

POSITION STATEMENT

Cervical cancer prevention



Key Recommendations

- Under the provisions of the current National Cervical Screening Policy, all women aged 18 to 70 are recommended to have a Pap test every two years as part of the National Cervical Screening Program. Screening should commence at age 18 to 20, or one to two years after commencing sexual activity, whichever is later.
- Under the National HPV Vaccination Program, it is recommended that girls aged 12-13 years be immunised against human papilloma virus types 16 and 18.
- In the absence of sufficient evidence to suggest that alternate technologies are more effective than the conventional Pap test, a patient-centred approach for individual decisions about the use of these technologies is recommended.
- Cancer Council Australia supports an evidenced based approach to reviewing the screening interval, age at first screen, impact of HPV vaccination and role of new technologies in the National Cervical Screening Program.

Background

Cervical screening has been available in Australia since the 1960's; however, it was not until 1991 that a coordinated program, known today as the National Cervical Screening Program was introduced.

Screening for cervical cancer is possible because the cervical cells pass through a series of detectable changes before they become cancerous. Cervical cancer may take ten years or more to develop. Through population screening at regular intervals, the Pap test has the potential to reduce up to 90% of cervical cancer and is currently the best protection against the disease. (1) Like all screening tests, the Pap test is not 100% accurate. The Pap test can detect the most common type of cervical cancer, squamous cell carcinoma. It is less effective at detecting adenocarcinoma, which is much less common.

Nearly all cervical cancer occurs as a consequence of human papilloma virus (HPV) infection. (2) A vaccine that protects against two types of HPV that cause 70% of cervical cancer is available in Australia. In 2007, the HPV vaccine was added to the National Immunisation Program and is available to girls in their first year of high school.

Early detection of pre-cancerous changes through Pap tests and the prevention of HPV infections that can cause these changes through vaccination are the major strategies for reducing death and illness from the disease (3).

Cervical cancer risk

In 2005, cancer of the cervix accounted for 734 new cancers in Australian women. The lifetime risk of a woman developing cervical cancer before the age of 75 years is one in 198. (4) It is the 19th most common cause of cancer death in Australian women and accounted for 224 deaths in 2006.(5)

Following the introduction of the National Cervical Screening Program, the incidence of cervical cancer among women aged 20 to 69 has almost halved from 17.1 per 100,000 in 1991 to 9.2 per 100,000 in 2005, and the mortality rate has declined from 5.2 per 100,000 in 1986 to 1.9 per 100,000 in 2006.(5) It

has been estimated that cervical screening saves over 1,200 women from developing cervical cancer each year.(6)

Data from 2003 to 2006 in Queensland, Western Australia, South Australia and the Northern Territory indicate that Aboriginal and Torres Strait Islander (A&TSI) women have a mortality rate attributable to cervical cancer of 10.3 per 100,000 women, compared with a rate of 2.0 per 100,000 for non-A&TSI women. (5) Targeted education, recruitment activities and dedicated funding are required to increase the participation of A&TSI women in cervical cancer prevention initiatives.

Studies have shown consistent associations between increased risk of cervical cancer and early age at first sexual activity, increasing numbers of sexual partners and/or partners who have had multiple partners. (7) These behaviours may place women at an increased risk of HPV infection and subsequently at increased risk of developing cervical cancer. However, infection with HPV is common even among women who have had only one sexual partner, and therefore all women who have been sexually active should be considered at risk.

To reduce the incidence of cervical cancer, all women, between the ages of 18 and 70 who have ever been sexually active should have regular two yearly Pap tests. This is regardless of disability, sexual orientation, culture and/or ethnicity.

Some women who have had a hysterectomy will need to continue having Pap tests. Women will still need regular Pap tests or vaginal smears (where a cell sample is taken from the top of the vagina) if they:

- Still have a cervix
- Had a hysterectomy as part of treatment for a gynaecological cancer
- Have ever had a significant abnormality detected on a Pap test, or
- Have never had a Pap test

Recommendation:

- Under the provisions of the current National Cervical Screening Policy, all women aged 18 to 70 are recommended to have a Pap test every two years as part of the National Cervical Screening Program. Screening should commence at age 18 to 20, or one to two years after commencing sexual activity, whichever is later.

