

Cervical Screening Essentials

Implementation of the revised NHMRC *Screening to prevent cervical cancer: guidelines for the management of asymptomatic women with screen detected abnormalities, 2005.*

This reference sheet includes

- a summary of the six major changes to management of asymptomatic women with screen detected abnormalities;
- information on
 - managing women who have been treated for a high grade abnormality;
 - HPV and cervical cancer;
 - using the HPV DNA test; and
- information on applying the guidelines in special circumstances.

It is intended to assist you in taking appropriate action on receipt of abnormal Pap smear reports.

BACKGROUND

The revised *Screening to prevent cervical cancer: guidelines for the management of asymptomatic women with screen detected abnormalities* (the guidelines) offer medical practitioners evidence-based recommendations to manage patients who have an abnormal Pap smear.

In 2001, a multidisciplinary expert Guideline Review Group, chaired by Professor Ian Hammond, was convened to review the NHMRC (1994) *Screening to prevent cervical cancer: Guidelines for the Management of women with screen detected abnormalities*. The group identified several key areas for consideration. A detailed literature review was commissioned, in addition to two outcomes studies involving data collected by Australian Pap test registers. New knowledge is now available regarding the natural history of HPV infection and the role of this agent in cervical carcinogenesis.

The rigorous NHMRC guideline development process was carefully followed. This involved consultation with all relevant professional bodies, a wide range of clinicians and consumers.

These guidelines are an evidence based population health package for Australian women. The NHMRC approved the revised guidelines in June 2005, and they will be implemented from 3 July 2006.

Key changes

There are six major changes to the management of women with screen detected abnormalities.

1. **New terminology system for Pap smear cytology.**
2. **Repeat Pap smear for most women with low grade squamous change.**
3. **Do not treat women with biopsy proven CIN 1.**
4. **Refer all women with atypical glandular cell reports for colposcopy.**
5. **Use HPV testing as test of cure following treatment for high grade abnormalities (CIN 2 & 3).**
6. **Do not report normal endometrial cells in post menopausal women.**

1. Terminology: the Australian Modified Bethesda System 2004 (AMBS 2004).

The need for new terminology arose from two concerns. First there was a need to move away from terminology that suggests an inevitable progression from CIN 1 through to CIN 2 and CIN 3 and to cancer. Such progression is now recognised to be a rare event. CIN 1 reflects an infective process. Progression to more significant disease is related to persistent HPV infection over many years.

The second concern was to provide terminology that was compatible with other systems allowing international research data to be relevant to Australia. The new terminology relates to cytology. The CIN terminology will be retained to describe histological diagnoses.

2. Repeat Pap smear for most women with low grade squamous abnormalities

The new terminology recognises two categories of low grade squamous intraepithelial lesions (LSIL)

- Possible LSIL, previously known as non specific minor changes; and
- LSIL, previously known as CIN1 and HPV.

This recommendation will affect the most women, with approximately 90,000 women each year receiving a Pap smear result of low-grade abnormality (LSIL). The high numbers of LSIL occur because young Australian women (<25yrs) are screened and the prevalence of HPV infection in young women is high. The two yearly screening interval in Australia results in high detection of transient abnormalities.

Outcome data from Australian Pap test registers was used to determine the final recommendations for the management of Australian women with these low grade abnormalities. These data and information from natural history studies on HPV infection support a delay in the timing of colposcopic assessment to allow spontaneous resolution of HPV infection.

What are the new recommendations for managing women whose Pap smear is reported as a low-grade abnormality (LSIL or possible LSIL)?

A woman with a Pap test report of LSIL should be managed in the same way irrespective of whether the abnormality is regarded as possible or definite LSIL. Women should be recommended for a repeat Pap test in 12 months.

An exception to the above recommendation is made for women over the age of 30 years without a history of negative cytology in the preceding two to three years.

Either repeat cytology within six months or early colposcopy (this decision is dependent on clinical judgement and the needs of the woman) is recommended for these women to facilitate diagnosis of any occult HSIL that may have advanced further in the sequence from HSIL towards cancer.

Why does the management differentiate between women aged under and over 30 years? Shouldn't all women be treated equally?

It is recognised that most low-grade abnormalities are viral infections caused by HPV. This is a common infection occurring most frequently in the early years after commencing sexual activity (typically women between the ages of 18 to 30). In this group, HPV is mostly transient, spontaneously regressing and clears in an average of one to two years (a mean of 8 to 14 months).

