the treating medical staff to fainting and anxiety/stress reactions.

References

Buttery JP, Madin S, Crawford NW, et al. Mass psychogenic response to human papillomavirus vaccination. *Medical Journal of Australia* 2008;189:261-2.

Centers for Disease Control and Prevention (CDC), Kroger AT, Sumaya CV, et al. General recommendations on immunization – recommendations of the Advisory Committee on Immunization Practices (ACIP). [erratum appears in MMWR Recomm Rep. 2011 Jul 29;60:993]. *MMWR Recommendations and Reports* 2011;60(RR-2):1-61.

Q5. How do we know the vaccine won't cause cancer? Surely if HPV can, a vaccine based on it might too?

Neither of the HPV vaccines in use in Australia can cause cancer. The viral proteins which can disrupt normal cell growth and repair mechanisms and ultimately result in cancer are well described in the scientific literature. They are not contained in the HPV vaccines.

HPV vaccines are made using recombinant DNA technology and contain only 'virus-like particles' (***see Q8***). The vaccines contain only proteins from the outer coat of the virus, with no viral DNA. It is not a live virus, and is not infectious.

References

Burd EM. Human papillomavirus and cervical cancer. *Clinical Microbiology Reviews* 2003;16:1-17.

Greenblatt RJ. Human papillomaviruses:diseases, diagnosis, and a possible vaccine. *Clinical Microbiology Newsletter* 2005;27:139-45.

Münger K, Howley PM. Human papillomavirus immortalization and transformation functions. *Virus Research* 2002;89:213-28.

Q6. I've heard the vaccine could cause infertility. Is that true?

No. There is no biologically plausible way in which the vaccine could cause infertility in either women or men. HPV infection, unlike some other sexually transmitted infections such as chlamydia, is not a cause of infertility. Studies of high doses of the vaccine in female and male rats showed no effect on fertility.

Some Internet sites report disturbing claims that one ingredient of the vaccine, polysorbate 80, causes infertility in rats. This is based on one study of newborn rats (weighing 10–17 grams) given extremely large doses (20–200 times the amount in Gardasil®) injected into the abdomen. However, the Therapeutic Goods Administration has reviewed available data regarding polysorbate 80 and fertility and concluded that there is no evidence that polysorbate 80 at a level of 50 µg per 0.5 mL dose of Gardasil® poses a hazard to human reproduction or fertility. Polysorbate 80 is used as an emulsifier and is found in numerous medications, including other vaccines, and is used as a food additive and in cosmetics.

Providers and the public should be aware that false scares about vaccines leading to infertility are sometimes used to disrupt immunisation campaigns. For example, scare campaigns in Nigeria in 2003 about the polio vaccine leading to infertility resulted in reduced vaccine uptake and consequent polio outbreaks.

References

Centers for Disease Control and Prevention (CDC). Resurgence of wild poliovirus type 1 transmission and consequences of importation – 21 countries, 2002–2005. *MMWR Morbidity and Mortality Weekly Report* 2006;55:145-50.

Raufu A. Nigeria postpones programme of polio immunisation. *BMJ* 2004;328:1278.

Wise LD, Pauley CJ, Michael B, Wolf JJ. Lack of effects on male fertility from a quadrivalent HPV vaccine in Sprague-Dawley rats. *Birth Defects Research Part B:*

Developmental and Reproductive Toxicology 2010;89:376-81.

Wise LD, Wolf JJ, Kaplanski CV, et al. Lack of effects on fertility and developmental toxicity of a quadrivalent HPV vaccine in Sprague-Dawley rats. *Birth Defects Research Part B: Developmental and Reproductive Toxicology* 2008;83:561-72.

Q7. Is it safe to get the vaccine when pregnant?

Although it is recommended that HPV vaccination be avoided during pregnancy, there is no indication that inadvertent administration of the vaccine to a pregnant woman will result in an increased risk of adverse pregnancy outcomes. Although participants were requested to avoid pregnancy, during Phase 3 trials of Gardasil® there were 1,796 pregnancies in women who received Gardasil® and 1,824 pregnancies in placebo recipients. The rate of adverse pregnancy outcomes was similar in vaccine and placebo recipients. In particular, there was no evidence of an impact on spontaneous abortion rates, foetal deaths or number of live births. Congenital anomalies were rare and the types of anomalies that occurred in both groups were consistent with those generally observed in pregnancies in women in the 16–26 years age group.

Post-licensure surveillance of HPV vaccination during pregnancy has also been reviewed using pregnancy registries established by the vaccine manufacturers. Data from the Gardasil® registry are published and do not indicate any issues or new safety signals.