Women exposed to diethylstilboestrol (DES)

Diethylstilboestrol (DES), a synthetic form of the female hormone oestrogen, was prescribed to pregnant women from the 1940s to early 1970 to prevent miscarriage and other pregnancy complications. Its use has been linked with the development of clear cell adenocarcinoma, a rare cancer of the vagina and/or cervix. A very small number of daughters of women who took DES while pregnant have developed this cancer. The overall risk of an exposed daughter developing this type of cancer is less than one in 1,000 women. (8) More information on DES is available on the Cancer Council NSW website <http://www.cancercouncil.com.au/editorial.asp?pageid=248>.

A routine Pap test is not adequate for DES daughters. These women are encouraged to have an annual DES pelvic examination, including separate Pap tests from the cervix and from the surfaces of the upper vagina, a visual and manual inspection of the vagina and an internal pelvic examination. The National Cervical Screening Program recommends annual Pap tests and colposcopy examinations for DES-exposed women.

Cervical cancer and the human papilloma virus (HPV)

Nearly all cervical cancer occurs as a consequence of HPV infection, although most HPV infections do not lead to cervical cancer. Over 100 types of HPV have been identified, with more than 40 of these affecting

the genital region. (9) Genital HPVs can be divided into high and low-risk types, based on the strength of their association with cervical cancer. (10) However, even for high-risk HPV types, only 2% of infections will eventually lead to cancer. Two high-risk HPV types, 16 and 18, together account for around 70% of all cervical cancer. (11) Up to 75% of people are infected with genital HPVs at some time in their lives, and most infections resolve without treatment. Most infected women are never aware that they have had the infection.(12)

Long-term infection with high-risk HPV is a necessary but not sufficient factor in the development of cervical cancer. Even infections present for many years can go away spontaneously. However, persistence of HPV infection is currently the best predictor of risk of cervical cancer, therefore screening programs are designed to detect the abnormalities associated with long term HPV infection.

Cofactors that increase the risk of cervical cancer in women who have had a long term HPV infection include:

- Increasing age
- Use of oral contraceptives for five or more years
- Five or more full-term pregnancies
- Exposure to tobacco smoke
- Immunosuppression, e.g. women infected with human immuno-deficiency virus (HIV)
- Presence of antibodies to Chlamydia trachomatis or to herpes simplex virus type 2 (genital herpes and less commonly, cold sores). (7)

However, these cofactors contribute only a small amount to the risk of developing cancer – the major risk is from long-term infection of the cervix with high-risk HPV.

HPV DNA testing

Due to the relationship between long-term infection with high-risk types of HPV and the development of cervical cancer, testing for the presence of HPV deoxyribonucleic acid (DNA) in cervical cell specimens has the potential to identify women at increased risk of developing cervical cancer.

Available HPV DNA testing kits can detect several high and low-risk types of HPV. HPV testing can be potentially employed for primary screening: used either alone or in combination with cytology. Infection with high-risk HPVs is very common in younger women, particularly in the first 10 years after commencement of sexual activity. HPV commonly resolves without treatment, therefore a single positive test for high-risk HPV is of little significance in an otherwise asymptomatic healthy young woman. HPV testing can also have applications in the triage of patients with low-grade epithelial abnormalities and surveillance of high-grade abnormalities following treatment. Studies continue to investigate the use of HPV DNA testing in these contexts.

A 2009 Commonwealth Government review in Australia by the Medical Services Advisory Committee (MSAC) assessed the available evidence regarding the use of one type of HPV DNA test, the Hybrid Capture-II (HC-II), as an aid in triaging women who had undergone cervical screening with a result of low-grade epithelial abnormality. (13) MSAC concluded that there was insufficient evidence relating to the use of the HPV HC-II test in these circumstances, and recommended that public funding should not be supported at this time. (13) However, for women already undergoing annual cytological review for follow-up of a previously treated high-grade abnormality, the National Cervical Screening Program's management guidelines recommend HPV testing, and in this instance, a Medicare rebate is available. (14)

HPV Vaccine

In 2006, the Australian Therapeutic Goods Administration approved a quadrivalent vaccine (Gardasil™) for use in immunising females between the ages of nine and 26 against infection with two high-risk HPV

types (16 and 18) that cause approximately 70% of cervical cancer. Gardasil™ also offers protection against two low-risk HPV types (6 and 11) that cause 90% of genital warts. In 2009, the approved age for Gardasil™ was extended to females aged nine to 45.

