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Foreword

Over one million New Zealand women are enrolled in the National Cervical Screening Programme (NCSP). The aim of these guidelines is to assist health professionals achieve best practice outcomes for these women. The guidelines have been developed for those providing services for the prevention of cervical cancer, including nurses, general practitioners, gynaecologists, scientists and pathologists.

The guidelines update and replace the *Guidelines for the Management of Women with Abnormal Smears*, published in 1999. The update has used an evidence-based process recommended by the New Zealand Guidelines Group (NZGG), and involved extensive consultation with experts throughout New Zealand and internationally. Where possible, New Zealand data was used as supporting evidence. The guidelines also take into account recent scientific developments in our understanding of the prevention of cervical cancer.

Although the guidelines are evidence-based where possible, they can only ever be a guide to best clinical practice. Clinicians must continue to exercise their judgement and make decisions – in consultation with their patients – that reflect individual clinical and social circumstances.

The guideline revision process was led by two teams, representing the nursing and medical professions, with consumer input and assistance from epidemiologists and the NZGG. We are grateful to the teams for their hard work over three years, their dedication to the process, and their patience in seeing the process through to its conclusion.

We would like to thank the large number of people – too numerous to mention individually – who revised drafts and fed back useful critique to the teams. We also acknowledge the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (in particular Professor Ian Hammond and Dr Louise Farrell) for their support and helpful comments. Special thanks are due to Anna Maxwell and Dr Harold Neal (NCSP staff), who contributed significantly to compiling the guidelines.

Finally, we would like to acknowledge permission from the Australian Department of Health and Aging to use their guideline as a key resource in the revision process.

The revised *Guidelines for Cervical Screening in New Zealand* will be carefully monitored by the NCSP, and your feedback is invited. We plan to revise the guidelines again in three to five years, depending on comments and future technological developments in screening tests and the human papillomavirus vaccine.

Dr Hazel Lewis  
Clinical Leader, NCSP

Dr Gary Fentiman  
Chair, Guidelines Development Team

Dr Peter Bethwaite  
Chair, HPV Working Group
PART A: Introduction
There is now overwhelming evidence that the primary underlying cause of cervical cancer is persistent infection with certain high-risk types of human papillomaviruses (HrHPV), and that these viruses are transmitted sexually. Most HPV infections resolve spontaneously, but those that persist may lead to the development of precancerous abnormalities. If untreated, they may progress to cancer.

Cervical cancer is a disease with a long latency period, taking on average 10 to 20 years to develop. This means that screening for the detection and treatment of precursor (precancerous) lesions can be very effective for women who participate regularly in a screening programme.

Cervical screening has changed little over the past 30 years or so, but is now witnessing the introduction of new technologies, including liquid-based cytology (LBC) and testing for HPV. These novel screening technologies will become increasingly important as widespread vaccination of the population against HPV necessitates improvements in techniques for the detection of cervical abnormalities.

Two vaccines (Gardasil® and Cervarix®) effective against HrHPV types 16 and 18, which are thought to cause up to 70% of cervical cancer, are now registered for use in New Zealand. A publicly funded HPV immunisation programme will begin in September 2008 and it is expected that over time this will have a marked effect not only on the incidence of and mortality from cervical cancer, but also on the volumes of abnormal cytology and colposcopy assessments. This is likely to result in the need for further changes to these guidelines.

The revised Guidelines for Cervical Screening in New Zealand take into account new evidence on the aetiology and pathogenesis of cervical cancer since the previous guidelines were published in 1999. They also signal the start of a change in cervical screening tests that will be used in future, leading to a change in recall intervals for women with abnormal results.
Background

There is now overwhelming evidence that the primary underlying cause of cervical cancer is persistent infection with certain high-risk types of human papillomaviruses (HrHPV), and that these viruses are transmitted sexually. Most HPV infections resolve spontaneously, but those that persist may lead to the development of precancerous abnormalities. If untreated, they may progress to cancer.

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How the Guidelines were developed

In 2005 the National Cervical Screening Programme (NCSP) established a Guideline Development Team (GDT) to help update the New Zealand Guidelines for the Management of Women with Abnormal Cervical Smears, published in 1999. An evidence-based methodology for this process, recommended by the New Zealand Guidelines Group (NZGG), was adopted. This involved an extensive review of the cervical screening literature, the development of clinical questions, and a group decision on what was to be included in the guidelines. In addition, a comprehensive search was made of all guidelines relating to the management of women with abnormal smears, which were then critically appraised using the AGREE tool (see Appendix 2).