Women who wish to conceive following a course of Gardasil® are able to commence trying to fall pregnant immediately following the third dose, as the vaccine is not a live virus.

For women who fall pregnant before completing the 3-dose vaccine schedule, the schedule can safely be resumed following pregnancy. As with other vaccines, there is no need to recommence the vaccine schedule from the first dose but recommence with the due dose (second or third).

References

Dana A, Buchanan KM, Goss MA, et al. Pregnancy outcomes from the pregnancy registry of a human papillomavirus type 6/11/16/18 vaccine. *Obstetrics and Gynecology* 2009;114:1170-8.

Garland SM, Ault KA, Gall SA, et al. Pregnancy and infant outcomes in the clinical trials of a human papillomavirus type 6/11/16/18 vaccine: a combined analysis of five randomized controlled trials. *Obstetrics and Gynecology* 2009;114:1179-88.

Q8. I've heard that it is a genetically modified vaccine. Is that true?

No, neither of the HPV vaccines contains viral DNA and they cannot 'interact' with your DNA. HPV vaccines are made using recombinant DNA technology which means they contain very pure protein rather than killed or live viruses. Hepatitis B vaccine is made using similar technology.

The technique of producing the protein found in the coat of the virus, which then naturally self-assembles into 'virus-like particles' (VLPs), was first discovered by Professor Ian Frazer and colleagues in Brisbane. Prior to this discovery, all attempts to create a vaccine against HPV had proven unsuccessful. The genetic code (or instructions) to make the protein of the viral coat is inserted into either a yeast (for Gardasil®) or insect cell (for Cervarix®). The yeast or insect cell then makes the protein which assembles itself into VLPs which have the same shape (a sphere) as HPV but contain no viral DNA.

Reference

Zhou J, Sun XY, Stenzel DJ, Frazer IH. Expression of vaccinia recombinant HPV 16 L1 and L2 ORF proteins in epithelial cells is sufficient for assembly of HPV virion-like particles. *Virology* 1991;185:251-7.

Questions about HPV and the HPV vaccine in general

Q9. Is the vaccine really needed if only a small proportion of HPV infections lead to cancer?

It is estimated that 3–10% of HPV infections persist for long periods which can lead to the development of pre-cancerous abnormalities. In most cases, the pre-cancerous lesions disappear on their own over time; however, in some cases they progress to cause cancer. Even though only a small *proportion* of HPV infections result in disease, many people still develop cellular abnormalities and cancers because HPV infections are so common in the population

Prior to HPV vaccination, every year Pap screening in Australia detected low-grade cervical abnormalities in about 90,000 women and high-grade cervical abnormalities in a further 15,000 women. Even though Pap screening is in place to detect these pre-cancerous lesions, it is estimated that in 2016 there will still be 905 cases (which translates to a rate of 7 per 100,000 women) and 255 deaths due to cervical cancer.

Apart from the cervix, HPV is also associated with cancers of several other body sites in both women and men. In 2011, 218 Australian women and 151 Australian men were diagnosed with anal cancer, of which approximately 85% of cases are caused by HPV. Additionally, about 600 new cases of cancer of the mouth and throat are detected every year in Australia, of which HPV causes about 60%. HPV is also associated with vulvar, vaginal and penile cancers. It is important to note that most of these cancers would have arisen from HPV infections that were acquired prior to the availability of vaccination.

The advantage of vaccination is that it *prevents* infections with the HPV types that are included in the vaccine and therefore also prevents the development of the pre-cancerous lesions and cancer that these infections may cause. Screening will only detect disease once it has already developed. When HPV vaccine is given prior to HPV exposure, vaccination is highly effective (in males and females) at preventing persistent infection with the HPV types included in the vaccine. In only 9 years since the HPV vaccination program was introduced in Australia in 2007, reductions in lesions caused by HPV are already being recorded (***see Q15 and Q16***).

References

Australian Institute of Health and Welfare (AIHW). Cancer in Australia: an overview, 2014. Cancer series no. 90. Cat. no. CAN 88. Canberra: AIHW; 2014. Available from: www.aihw.gov.au/publication-detail/?id=60129550047 (Accessed 4 March 2016).

Brotherton JM, Saville AM, May CL, et al. Human papillomavirus vaccination is changing the epidemiology of high-grade cervical lesions in Australia [letter]. *Cancer Causes and Control* 2015;26:953-4.

Georgousakis M, Jayasinghe S, Brotherton J, et al. Population-wide vaccination against human papillomavirus in adolescent boys: Australia as a case study. *The Lancet Infectious Diseases* 2012;12:627-34.