In 2007, a bivalent HPV vaccine (Cervarix™) was also approved for use in Australian girls and women aged 12 to 45. This vaccine provides protection against HPV types 16 and 18.

In 2007, Gardasil™ was added to the National Immunisation Program and is currently offered to girls in their first year of high school. Additionally, for a two-year period, the vaccine was also offered to females aged 13 to 26. Those outside of the National Immunisation Program who wish to have either the Gardasil™ or Cervarix™ vaccine can do so at their own cost from their medical practitioner.

Current evidence suggests that the available HPV vaccines are of most benefit to females who have not yet been infected with HPV, and will therefore give the best protection against cervical cancer if given before the onset of sexual activity. There may be some benefit in vaccinating sexually active women, as a number of women may not yet have been infected with any or all of the HPV types included in the vaccine. The level of protection provided to boys and older, sexually active women is under evaluation in clinical trials. (15)

HPV vaccine doses administered in Australia are recorded through the National HPV Vaccination Program Register. The registry sends reminders to girls overdue for vaccination, advises females when they have completed the vaccination course, provides reports on vaccination status and provides de-identified data to inform policy making and research. In the future, the registry will facilitate cross-referencing of vaccination data with information from cervical cytology (Pap tests) or cervical cancer registries for evaluation purposes.

As the HPV vaccine does not protect against all types of cancer-causing HPV, regular Pap tests continue to be important. Even young girls who have been vaccinated will still need Pap tests when they are older.

Recommendation:

- Under the National HPV Vaccination Program, it is recommended that girls aged 12-13 years be immunised against HPV types 16 and 18.

Further advances in preventing cervical cancer

Worldwide it is estimated that there are 100 million women infected with high-risk HPV types. (16) In light of this, therapeutic HPV vaccines are being developed and trialled to determine their effectiveness in regressing and eliminating established HPV infection. (17) However, these vaccines are not likely to be available in the foreseeable future.

A desire to improve the sensitivity and/or specificity of the Pap test has led to the development of several new technologies.

One approach is liquid-based cytology (LBC). With this method, cervical cells collected on the sampling instruments during a conventional Pap test are suspended in liquid. At the laboratory, the liquid sample is filtered to remove blood and cellular debris. The cells are then deposited as a single layer onto a slide, stained and examined.

Automated LBC (where slides are read by an imager which marks fields of interest for examination by a cytologist) has been reported as detecting more high-grade cervical abnormalities compared to conventional cytology, although the imager also detected a larger amount of low-grade lesions. (18) However, a 2009 review by the Medical Services Advisory Committee concluded that in the current Australian setting conventional cytology was as effective as automated LBC, and recommended that

public funding not be supported for LBC at this time. (19) Therefore, women choosing LBC will pay an additional charge of approximately \$40, for which there is no Medicare rebate.

A second approach that has recently emerged is self-sampling. This involves the woman collecting their own cervical cell and/or HPV DNA sample in the privacy of their home. Self-sampling kits are available from medical practitioners and come at an additional cost, for which there is no Medicare rebate. The role of self-sampling in Australia is undetermined, and it should not replace the conventional Pap test.

Recommendation:

- In the absence of sufficient evidence to suggest that alternate technologies are more effective than the conventional Pap test, a patient-centred approach for individual decisions about the use of these technologies is recommended.

The introduction of the HPV vaccination program, the identification of women at higher risk of developing cervical cancer through HPV DNA testing, and the development of other medical advances may lead to a different approach to preventing cervical cancer in the future.

The Australian Government recently announced that the National Cervical Screening Program would undertake a renewal process, examining program and policy aspects such as the screening interval, age at first screen, impact of HPV vaccination and role of other medical advances.

Recommendation:

- The Cancer Council Australia supports an evidenced based approach to reviewing the screening interval, age at first screen, impact of HPV vaccination and role of new technologies in the National Cervical Screening Program.

For further information

- The Cancer Council Australia – www.cancer.org.au
- The Cancer Council's Cancer Helpline – 13 11 20 (cost of a local call)
- National Cervical Screening Program – www.cervicalscreen.health.gov.au, 13 15 56
- National HPV Immunisation Program – www.immunise.health.gov.au
- National HPV Vaccination Program Register – www.hpvregister.org.au
- PapScreen Victoria – www.papscreen.org.au

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