However, for many clinical questions there was insufficient or inconsistent external evidence to provide direct answers. In these cases recommendations were developed by discussion, ‘considered judgment’ and the consensus of the multidisciplinary group. Grading of recommendations was based on the strength of the evidence using the NZGG Grading system (see ‘Using the Guidelines’ in Part B).

The Australian guidelines, Screening to Prevent Cervical Cancer: Guidelines for the Management of Asymptomatic Women with Screen Detected Abnormalities (2005) was used as a key resource.
Overview of Cervical Screening in New Zealand

In New Zealand, approximately 160 women are diagnosed with cervical cancer every year and 60 die from this largely preventable disease, despite the availability of an organised screening programme. About half the women who develop or die from cervical cancer have never been screened, and about a third have only been screened irregularly and infrequently.

The New Zealand National Cervical Screening Programme (NCSP) was established in 1990 to reduce the number of women who develop cervical cancer and those who die from it. Through routine screening at regular intervals, the programme aims to detect precancerous squamous cell changes, which, if not treated, may lead to cancer.

The programme has a number of separate components (Figure 1), each of which must operate effectively for the programme to meet its objectives.

**Figure 1: The Screening Pathway**

Successful cervical screening requires a high standard of quality at each step in the screening pathway, from invitation and recall of women, through smear taking, laboratory testing, colposcopy and the management and information systems that support these processes. The Health (National Cervical Screening Programme) Amendment Act, which came into effect in 2004, underpins the NCSP’s operations to ensure the co-ordination of a high-quality screening programme for all women in New Zealand.
Coverage

Overall programme coverage is currently approximately 70–75% (hysterectomy adjusted) for the total population and approximately 50–60% for Māori, Pacific and Asian women. Coverage increased rapidly following the change to an ‘opt off’ register in 1993 but has remained stable for over a decade. Nevertheless, New Zealand is in the top five of OECD countries in terms of cervical screening rates. This overall level does, however, disguise important ethnic inequalities in coverage among Māori, Pacific and Asian women. Coverage is also lower among women living in the most deprived areas of the country.

Cervical cancer incidence and mortality

Since the introduction of the NCSP in 1990 the age-standardised incidence rate of invasive cervical cancer has fallen by approximately 50% (Figure 2). The rate has fallen more rapidly among Māori, so that the inequality in incidence between Māori and non-Māori women has narrowed, although Māori rates remain higher than those for non-Māori (Figure 3).

Cervical cancer mortality began to decline many years before the introduction of the NCSP, possibly reflecting opportunistic screening and improvements in treatment. However, mortality has fallen more rapidly since the introduction of the NCSP: by approximately 60% since 1990 (Figure 2). This improvement has been much greater for Māori women, which means the mortality gap between Māori and non-Māori women has substantially narrowed (Figure 4).

Figure 2: Cervical cancer incidence and mortality trends, total population, 1996–2004

![Cervical cancer incidence and mortality trends, total population, 1996–2004](image)

Note: Rates per 100,000, age-standardised to Segi's world population
Guidelines for Cervical Screening in New Zealand

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Note: Rates per 100,000, age-standardised to Segi’s world population.

Figure 3: Cervical cancer incidence trends, by ethnicity, 1996–2004

Figure 4: Cervical cancer mortality trends, by ethnicity, 1996–2004
When to screen and how often

Regular cervical screening for the prevention of cervical cancer is recommended for all women who are, or have ever been, sexually active. NCSP policy on screening age and interval remains unchanged.

**NCSP policy on screening age and interval**

All women who have ever had sexual intercourse should be offered a three-yearly cervical smear test from age 20 to age 69.

If this is the first ever smear, or more than 5 years have elapsed since the previous smear, a second smear is recommended one year after the first, with three-yearly smears thereafter.

**Age to start screening**

Understanding of the natural history of cervical cancer, and in particular of the role of human papillomavirus (HPV) infection in the pathogenesis of this cancer, has advanced considerably since the previous New Zealand guidelines were published. Much more is now known about the association between HPV and cervical cancer. In particular, specific high risk subtypes have been identified as being necessary for the development of cervical cancer. The implication is that in the absence of persistent infection with these high-risk HPV genotypes, cervical cancer is not expected to develop. This epidemiological finding is highly relevant to the screening recommendations.