Giuliano AR, Harris R, Sedjo RL, et al. Incidence, prevalence, and clearance of type-specific human papillomavirus infections: the Young Women's Health Study. *Journal of Infectious Diseases* 2002;186:462-9.

Grulich AE, Jin F, Conway EL, et al. Cancers attributable to human papillomavirus infection. *Sexual Health* 2010;7:244-52.

Moscicki AB, Schiffman M, Burchell A, et al. Updating the natural history of human papillomavirus and anogenital cancers. *Vaccine* 2012;30 Suppl 5:F24-33.

Q10. I've heard there are many HPV types that can infect people, but the vaccine only protects against four. Can I still get cancer caused by HPV even if I am vaccinated?

There are 40 known HPV types which can infect the mucosal surfaces of humans and potentially cause disease. The HPV types included in the quadrivalent HPV vaccine (Gardasil®) were specifically chosen because they are the types which are most commonly associated with cancers (HPV types 16 and 18) or non-cancerous lesions such as genital warts (HPV types 6 and 11). For example, a worldwide study looking at HPV types found that, in cases of cervical cancer, HPV types 16 and 18 were detected in more than 70% of the samples. In other cancers caused by HPV that occur in males and females, such as anal cancer, HPV types 16 and 18 are found in approximately 85%. HPV types 6 and 11 are not commonly detected in cancers; however, they are responsible for nearly all cases of genital warts in males and females.

Although the quadrivalent HPV vaccine protects against the HPV types which most commonly cause serious disease, some of the HPV types not included in the vaccine can still cause cancer. It is for this reason that it is still important that women over the age of 18 years have a Pap test every 2 years after they have commenced sexual activity. After 1 May 2017, under the renewed National Cervical Screening Program, screening for women aged 25–74 years will be recommended every 5 years. In the interim, it is very important to follow the current recommendations. More information about the future changes to the National Cervical Screening Program can be found at www.cancerscreening.gov.au.

There is some evidence from clinical trials that vaccination might result in some cross-protection against other HPV types not included in the vaccine. However, the level of protection against other HPV types is less than for vaccine HPV types and it is still not known how long cross-protection lasts.

A 9-valent HPV vaccine (Gardasil®9) is now registered but not yet available in Australia. In addition to the same four types in the quadrivalent vaccine, it protects against additional HPV types: 31, 33, 45, 52 and 58. The extra HPV types covered in the 9-valent HPV vaccine are the next five most frequently detected HPV types in cervical cancers globally. In a large international randomised control trial with 14,215 women aged 16–26 years, the 9-valent HPV vaccine was safe and highly efficacious against infection and disease due to the additional five HPV types and it elicited similar levels of antibody to the four common HPV types. In further trial data in adolescent girls and boys, the 9-valent HPV vaccine was as safe and immunogenic as in 16–26-year-old females.

References

de Sanjose S, Quint WG, Alemany L, et al. Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. *The Lancet Oncology* 2010;11:1048-56.

Grulich AE, Jin F, Conway EL, et al. Cancers attributable to human papillomavirus infection. *Sexual Health* 2010;7:244-52.

Joura EA, Giuliano AR, Iversen OE, et al. A 9-valent HPV vaccine against infection and intraepithelial neoplasia in women. *New England Journal of Medicine.* 2015;372:711-23.

Malagón T, Drolet M, Boily MC, et al. Cross-protective efficacy of two human papillomavirus vaccines: a systematic review and meta-analysis. *The Lancet Infectious Diseases* 2012;12:781-9.

Petrosky E, Bocchini JA, Jr, Hariri S, et al. Use of 9-valent human papillomavirus (HPV) vaccine: updated HPV vaccination recommendations of the Advisory Committee on Immunization Practices. *MMWR Morbidity and Mortality Weekly Report*. 2015;64:300-4.

Van Damme P, Olsson SE, Block S, et al. Immunogenicity and safety of a 9-valent HPV vaccine. *Pediatrics*. 2015;136:e28-39.

Q11. Is it true that the risk of cervical cancer in Australia is really low, even without vaccination?

Due to the very successful Pap screening program in Australia, mortality due to cervical cancer is one of the lowest in the world (1.8 deaths per 100,000 women in 2014). However, the likelihood of a woman who lives up to 85 years of age dying of cervical cancer is 1 in 496. The highest mortality rate due to cervical cancer in Australia is among women who are unscreened or under-screened. Although screening prevents a large majority of cervical cancers, prior to the introduction of the HPV vaccination program it was estimated that nearly 560 cervical cancers per year were preventable by HPV vaccines that covered HPV types 16 and 18. In addition, Pap screening identified pre-cancerous lesions due to vaccine HPV types in tens of thousands of women each year. These women then had to undergo further tests and sometimes treatment (such as surgery) to remove the lesions to prevent development of cancer.