Some HPV infections can take up to three years to clear, depending on the individual's immune system.

In women over 30 years of age there is a stronger association between persistent HPV infection and the development of high-grade cervical abnormalities. It is the persistence of the HPV infection, coupled with the increasing age of the woman, that increases the risk of developing cancer.

Women over 30 years of age who have had regular normal Pap smears can be reassured that they do not have a persistent HPV infection, so it is quite safe for them to have a repeat Pap smear in 12 months. For women who have not had the reassurance of a normal smear in the past two to three years, it is safer to have a colposcopy or an early repeat smear.

3. Do not treat women with biopsy proven CIN 1 or HPV lesions

The previous guidelines were equivocal regarding treatment for biopsy proven low grade lesions. Evidence does not support treatment of these lesions, which are likely to spontaneously resolve. The new guidelines recommend that treatment of biopsy proven CIN 1 and HPV should not be undertaken. Treatment is reserved for women who have, or subsequently develop, a high grade epithelial abnormality.

4. Refer all women with atypical glandular cells for colposcopy

In contrast to low grade squamous epithelial abnormalities, women who have any glandular cytologic abnormality are recommended to have colposcopic assessment by an expert in the colposcopic evaluation of suspected malignancies, or by a gynaecological oncologist.

Colposcopic assessment of these lesions is difficult, requiring considerable expertise. The higher rate of invasive cancer diagnosis within two years of a report of glandular abnormality justifies this recommendation.

Glandular abnormalities are very rare. There are only 800 women with low grade glandular reports annually in Australia. These abnormalities develop within the endocervical region of the cervix, rather than the ectocervix, the part visible at the top of the vagina. It can be quite difficult to sample the cells of the endocervical region, so repeat Pap smears may not give an accurate report on the state of the cervix. **This is the reason for the new recommendation for colposcopy in these women.**

5. Use HPV & cytology as a test of cure for women treated for CIN 2 and 3

Women who test negative for high risk HPV subtypes following treatment for CIN 2 or 3 have a very low risk of further high grade cervical abnormality. Because the prevalence of HPV positivity falls quite sharply during the first year post treatment, it is recommended that HPV testing is introduced at 12 and 24 months (after treatment) in conjunction with cytology. Once a woman has tested negative by both tests on two consecutive occasions, it is recommended that she return to the normal two yearly screening interval rather than annual cytology.

6. Do not report normal endometrial cells in post menopausal women

Laboratories have reported the presence of normal endometrial cells found in the Pap smear of women over the age of 45 years. Reporting of this finding is no longer recommended in **asymptomatic women** because of the very low incidence of endometrial cancer (0.2%) and because the presence of normal endometrial cells in these women does not indicate underlying cancer. Normal endometrial cells do not require any further investigation in the asymptomatic woman.

OTHER KEY INFORMATION

What are the new recommendations for managing women who have been treated for a high-grade abnormality?