The appropriate age at which to start cervical screening (screening initiation) and the most appropriate frequency of screening (screening interval) will depend on the age-related risk of cervical cancer in the population, and must take into account the costs of screening and the risk of harm from screening and consequential (unnecessary) treatment, alongside the potential benefits.

The International Agency on Research on Cancer (IARC) recommends that the age at which screening begins should aim to maximise the detection of cervical pre-cancer cases while avoiding the large number of transient HPV infections. Because the high rate of abnormalities seen in younger women (caused by transient HPV infections) can lead to frequent treatments, the age for starting screening has been controversial. Although treatment has a low complication rate, it is now recognised that the consequences of treatment complications are greater for younger women who have not completed their family than they are for older women.

The age-specific incidence of cervical cancer in New Zealand shows that there is no need to screen sexually active women under 20 years of age. In other words, invasive squamous or adenocarcinoma of the cervix has rarely been diagnosed in New Zealand in a woman less than 20 years of age. Unnecessary screening of women under 20 years wastes precious resources, diverts attention from women who could genuinely benefit from screening, and is unlikely to be of any benefit to these young women – in fact early and unnecessary screening can potentially cause them serious harm.
**Age to stop screening**

At the other end of the age range, many countries do not screen women over 60 or 65 years. This is due to the fact that good-quality smears are difficult to obtain in women many years after menopause, and if they have had many smears with a normal outcome in the past, particularly if they have had three normal smears in the past 10 years, women aged 65 years and over are considered to be at low risk of developing cervical cancer. However, the current policy in New Zealand is to continue regular screening until aged 69 years.

**Future changes to screening age and interval**

In other developed countries with organised cervical screening programmes, such as the United Kingdom, it is now recommended that women should not be screened before age 25 years, should continue to be screened three-yearly until 50 years of age, and thereafter should be screened five-yearly until 65 years. In the Netherlands and Finland cervical screening targets women aged 30 to 60 years with five-yearly screening; women in these countries are not screened after 60 years of age. A recent comparison of the Australian policy of two-yearly screening with the three to five-yearly screening policy in the United Kingdom found similar reductions in incidence and mortality in both countries, and recommended a review of the Australian policy of two-yearly screening.⁴

A recent World Health Organization (WHO) guide on cervical cancer control⁵ recommends that:

- new programmes should start screening women aged 30 years or more
- existing programmes should not include women less than 25 years of age
- a five-year screening interval is appropriate for women over 50 years
- a three-year interval is appropriate in the age group 25–49 years
- annual screening is not recommended at any age
- screening is not necessary for women over 65 years provided the last two smears were negative.

At the request of the NCSP, the Public Health Intelligence unit of the Ministry of Health recently undertook a review of relevant New Zealand data held on the NCSP Register, the New Zealand Cancer Registry and the New Zealand Health Information Service Mortality Collection, together with an updated review of the international literature on the efficacy of cervical cytological screening.⁶ Statistical models were built to explore policy options for age at first screen and screening interval in the light of this data and recent policy changes in other countries, as well as the revised WHO recommendations.

As a result, the NCSP has decided against a change in policy at this stage. The current policy of screening women between the ages of 20 and 69 every three years if they have ever been sexually active remains in place. This policy will be reviewed again in another three to five years in light of the changes in screening outlined in these guidelines and the introduction of routine HPV vaccination in New Zealand.
PART B: The Guidelines
The following guidelines use technical terminology that will be familiar to many health professionals but may be foreign to those outside the health system who may wish to access these guidelines. The glossary explains a number of key terms and abbreviations.

The guidelines are presented as shown in the example below.

**Example of a guideline**

<table>
<thead>
<tr>
<th>ASSESSMENT/ REPORT GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histologically confirmed low-grade squamous abnormalities</td>
<td>Treatment is not recommended because such lesions are considered to be an expression of a productive HPV infection.</td>
</tr>
</tbody>
</table>

The first column gives the result of the smear or assessment, the second column provides the guidelines for management, and the third column gives a grading of the level of evidence on which the guideline is based. The grades given are A, B, C, I and 3, and are explained below.