HPV vaccination is a preventive healthcare measure to be used in conjunction with Pap screening. As vaccination prevents infection with the most common HPV types associated with cancer, it means that, for these types, the initial persistent infection, and the subsequent progression to pre-cancerous lesions and then cancer, doesn't occur at all (***see Q9***). Due to the lead time of several years from HPV infection to development of cervical cancer, the impact of HPV vaccine on cancer incidence is not expected to be observed for decades after program introduction. However, studies have already demonstrated a substantial reduction in the incidence of cervical pre-cancerous lesions in young vaccine-eligible women. Although vaccination reduces the risk of pre-cancerous lesions being detected and requiring invasive treatment, vaccination does not protect against all HPV types, so screening is still required for vaccinated women.

In addition to reducing the risk of cervical cancer, HPV vaccination also protects against HPV infections and associated disease in other sites, such as the anus, vulva, vagina, penis, and head and neck (***see Q12***). There are no screening programs in place to detect cancers at these sites.

References

Australian Institute of Health and Welfare (AIHW). Cancer in Australia: an overview, 2014. Cancer series no. 90. Cat. no. CAN 88. Canberra: AIHW; 2014. Available from: www.aihw.gov.au/publication-detail/?id=60129550047 (Accessed 4 March 2016).

Australian Institute of Health and Welfare (AIHW). Cervical screening in Australia 2012–2013. Cancer series no. 93. Cat. no. CAN 91. Canberra: AIHW; 2015. Available from: www.aihw.gov.au/publication-detail/?id=60129550871 (Accessed 4 March 2016).

Crowe E, Pandeya N, Brotherton JM, et al. Effectiveness of quadrivalent human papillomavirus vaccine for the prevention of cervical abnormalities: case-control study nested within a population based screening programme in Australia. *BMJ* 2014;348:g1458.

Gertig DM, Brotherton JM, Budd AC, et al. Impact of a population-based HPV vaccination program on cervical abnormalities: a data linkage study. *BMC Medicine* 2013;11:227.

Grulich AE, Jin F, Conway EL, et al. Cancers attributable to human papillomavirus infection. *Sexual Health* 2010;7:244-52.

Stanley M, Lowy DR, Frazer I. Chapter 12: Prophylactic HPV vaccines: underlying mechanisms. *Vaccine* 2006;24 Suppl 3:S3/106-13.

Q12. I thought HPV vaccine prevents against cervical cancer. Why is it now being offered to boys too?

Cervical cancer is the most common HPV-associated cancer worldwide, so the majority of HPV research has been focused on understanding the role of HPV in causing that cancer type specifically. Because HPV vaccine development was initially focused on preventing cervical cancer, the first clinical trials involved only girls and women. However, as research has continued, much more is now known about the role of HPV in causing other cancers that affect men (such as penile cancer) and both men and women (such as head, neck and anal cancers). For example, in 2011, 75% of the approximate 600 cases of mouth and throat cancer, mostly attributable to HPV, occurred in men (***see Q9***).

A major clinical trial of the quadrivalent HPV vaccine in males 16–26 years of age showed the vaccine prevented more than 85% of persistent anogenital infections and external genital lesions (primarily genital warts) due to vaccine HPV types among participants not already infected by those types. Immunogenicity of the quadrivalent HPV vaccine in adolescent boys aged 9–15 was non-inferior to that in men aged 16–26 years, in whom vaccine efficacy has been demonstrated. Additionally, the immunogenicity and safety of the vaccine in boys was similar to that in girls and young adult women. Not only will HPV vaccination help prevent HPV infection and associated diseases in individual males, but research suggests vaccinating boys will contribute to increasing protection against HPV in girls due to 'community (herd) immunity'.

References

Australian Institute of Health and Welfare (AIHW). Cervical screening in Australia 2012–2013. Cancer series no. 93. Cat. no. CAN 91. Canberra: AIHW; 2015. Available from: www.aihw.gov.au/publication-detail/?id=60129550871 (Accessed 4 March 2016).

Block SL, Nolan T, Sattler C, et al. Comparison of the immunogenicity and reactogenicity of a prophylactic quadrivalent human papillomavirus (types 6, 11, 16, and 18) L1 virus-like particle vaccine in male and female adolescents and young adult women. *Pediatrics* 2006;118:2135-45.