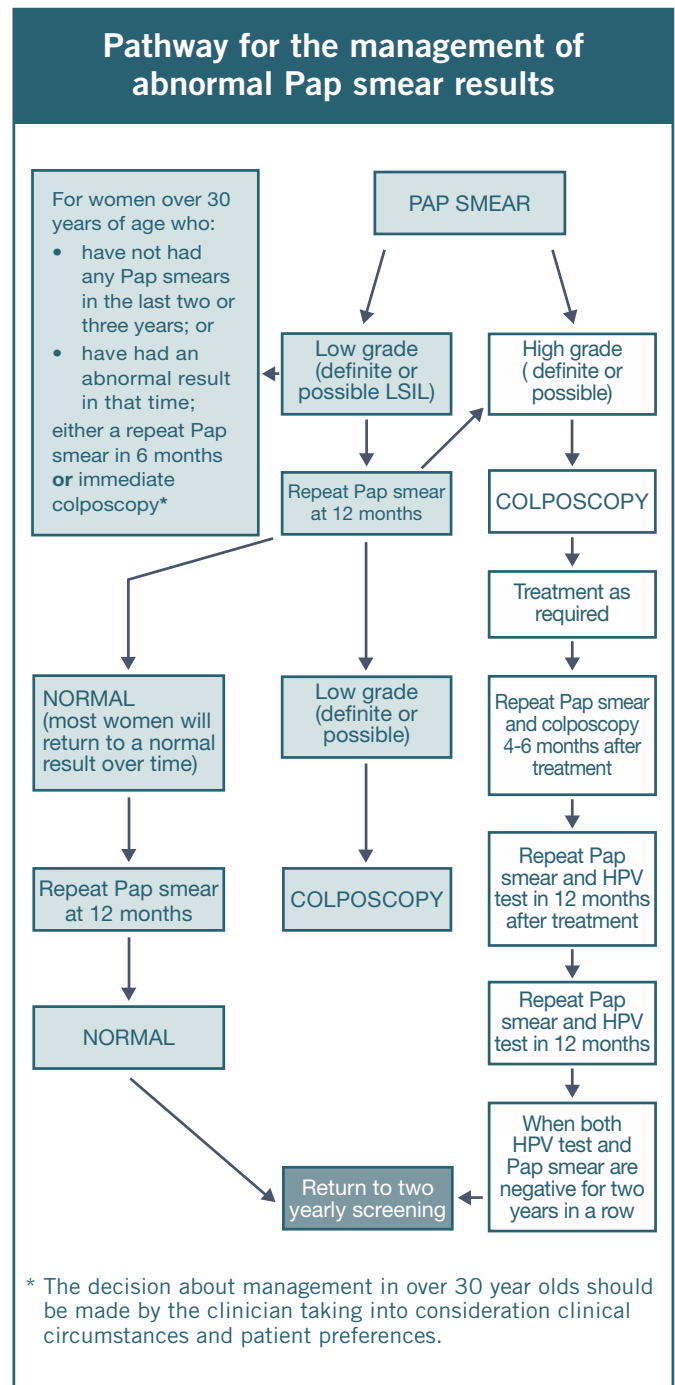
When a biopsy is reported as HSIL (previously CIN 2 or CIN 3), the recommended treatment is ablative or excisional treatment to remove the area of abnormality. Despite apparently successful treatment, published studies show that this group of women remain at slightly higher risk of cervical cancer than women who have never had an abnormality.

Previously this risk was managed through annual Pap smears. The revised guidelines now recommend that a woman who has had treatment for HSIL should:

- have colposcopy and cervical cytology at 4-6 months after treatment;
- have cervical cytology and HPV typing at 12 months after treatment and then annually until she has tested negative by both tests on two consecutive occasions;
- then return to the usual two yearly screening interval.

Even if the Pap smear shows a low grade abnormality or the HPV DNA test is positive, there is no need for a colposcopy unless the Pap smear shows a high grade change or the woman develops symptoms, such as abnormal bleeding.

Management after treatment for HSIL
4 - 6 months after treatment - <i>Pap smear and colposcopy</i>
12 months after treatment - <i>Pap smear and HPV test</i>
24 months after treatment - <i>Pap smear and HPV test</i>



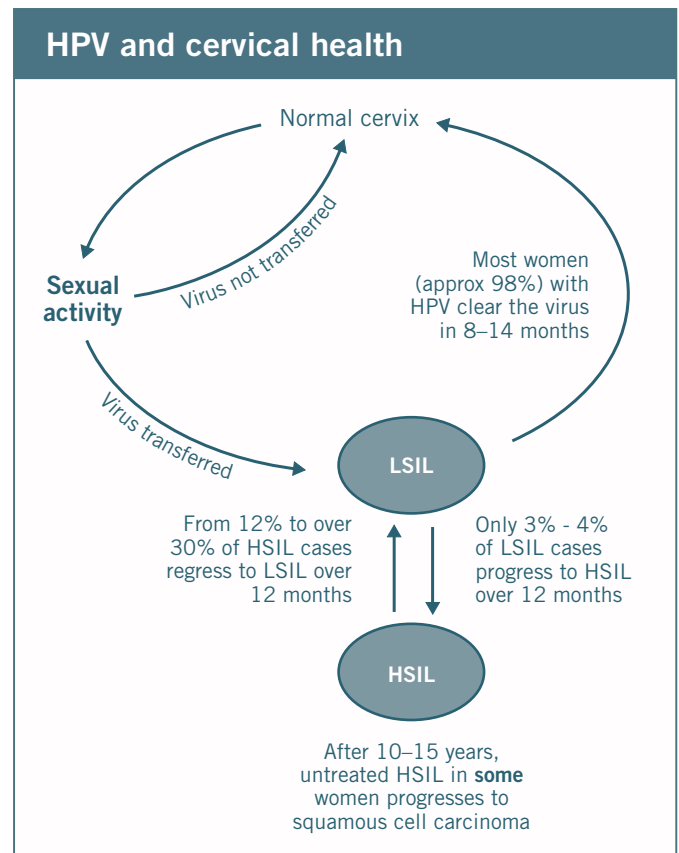
How is HPV linked to cervical cancer?