**GRADE DETAILS**

- **A**: The recommendation is supported by GOOD evidence. There are a number of studies that are valid, consistent, applicable and clinically relevant.
- **B**: The recommendation is supported by FAIR evidence based on studies that are valid, but there are some concerns about the volume, consistency, applicability and/or clinical relevance of the evidence that may cause some uncertainty (but they are not likely to be overturned by other evidence).
- **C**: The recommendation is supported by EXPERT OPINION only, from external opinion, published or unpublished (e.g., consensus guidelines).
- **I**: No recommendation can be made. The evidence is lacking, of poor quality or conflicting, and the balance of benefits and harms cannot be determined.
- **3**: Good practice point. Where no external evidence is available, best practice recommendations are made by consensus, based on the experience of the Guideline Development Team, or feedback from consultation within New Zealand.

Source: New Zealand Guidelines Group www.nzgg.org.nz
Using the Guidelines

The following guidelines use technical terminology that will be familiar to many health professionals but may be foreign to those outside the health system who may wish to access these guidelines. The glossary explains a number of key terms and abbreviations.

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<tbody>
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<td>Grade B</td>
</tr>
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</table>

The first column gives the result of the smear or assessment, the second column provides the guidelines for management, and the third column gives a grading of the level of evidence on which the guideline is based. The grades given are A, B, C, I and ✓, and are explained below.

<table>
<thead>
<tr>
<th>GRADE</th>
<th>DETAILS</th>
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<tbody>
<tr>
<td>A</td>
<td>The recommendation is supported by GOOD evidence. There are a number of studies that are valid, consistent, applicable and clinically relevant.</td>
</tr>
<tr>
<td>B</td>
<td>The recommendation is supported by FAIR evidence based on studies that are valid, but there are some concerns about the volume, consistency, applicability and/or clinical relevance of the evidence that may cause some uncertainty (but they are not likely to be overturned by other evidence).</td>
</tr>
<tr>
<td>C</td>
<td>The recommendation is supported by EXPERT OPINION only, from external opinion, published or unpublished (eg, consensus guidelines).</td>
</tr>
<tr>
<td>I</td>
<td>No recommendation can be made. The evidence is lacking, of poor quality or conflicting, and the balance of benefits and harms cannot be determined.</td>
</tr>
<tr>
<td>✓</td>
<td>Good practice point. Where no external evidence is available, best practice recommendations are made by consensus, based on the experience of the Guideline Development Team, or feedback from consultation within New Zealand.</td>
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</tbody>
</table>