Giuliano AR, Palefsky JM, Goldstone S, et al. Efficacy of quadrivalent HPV vaccine against HPV infection and disease in males. [erratum appears in N Engl J Med 2011 Apr 14;364(15):1481] *New England Journal of Medicine* 2011;364:401-11.

Giuliano AR, Anic G, Nyitray AG. Epidemiology and pathology of HPV disease in males. *Gynecologic Oncology* 2010;117(2 Suppl):S15-9.

Reisinger KS, Block SL, Lazcano-Ponce E, et al. Safety and persistent immunogenicity of a quadrivalent human papillomavirus types 6, 11, 16, 18 L1 virus-like particle vaccine in preadolescents and adolescents: a randomized controlled trial. *Pediatric Infectious Disease Journal* 2007;26:201-9.

Smith MA, Lew JB, Walker RJ, et al. The predicted impact of HPV vaccination on male infections and male HPV-related cancers in Australia. *Vaccine* 2011;29:9112-22.

Q13. How do we know that other HPV types won't replace those we vaccinate against?

Virological studies of HPV indicate that there is very little, if any, interaction between virus types, that is, they don't compete with each other. HPV16 appears to be unique in terms of its propensity to cause disease. Therefore, it is unlikely that other HPV types will replace the cancer-causing types 16 and 18 if infection with these two types is prevented through vaccination. The types of HPV infection occurring over time in Australia are being closely monitored.

Although it is unlikely that there will be 'replacement disease' following the prevention of HPV type 16 and 18 infection, we will still see disease from the remainder of the 40 or so HPV types that cause disease. This is why continuing to have Pap tests is important (***see Q10***).

References

Bernard HU. The clinical importance of the nomenclature, evolution and taxonomy of human papillomaviruses. *Journal of Clinical Virology* 2005;32 Suppl 1:S1-6.

Bernard HU, Calleja-Macias IE, Dunn ST. Genome variation of human papillomavirus types: phylogenetic

and medical implications. *International Journal of Cancer* 2006;118:1071-6.

Chan SY, Delius H, Halpern AL, Bernard HU. Analysis of genomic sequences of 95 papillomavirus types: uniting typing, phylogeny, and taxonomy. *Journal of Virology* 1995;69:3074-83.

Lowndes CM. Vaccines for cervical cancer. *Epidemiology and Infection* 2006;134:1-12.

Questions about HPV vaccine efficacy and impact

Q14. I've heard the vaccine doesn't work if you get it after you've already become sexually active. Is that true?

HPV vaccine works by stimulating the body's immune system to produce antibodies. These antibodies prevent infection with the four HPV types targeted by the vaccine but they do not treat infection that is already there. For the vaccine to work, it *must* be given before a person is exposed to the virus (i.e. come into contact with it). As HPV infection is commonly transmitted during sexual activity, HPV infection rates are highest in young people. Because of this, the best time to vaccinate is in early adolescence as most young adolescents haven't already been exposed to HPV. Additionally, younger adolescents respond better to the vaccine: those who receive their first HPV vaccine dose when aged 9–12 years develop approximately 1.5 times higher levels of HPV antibodies than older adolescents.

If the vaccine is given to people who are already sexually active, there is a higher chance they would have already been exposed to one or more of the vaccine HPV types and, in turn, the benefit of the vaccine will be reduced. This has been demonstrated in clinical trials of HPV vaccines. In women aged 16–26 years who had not yet been infected with any vaccine HPV types, vaccination prevented more than 98% of high-grade cervical lesions (CIN2 or worse) associated with those types. However, when all women enrolled in the trials were considered (including those who were already infected with any HPV type) protection for the whole group was lower at only 52%.

References

Kjaer SK, Sigurdsson K, Iversen OE, et al. A pooled analysis of continued prophylactic efficacy of quadrivalent human papillomavirus (types 6/11/16/18) vaccine against high-grade cervical and external genital lesions. *Cancer Prevention Research* 2009;2:868-78.

Reisinger KS, Block SL, Lazcano-Ponce E, et al. Safety and persistent immunogenicity of a quadrivalent human papillomavirus types 6, 11, 16, 18 L1 virus-like particle vaccine in preadolescents and adolescents: a randomized controlled trial. P*ediatric Infectious Disease Journal* 2007;26:201-9.

Smith JS, Melendy A, Rana RK, Pimenta JM. Age-specific prevalence of infection with human papillomavirus in females: a global review. *Journal of Adolescent Health* 2008;43:S5-25.

Q15. How do we know the vaccine will prevent cancers caused by HPV when cancer takes years to develop and the clinical trials ran for less than 5 years?

