

POSITION STATEMENT

CERVICAL CANCER SCREENING

Recommendations:

- Under the provisions of the current National Cervical Screening Policy, all women aged 18 to 70 who have ever been sexually active are recommended to have a Pap test every two years as part of the National Cervical Screening Program.
- In the absence of sufficient evidence to suggest that alternate screening technologies are more effective than the conventional Pap test, a patient centred approach for individual decisions about screening methodologies is recommended.
- In line with emerging evidence, The Cancer Council Australia supports the move towards the introduction of a three-yearly cervical screening interval for Australian women in conjunction with long-term evaluation in terms of invasive cervical cancer incidence and mortality.

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, the Pap test has the potential to reduce up to 90 per cent of cervical cancer and is currently the best protection against the disease.¹ Like all screening tests, the Pap test is not 100 per cent 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. At this stage, early detection remains the major strategy for reducing death and illness from the disease.

Cervical cancer risk

In 2004, cancer of the cervix accounted for 718 new cancers in Australian women². The lifetime risk of a woman developing cervical cancer before the age of 75 years is one in 205³. It is the eighteenth most common cause of cancer death in Australian women and accounted for 210 deaths in 2004.⁴

Following the introduction of the National Cervical Screening Program, the incidence of cervical cancer among women aged 20 to 69 has halved from 17.1 per 100,000 in 1990 to 8.9 in 2004 and the mortality rate has declined from 5.4 per 100,000 in 1983 to 1.9 in 2004.⁵ It has been estimated that cervical screening saves over 1,200 women from developing cervical cancer each year.⁶

Mortality data from 2000 to 2003 in Queensland, Western Australia, South Australia and the Northern Territory indicates that Indigenous women have a mortality rate attributable to cervical cancer of 12.0 per 100,000 women, compared with a rate of 2.5 per 100,000 non-Indigenous women.⁷ Targeted education, recruitment activities and dedicated funding are required to increase the participation of Indigenous women in cervical screening.

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.⁸

These behaviours may place women at an increased risk of human papilloma virus (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.

Cervical cancer screening is not required for women who have undergone hysterectomy for reasons other than cancer.

Recommendation:

- Under the provisions of the current National Cervical Screening Policy, all women aged 18 to 70 who have ever been sexually active are recommended to have a Pap test every two years as part of the National Cervical Screening Program.

Women exposed to diethylstilboestrol (DES)

Diethylstilboestrol (DES), a synthetic form of the female hormone oestrogen, was prescribed to pregnant women from late 1930 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 around 1 in 1,000 women.⁹

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.

Cervical cancer and the human papilloma virus (HPV)

Nearly all cervical cancer occurs as a consequence of HPV infection, although almost all HPV infections do not lead to cervical cancer. Over 200 types of HPV have been identified, with more than 40 of these affecting the genital region.¹⁰ Genital HPVs can be divided into high and low-risk types, based on the strength of their association with cervical cancer.¹¹ Only high-risk types of HPV have been associated with the development of cervical cancer. However, even for high-risk HPV types, only two per cent of infections will eventually lead to cancer. Two high-risk types, HPV types 16 and 18, together account for around 70 per cent of all cervical cancer.¹² Up to 75 per cent 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.¹³

Persistent 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 and prevention programs are designed to detect the abnormalities associated with persistent HPV infection.

Cofactors that increase the risk of cervical cancer in women who have had a persistent 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, eg. 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).¹⁴

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

HPV DNA testing

Due to the relationship between persistent 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.

Commercially 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 2002 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.¹⁵ 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.¹⁶ However, for women already undergoing annual cytological review for follow-up of a previously treated high-grade abnormality, the management guidelines recommend HPV testing, and in this instance, a Medicare rebate is available.¹⁷

HPV Vaccine

Vaccines designed to help prevent cervical cancer have shown encouraging results and should be available soon. These vaccines work by immunising young women against infection with some of the high-risk HPVs that cause cervical cancer, and thereby have the potential to significantly reduce the risk of cervical cancer.

In the FUTURE II study, 12,167 women from 13 countries participated in a trial for a quadrivalent vaccine with HPV types 6, 11, 16 and 18. Women were randomised to receive three doses of either the vaccine or placebo over six months. The reported efficacy of the vaccine after an average follow-up of 17 months was 100 per cent, with no observed cases of high-grade pre-cancer or non-invasive cancer related to HPV 16 and 18 among the women vaccinated.¹⁸ Similar results have been observed in other smaller trials of bivalent (HPV 16 and 18) and quadrivalent (HPV 6, 11, 16 and 18) vaccines.

HPV vaccines can only benefit women 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 is also benefit in vaccinating sexually active women, as many have not yet been infected with a high-risk HPV. HPV vaccines do not protect women already infected with a high-risk HPV from cervical cancer. The currently available vaccines are targeted only at the HPVs responsible for two thirds of cervical cancers, therefore all vaccinated and unvaccinated women should continue having regular Pap tests.

Therapeutic HPV vaccines are also being developed and trialed to determine their effectiveness in regressing and eliminating established HPV infection.¹⁹ However, these vaccines are not likely to be available in the foreseeable future.

The introduction of a prophylactic and therapeutic HPV vaccine and the identification of women at higher risk of developing cervical cancer through HPV DNA testing are prospects for the future. If proven safe and affordable, these developments may represent a very different approach to the prevention of cervical cancer.

New screening technologies

In the past decade, a desire to improve the Pap test has led to the development of new screening technologies. Although nothing has yet replaced the need for direct examination of the cervix, technological advances are changing the way Pap tests are conducted, prepared and screened.

One new approach is liquid-based cytology (LBC). 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 under a microscope.

A 2002 review by the MSAC concluded there was insufficient evidence to suggest that LBC was superior to the conventional Pap test, and recommended that public funding not be supported for this screening test in Australia at this time.²⁰ Therefore, women choosing LBC will pay an additional charge of approximately \$30, for which there is no Medicare rebate.

Other ways to detect cervical epithelial abnormalities include screening of the Pap test slide via computerised microscope and optoelectronic screening: where a pen-like wand is used to measure the response to electrical and optical stimulation of the cervix. The collected data is then compared to a databank of cervical tissue types. These technologies are not widely available and incur an additional charge.

Recommendation:

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

Screening intervals

Australian women without any symptoms are currently recommended to have a Pap test every two years. Throughout 2002 and 2003, 60.7 per cent of Australian women aged 20 to 69 years participated in cervical cancer screening.²¹

Australia's current two yearly screening interval is conservative, with many countries recommending three years or more between tests.²² The International Agency for Research on Cancer suggests three yearly screening for women aged 25 to 49, five yearly screening for women aged 50 to 64, and for women aged 65 or over, screening only of those who had not been screened since age 50.²³

The benefit of annual screening compared to three-yearly screening is small. Research has shown that women aged 30 to 64 years, with three or more consecutive negative Pap test results who are screened once every three years rather than annually, have an excess risk of cervical cancer of approximately three in 100,000.²⁴

Given that increasing the screening interval does not significantly affect cervical cancer incidence, the associated cost savings with screening women less frequently could be directed towards communication and recruitment strategies aimed at increasing the participation of unscreened and underscreened women in the cervical screening program.

Recommendation:

- In line with emerging evidence, The Cancer Council Australia supports the move towards the introduction of a three-yearly cervical screening interval for Australian women in conjunction with long-term evaluation in terms of invasive cervical cancer incidence and mortality.

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
- PapScreen Victoria – www.papscreen.org.au

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