Source: New Zealand Guidelines Group www.nzgg.org.nz
Glossary

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tr>
<td>Adenocarcinoma</td>
<td>A cancer affecting the cervix, but involving the columnar (endocervical) cells rather than the squamous cells. The columnar cells are involved in glandular activity.</td>
</tr>
<tr>
<td>AGC</td>
<td>Atypical glandular cells (now replaces AGUS).</td>
</tr>
<tr>
<td>AIS</td>
<td>Adenocarcinoma in situ. High-grade changes to the glandular (endocervical) cells of the cervix.</td>
</tr>
<tr>
<td>ASC-US</td>
<td>Atypical squamous cells of undetermined significance.</td>
</tr>
<tr>
<td>ASC-H</td>
<td>Atypical squamous cells - cannot exclude HSIL.</td>
</tr>
<tr>
<td>Carcinoma in situ (CIS)</td>
<td>An older classification of CIN3. Abnormal cells that are confined to the surface epithelium of the cervix. The abnormal cells are evident throughout each of the layers of the epithelium, but they have not extended into other, deeper tissue or surrounding areas. Without treatment they may develop into invasive cancer.</td>
</tr>
<tr>
<td>Cervical intra-epithelial neoplasia (CIN)</td>
<td>Abnormal squamous cell changes or growth in the surface layers of the cervix. These changes are not cancer but some could develop into cancer if not treated. CIN is graded as low-grade CIN1, or high-grade CIN2 or 3; CIN3 means the most severe changes and is the same as carcinoma in situ.</td>
</tr>
<tr>
<td>Cervical smear</td>
<td>This may be either a conventional Pap smear or liquid-based cytology (LBC).</td>
</tr>
<tr>
<td>Coverage</td>
<td>The proportion of women aged 20-69 years who have had a screening result recorded on the NCSP-Register in the previous three years.</td>
</tr>
<tr>
<td>Cytopathological review</td>
<td>A review of the smear test and histology slides by a pathologist/cytologist. This may be undertaken during multidisciplinary case review by a group of health professionals (eg, pathologist, colposcopist, cytologist and colposcopy nurse).</td>
</tr>
<tr>
<td>Dysplasia</td>
<td>Abnormal changes in the cervix graded as mild (CIN1), moderate (CIN2) or severe (CIN3).</td>
</tr>
<tr>
<td>Ectocervix</td>
<td>The outer surface layer of the outer cervix.</td>
</tr>
<tr>
<td>Endocervix</td>
<td>The surface layer of the inner cervix that forms the canal of the cervix.</td>
</tr>
<tr>
<td>Endometrium</td>
<td>The tissue lining the uterus.</td>
</tr>
<tr>
<td>HPV</td>
<td>Human papillomavirus.</td>
</tr>
<tr>
<td>HrHPV</td>
<td>High-risk human papillomavirus.</td>
</tr>
<tr>
<td>HSIL</td>
<td>High-grade squamous intra-epithelial lesion (equivalent to CIN2/3).</td>
</tr>
<tr>
<td>Liquid-based cytology (LBC)</td>
<td>An alternative method to the conventional Pap smear for preparing cells from the cervix for cytology testing. Instead of the cells being smeared on to a glass slide, they are put into a liquid preserving solution. May also be used for HPV testing.</td>
</tr>
<tr>
<td>Low-grade abnormality</td>
<td>A low-grade squamous intra-epithelial lesion (LSIL) involving mild changes to the cells of the cervix, which include abnormalities due to HPV changes and CIN1. These changes need careful follow-up but may not need treatment.</td>
</tr>
<tr>
<td>LSIL</td>
<td>Low-grade squamous intra-epithelial lesion.</td>
</tr>
<tr>
<td>RANZCOG</td>
<td>Royal Australian and New Zealand College of Obstetricians and Gynaecologists.</td>
</tr>
<tr>
<td>Specialist colposcopist</td>
<td>A gynaecologist with special expertise in colposcopy.</td>
</tr>
<tr>
<td>Transformation zone</td>
<td>The region of the cervix where the glandular (columnar) precursor cells have changed or are changing to squamous cells. Most cervical abnormalities in the squamous cells occur in the transformation zone as a result of HPV infection.</td>
</tr>
<tr>
<td>Triage</td>
<td>The clinical process of sorting people into groups based on their need for or likely benefit from treatment.</td>
</tr>
<tr>
<td>Unsatisfactory smear</td>
<td>An inadequate smear that cannot be assessed by the laboratory.</td>
</tr>
<tr>
<td>Vault smear</td>
<td>A smear taken from the top of the vagina in women who have had their cervix removed during a hysterectomy.</td>
</tr>
</tbody>
</table>
Management of Women with Normal Cervical Smears

The cervical smear is a screening test of usually asymptomatic women to detect and treat pre-invasive abnormalities of the cervix. If the first-ever smear result is negative, a follow-up smear is recommended in 12 months in order to reduce the risk of a false negative result. If this follow-up smear is also negative, recall should be every three years.

If a woman is symptomatic or there is a concern about the clinical appearance of the cervix, she should be referred for colposcopic assessment according to RANZCOG guidelines.

**Guideline 1: Negative (normal) cervical smear**

<table>
<thead>
<tr>
<th>CERVICAL SMEAR REPORT</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative for squamous or glandular epithelial lesion or malignancy</td>
<td>Recall in 3 years for cervical smear unless it falls into the following category.</td>
<td>Grade B</td>
</tr>
<tr>
<td>Negative for squamous or glandular epithelial lesion or malignancy, but this is the first smear, or more than 5 years have elapsed since the previous smear</td>
<td>Recall in 12 months for cervical smear.</td>
<td>Grade C</td>
</tr>
</tbody>
</table>
Management of Women with Unsatisfactory Cervical Smears

An unsatisfactory cervical smear is one that is inadequate for some reason and therefore cannot be reported on by the laboratory. The adequacy of a cervical cytology sample is based on the number of well-visualised, well-preserved squamous cells that have been sampled. Laboratories reading cervical samples have a standardised procedure for assessing the adequacy of a cervical cytology sample. Note that the presence or absence of cells from the endocervical canal/transformation zone does not affect the adequacy of a cervical smear.