Although most HPV infections are cleared by the body naturally and never result in cancer, if an HPV infection persists the virus can eventually integrate into cells and prevent them from repairing themselves normally, causing pre-cancerous lesions. Over time, a proportion of these pre-cancerous lesions can progress into cancer. So, while not all HPV infections cause cancer, infection is the necessary first step for the development of cervical and other HPV-related cancers. Although other factors may be important in determining progression to cancer (***see Q17***), cancer does not occur without HPV infection.

Because of the long time it takes for cancer to develop, HPV vaccine trials needed to assess the efficacy of the HPV vaccine against the early stages of the disease process (i.e. 'surrogate' outcomes), rather than cancer as the end result. These surrogate outcomes included the vaccine's ability to prevent an initial HPV infection, as well as pre-cancerous lesions.

In clinical trials, HPV vaccination has been shown to prevent cervical, penile and anal infections due to the vaccine HPV types. More importantly the vaccines were also highly effective (90 to 100%) in preventing the step closer to cancer: pre-cancerous lesions caused by HPV. This outcome is taken as the most practical measure of the success of vaccination over time. This is accepted in much the same way that detection and removal of such lesions in the cervix, through Pap screening programs, is accepted as a means to reduce cervical cancer. Studies are now emerging that show substantial reductions in high

grade pre-cancerous cervical lesions in women eligible to receive HPV vaccination in Australia (***see Q16***).

References

FUTURE II Study Group. Effect of prophylactic human papillomavirus L1 virus-like-particle vaccine on risk of cervical intraepithelial neoplasia grade 2, grade 3, and adenocarcinoma in situ: a combined analysis of four randomised clinical trials. *The Lancet* 2007;369:1861-8.

Garland SM, Hernandez-Avila M, Wheeler CM, et al. Quadrivalent vaccine against human papillomavirus to prevent anogenital diseases. *New England Journal of Medicine* 2007;356:1928-43.

Gertig DM, Brotherton JM, Budd AC, et al. Impact of a population-based HPV vaccination program on cervical abnormalities: a data linkage study. BMC Medicine 2013;11:227.

Giuliano AR, Palefsky JM, Goldstone S, et al. Efficacy of quadrivalent HPV vaccine against HPV infection and disease in males. [erratum appears in N Engl J Med 2011 Apr 14;364(15):1481]. *New England Journal of Medicine* 2011;364:401-11.

Pagliusi SR, Aguado MT. Efficacy and other milestones for human papillomavirus vaccine introduction. *Vaccine* 2004;23:569-78.

Q16. Is it true that there are already reductions in HPV disease in Australia since vaccination was introduced in 2007?

Data are already showing that since the Australian HPV vaccination program commenced in April 2007, there has been an overall decline in HPV disease in females and males. For example, the number of pre-cancerous lesions detected in 20–24-year-old women has dropped from 18.1 per 1,000 women screened in 2007 to 13.5 per 1,000 women in 2013. This decline will be reflected in declines in cervical cancer in the coming decades.

Additionally, reductions in HPV infection and HPV-genital warts are also being recorded in Australian females and males. One study has demonstrated a near disappearance of genital warts among young women <21 years of age (eligible for vaccine) since the introduction of the vaccine.

There is also evidence of a herd protection benefit in unvaccinated males. There has been a significant decline in new genital wart diagnoses observed in heterosexual males of the same age as the girls targeted by the HPV vaccination program. However, there has been no significant reduction in new cases of genital warts reported by men who have sex with men which suggests they get limited benefit from the female program.

As cancer can take many decades to develop after an initial HPV infection, definitive evidence of a reduction in the incidence of cervical cancer resulting from the HPV vaccination program is expected in years to come (***see Q15***).

References

Ali H, Donovan B, Wand H, et al. Genital warts in young Australians five years into national human papillomavirus vaccination programme: national surveillance data. [erratum appears in BMJ 2013 May 7;346:f2942] *BMJ* 2013;346:f2032.

Brotherton JM, Saville AM, May CL, et al. Human papillomavirus vaccination is changing the epidemiology of high-grade cervical lesions in Australia [letter]. *Cancer Causes and Control.* 2015;26:953-4.

Chow EP, Read TR, Wigan R, et al. Ongoing decline in genital warts among young heterosexuals 7 years after the Australian human papillomavirus (HPV) vaccination programme. *Sexually Transmitted Infections* 2015;91:214-9.

Crowe E, Pandeya N, Brotherton JM, et al. Effectiveness of quadrivalent human papillomavirus vaccine for the prevention of cervical abnormalities: case-control study nested within a population based screening programme in Australia. *BMJ* 2014;348:g1458.