Over 100 types of HPV have been identified. Of these, approximately 30 infect the ano-genital region, of which about 13 are considered “high risk” as these have the potential to cause high-grade abnormalities of the cervix. The association between these “high risk” types (especially types 16 and 18) of HPV and the development of cervical cancer is now certain.

HPV is spread via genital skin-to-skin contact, so using condoms or other barrier methods does not prevent transmission. Around 80% of the population will have HPV at some time, and most will never know, unless it is noticed on a Pap smear result. HPV is not actually detected on the Pap smear, but sometimes the Pap smear may show that the cells appear to be affected by the virus.

HPV could be considered a normal part of being sexually active. Normalising HPV may help women who are worried about the stigma of a sexually transmissible virus. Women may be worried about the need to tell their current or prospective partners. Given that it is so common, it is likely that partners will have or have had HPV themselves.

For many women, partner infidelity may be a concern. It is important to remind women that HPV can remain latent for months or even years, so a current infection is not necessarily a sign of infidelity.



When should the HPV DNA test be used?

A DNA test for detecting HPV types associated with cervical cancer is available, but is of limited value for women under the age of 30 where HPV infections are very common and usually transient.

The NHMRC guidelines recommend use of high-risk HPV testing at 12 and 24 months following treatment of HSIL of the cervix to monitor the effectiveness of treatment. Medicare will cover the cost of the HPV test in this instance.

In these women, a HPV test should be performed along with a Pap smear at annual intervals. Once both the Pap smear and the HPV test are reported as negative on two successive occasions, the woman can return to two yearly screening.

How will the new guidelines be monitored?

Processes for monitoring the guidelines have been established. The Australian Government, Department of Health and Ageing has undertaken responsibility to monitor their safety on a six-monthly basis. NHMRC requires the guidelines to be reviewed by 2010.

APPLYING THE GUIDELINES IN SPECIAL CIRCUMSTANCES

Abnormality during pregnancy

The investigation of screen-detected abnormalities during pregnancy should follow the same guidelines as for the non-pregnant woman. In general, women who present with a low-grade abnormality should have a repeat smear in 12 months. High grade lesions need early referral for colposcopic assessment, preferably by a colposcopist experienced in assessing the pregnant cervix.

Immunosuppressed women

Immunosuppression in this context is defined as:

- CD4 count of < 400 in HIV-positive women; or
- transplantation with immunosuppressive therapy > 3 years.

If an immunosuppressed woman has a screen-detected abnormality she should be referred for colposcopy, even if the lesion is low-grade.

Management of immunosuppressed women is complex and should be carried out in specialist centres.

Women exposed in utero to diethylstilboestrol (DES)

DES-exposed women should be offered annual cytological screening and colposcopic examination of both the cervix and the vagina.

Previous hysterectomy

1. **For documented benign reasons** (e.g. menorrhagia, fibroids) - no further smears required if previous smears were negative.
2. **Unknown smear history** - baseline smear: if negative, no further smears required.
3. **Subtotal hysterectomy** - continue normal routine surveillance.
4. **Hysterectomy after CIN 2 or 3.** These women require continued screening because of their increased risk of vaginal neoplasia. The role of HPV testing in this situation requires further investigation.

Cervical Screening Essentials

The revised NHMRC *Screening to prevent cervical cancer: Guidelines for the management of asymptomatic women with screen detected abnormalities* will assist health practitioners in the care of women with screen detected abnormalities. All health practitioners in relevant fields are encouraged to read this document.

The guidelines are available at www.nhmrc.gov.au/publications/synopses/wh39syn.htm.

FURTHER INFORMATION

www.cancerscreening.gov.au - you can order free copies of publications from this website

www.healthinsite.gov.au

State/Territory Cervical Screening Program
13 15 56

Translating & Interpreting Service 13 14 50

**National Cervical
Screening Program**

A joint Australian, State and Territory Government Initiative