There are three main kinds of factors that cause unsatisfactory samples:
- taking the smear – there is inadequate sampling of cells, contact bleeding, poor fixation or unwanted artefacts
- clinical factors eg, bleeding, inflammation or cytolysis
- laboratory technical factors.

An unsatisfactory cytology sample is recorded as a non-result on the NCSP Register. Three consecutive unsatisfactory samples will result in a recommendation for colposcopy to exclude a high-grade lesion. Smear takers should consider using the LBC technique for the collection and transport of a cervical sample following an unsatisfactory smear result.

Guideline 2: Unsatisfactory cervical smear

<table>
<thead>
<tr>
<th>CERVICAL SMEAR REPORT</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
</table>
| Unsatisfactory        | Repeat the cervical smear within 3 months. Refer for colposcopy after 3 consecutive unsatisfactory smear reports. Note: NCSP LBC Policy Statement (2006): There may be situations where liquid-based cytology (LBC) offers some advantage over conventional smears, such as women with:  
  - excessive cervical mucus, discharge or blood  
  - recurrent inflammatory smears  
  - recurrent unsatisfactory smears. (see www.nsu.govt.nz) | Grade B |
Management of Women with Abnormal Cervical Smears

Low-grade Squamous Abnormalities: ASC-US and LSIL

Introduction

Cervical cancer is a very rare outcome of a low-grade abnormality.\textsuperscript{7,8} Cancer diagnosed after a low-grade cytology result represents a combination of two main influences: under-calling on the index cytology and true progression over time from an intra-epithelial abnormality.

Recent studies indicate that the risk for CIN2/3 is similar for women with low-grade squamous intra-epithelial lesions (LSIL) and atypical squamous cells of undetermined significance (ASC-US).\textsuperscript{5} Both categories also show similar high regression rates, and so both are managed similarly.

An analysis of data held on the NCSP Register was undertaken to help inform the management of women with low-grade abnormalities. This paper is published on the NCSP website (see www.nsu.govt.nz).

Management of women with a cervical smear report of ASC-US or LSIL

Low-grade cytology is a manifestation of a viral infection that will resolve spontaneously in the majority of women under 30 years old.\textsuperscript{10,11} The recall timeframe has been extended to 12 months for women aged 20–29 years given the evidence that the median time for clearance of HPV infection is 6-18 months (see Guideline 3).\textsuperscript{12}

Evidence shows that women 30 years and over with a HrHPV infection are at increased risk of developing a high-grade lesion, because the infection is more likely to be persistent.\textsuperscript{13} HPV triage for women in this age group with a first ASC-US/LSIL cytology result is of greater benefit than repeated cytology to assess the underlying risk of HSIL.\textsuperscript{14,15} (Refer also to NCSP Best Practice Guidance on HPV Testing (2008), page 47).

If a woman is symptomatic or there is concern about the clinical appearance of the cervix, she must be investigated appropriately with colposcopic assessment.

All women should be advised of the significance of their low-grade cytology results and their low risk of harbouring or developing a cancer. If a woman is unduly anxious or specifically requests specialist reassurance, referral for colposcopic assessment may alleviate her anxiety, even though this is not a complete safeguard against a diagnosis of underlying HSIL or cervical cancer.
Guideline 3: Cervical smear report ASC-US/LSIL (See Flowchart 1)