Gertig DM, Brotherton JM, Budd AC, et al. Impact of a population-based HPV vaccination program on cervical abnormalities: a data linkage study. *BMC Medicine* 2013;11:227.

Tabrizi SN, Brotherton JM, Kaldor JM, et al. Fall in human papillomavirus prevalence following a national vaccination program. *Journal of Infectious Diseases* 2012;206:1645-51.

Q17. Isn't leading a healthy lifestyle enough to prevent cancer?

Although there is evidence that a healthy diet and exercise can help protect against certain other cancers, such as bowel cancer, there is no definitive evidence that these factors will protect against cancers associated with HPV. The only way to ensure protection from infection with HPV (which is the necessary first step in the cancer development process) is to remain completely sexually abstinent. Although the risk of acquiring HPV infection increases with the number of sexual contacts, even having only one partner who is infected can result in getting an

HPV infection and HPV-related cancer. Most people with a current HPV infection do not display any symptoms or signs – that is, you can't tell if you or your partner have the virus. Similarly, if infected, there is no way to ensure or know if the body's immune system will be able to clear the virus on its own, or if that infection is silently progressing to cancerous changes.

Factors which have been shown to increase a person's risk of persistent HPV infection, and thus of developing related cancers, include:

- genetic factors
- smoking
- the presence of a co-infection with other sexually transmitted infections, such as herpes or chlamydia
- whether there is severe immune suppression, such as HIV infection.

Other factors that increase the risk for cervical cancer in particular include having had a very large number of births (seven or more) and long-term oral contraceptive use.

A person may be able to reduce their risk of HPV infection somewhat by consistent condom use, but it should be emphasised that HPV can be transferred via contact between genital and mucosal surfaces that are not covered by the condom.

References

Goldstone S, Palefsky JM, Giuliano AR, et al. Prevalence of and risk factors for human papillomavirus (HPV) infection among HIV-seronegative men who have sex with men. *Journal of Infectious Diseases* 2011;203:66-74.

Green J, Berrington de González A, Sweetland S, et al. Risk factors for adenocarcinoma and squamous cell carcinoma of the cervix in women aged 20–44 years: the UK National Case–Control Study of Cervical Cancer. *British Journal of Cancer* 2003;89:2078-86.

Hildesheim A, Wang SS. Host and viral genetics and risk of cervical cancer: a review. *Virus Research* 2002;89:229-40.

International Collaboration of Epidemiological Studies of Cervical Cancer. Carcinoma of the cervix and tobacco smoking: collaborative reanalysis of individual data on 13,541 women with carcinoma of the cervix and 23,017 women without carcinoma of the cervix from 23 epidemiological studies. *International Journal of Cancer* 2006;118:1481-95.

International Collaboration of Epidemiological Studies of Cervical Cancer. Cervical carcinoma and reproductive factors: collaborative reanalysis of individual data on 16,563 women with cervical carcinoma and 33,542 women without cervical carcinoma from 25 epidemiological studies. *International Journal of Cancer* 2006;119:1108-24.

Madeleine MM, Brumback B, Cushing-Haugen KL, et al. Human leukocyte antigen class II and cervical cancer risk: a population-based study. *Journal of Infectious Diseases* 2002;186:1565-74.

Winer RL, Feng Q, Hughes JP, et al. Risk of female human papillomavirus acquisition associated with first male sex partner. *Journal of Infectious Diseases* 2008;197:279-82.

Other issues

Q18. If all the trials were sponsored by the vaccine manufacturer, can we trust their data?

There are many processes in place to ensure the integrity of the data presented by manufacturers of vaccines. The regulatory requirements for vaccines are very stringent. Prior to undertaking vaccine trials, manufacturers consult large regulatory agencies, such as the Food and Drug Administration (FDA) in the USA, to ensure that all required information is collected and presented.

Trials are conducted by academic research organisations, rather than by the sponsor company themselves, requiring approval from independent ethics committees. To reduce bias, all key trials of Gardasil® were conducted in a blinded, randomised fashion which means that neither the participant nor the doctor/study personnel knew who had received the active vaccine. In addition, trials are overseen by independent safety panels that are also blinded.

Results from clinical trials submitted to scientific journals for publication are subject to 'peer review'. This means that the results are independently scrutinised by experts in the field prior to publication.

Before vaccines are licensed for use, regulatory authorities request specific data from the manufacturers

and conduct their own analyses of the trial data. In Australia, the Therapeutic Goods Administration evaluates the safety and efficacy of the vaccine in detail before recommending that it be registered for use.

Once a vaccine is registered, the Australian Technical Advisory Group on Immunisation (ATAGI) provides independent expert advice to government regarding the potential use of the vaccine in Australia, after considering the data on the vaccine as well as information on the disease in the Australian setting. Recommendations on vaccine use in Australia are published in *The Australian Immunisation Handbook* endorsed by the National Health and Medical Research Council.

References

Jüni P, Altman DG, Egger M. Systematic reviews in health care: assessing the quality of controlled clinical trials. *BMJ* 2001;323:42-6.

Nolan TM. The Australian model of immunization advice and vaccine funding. *Vaccine* 2010;28 Suppl 1:A76-83.

Q19. Why is there information on the Internet and social media saying the vaccine is dangerous if it isn't?

There are many competing interests and a wide range of views available on the Internet and it is often difficult to determine whose opinion it is that you are reading.

Some people who choose alternative lifestyles may reject mainstream medicine including vaccinations. While this position should be respected as their choice, it is important for others who are considering vaccination to be aware that some information provided on the Internet comes from organisations or people who are philosophically completely opposed to vaccination.

Anti-vaccination groups voice concern about most vaccines and this now includes HPV vaccines. Their perceptions can be found at websites such as those of the Australian Vaccination Skeptics Network (AVN) and the National Vaccination Information Center (NVIC). Press releases from such organisations may often be alarming and controversial and thus generate considerable media interest.

The American College of Pediatricians, a highly conservative small group of approximately 200 members, distinct from the highly respected American Academy of Pediatrics (that represents over 64,000 paediatricians in the USA) released a statement in January 2016 raising concerns around the HPV vaccine. They point to reports that 'hypothesise' that the vaccine may induce premature ovarian failure (POF). However, it is important to realise that these concerns are ideologically, and not scientifically, based. Due to its non-medical agenda, this organisation does not represent the views and recommendations of the main medical or scientific bodies in the USA, Australia or many other countries. It is very important to be assured that information on HPV vaccines is balanced and obtained from credible and trusted sources (***see Q3***).

References

Australian Academy of Science. The science of immunisation: questions and answers. Canberra: Australian Academy of Science; 2012. Available from: www.science.org.au/files/userfiles/learning/documents/immunisation/immunisation-lr.pdf (Accessed 4 March 2016).

Offit PA, Jew RK. Addressing parents' concerns: do vaccines contain harmful preservatives, adjuvants, additives, or residuals? *Pediatrics* 2003;112:1394-401.

Myths and realities: responding to arguments against vaccination. A guide for providers. 5th ed. Canberra: Australian Government Department of Health and Ageing; 2013. Available from: www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/uci-myths-guideprov (Accessed 4 March 2016)

Q20. Could receiving HPV vaccine make my daughter or son promiscuous?

No, there is no evidence that receiving HPV vaccine could lead to promiscuity. The assumption that underlies this is that adolescents will not engage in 'risky' sexual behaviour if they fear HPV infection and thus vaccination against HPV removes the motivation for abstinence/safe sex. However, this is not supported by evidence. A US study found that only 7% of women cited fear of sexually transmitted diseases as a main reason for not having sex.

Among the participants in the HPV vaccine trials there was no increase in number of sexual partners in those who were vaccinated compared with those who were not. In addition, surveys of young women who had received HPV vaccination have found that there is no association with HPV vaccination and risky sexual behaviours such as number of sexual partners. In addition, adolescent women who were sexually active and received HPV vaccine were more likely to always wear a condom. This has been supported by data comparing sexual activity-related healthcare outcomes among girls who had received HPV vaccine at 11–12 years of age with those who hadn't. In this study, the risk of any pregnancy, STI

testing or diagnosis, or contraceptive counselling was not increased in girls who had received HPV vaccine.

Initiation of sexual activity is influenced by many other factors such as individual psychological factors, drug and alcohol use, family communication and support, community relationships, school factors, and perceptions of peer sexual activity. There is good evidence that receiving information about sexually transmitted infections, providing condoms or discussing sex *does not* result in earlier or more sexual activity.

References

Bednarczyk RA, Davis R, Ault K, et al. Sexual activity-related outcomes after human papillomavirus vaccination of 11- to 12-year-olds. *Pediatrics* 2012;130:798-805.

Liddon NC, Leichliter JS, Markowitz LE. Human papillomavirus vaccine and sexual behavior among adolescent and young women. *American Journal of Preventive Medicine* 2012;42:44-52.

Monk BJ, Wiley DJ. Will widespread human papillomavirus prophylactic vaccination change sexual practices of adolescent and young adult women in America? *Obstetrics and Gynecology* 2006;108:420-4.