<table>
<thead>
<tr>
<th>CERVICAL SMEAR REPORT</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASC-US/LSIL</td>
<td><strong>Women aged 20 – 69 years with an abnormal smear report within the last 5 years</strong> Refer for colposcopy.</td>
<td>Grade B</td>
</tr>
<tr>
<td></td>
<td><strong>Women aged 20 – 29 years with no abnormal smear reports within the last 5 years</strong> Repeat cervical smear in 12 months.</td>
<td>Grade B</td>
</tr>
</tbody>
</table>
|                        | **Until 1 July 2009:**
|                        | **Women aged 30 years and over with one (or more) normal smear reports in the last 5 years** Repeat cervical smear in 12 months. | Grade B |
|                        | **Women aged 30 years and over who have not had a smear in the last 5 years** should be offered either a repeat smear within 6 months or a referral to colposcopy. | |
|                        | **From 1 July 2009:**
|                        | **Women aged 30 years and over who have not had an abnormal smear report within the last 5 years** should be offered an HPV test, as per the NCSP Best Practice Guidance on HPV Testing (2008). |
|                        | 1. If the reflex HrHPV test is negative, repeat cytology in 12 months. If the repeat cytology is negative, return to normal screening. |
|                        | 2. If the HrHPV test is positive, refer for colposcopy. |
|                        | *See Flowchart HPV Testing Guidance 1: Triage of women 30 years and over with ASC-US or LSIL* |
| 12-month repeat smear report after ASC-US/LSIL | If the 12-month repeat smear is reported as: |
| | • HSIL or ASC-H, refer for colposcopy |
| | • ASC-US/LSIL, refer for colposcopy |
| | • negative, repeat the smear in 12 months (ie, 24 months after the index smear). | Grade B/C |
Flowchart 1: Management of women with low-grade abnormalities: ASC-US or LSIL

Cervical smear report ASC-US/LSIL

women 20-29 years

- Previous abnormal report within last 5 years → Colposcopy
- No abnormal report within last 5 years → Repeat smear in 12 months

women 30 years and over

- Previous abnormal report within last 5 years → Colposcopy
- 1 or more normal reports within the last 5 years → Repeat smear in 12 months
- No smear within the last 5 years → Either
  - Repeat smear in 6 months OR Colposcopy

As from 1 July 2009 triage with HPV testing as per NCSP Best Practice Guidance on HPV Testing
Colposcopic assessment of women with ASC-US/LSIL

The colposcopic assessment and management of women with a cytology result of ASC-US/LSIL should comply with the guidelines published by RANZCOG and the Australian Society of Colposcopy and Cervical Pathology.\textsuperscript{16}

A fluctuating status between low-grade change and negative cytology is not uncommon, but the significance of this is unclear. It could reflect a transition from active HPV infection to resolution followed by re-infection, or there could be an underlying persistent lesion that is not being consistently sampled or is not being detected on cytology. HrHPV testing may help with the further management of these women.

If there is inter-menstrual bleeding or post-coital bleeding, refer to the RANZCOG guidance.\textsuperscript{17}

Guideline 4: Colposcopic assessment of women with ASC-US/LSIL (See Flowchart 2)

<table>
<thead>
<tr>
<th>COLPOSCOPIC ASSESSMENT</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Satisfactory and normal</td>
<td>Refer back to the smear-taker for 2 annual smears. 1. If either smear is abnormal, refer for repeat colposcopy. 2. If both smears are negative, resume routine screening.</td>
<td>Grade C</td>
</tr>
<tr>
<td>Satisfactory and abnormal</td>
<td>Perform target biopsy to make a diagnosis.</td>
<td>Grade C</td>
</tr>
<tr>
<td>Unsatisfactory</td>
<td>Cytology review is recommended. 1. If low-grade cytology is confirmed on review, repeat colposcopy and cytology is recommended in 12 months. 2. Management may be individualised, based on age, reproductive status and clinical risk. Treatment is not usually indicated.</td>
<td>✓ Grade C</td>
</tr>
</tbody>
</table>
Management of women with histologically confirmed LSIL

**Guideline 5: Histologically confirmed LSIL (See Flowchart 2)**

<table>
<thead>
<tr>
<th>HISTOLOGY REPORT</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histologically confirmed low-grade squamous abnormalities</td>
<td>Treatment is not recommended because such lesions are considered to be an expression of a productive HPV infection. Refer back to the smear-taker for repeat cytology at 12 and 24 months. If both smears are negative, it is recommended that the woman return to routine screening. If either repeat smear shows ASC-US/LSIL or higher (ie, HSIL, ASC-H, AGC or AIS), refer back to colposcopy.</td>
<td>Grade B, C</td>
</tr>
</tbody>
</table>
**Flowchart 2: Colposcopic assessment of ASC-US/LSIL and management of confirmed histology**

**Guidelines for Cervical Screening in New Zealand**

- **Routine 3 yearly screening**
- **Any abnormal smears**
  - Repeat smear at 12 months
  - Repeat smear at 12 months
  - Routine 3 yearly screening

**Flowchart Details**

- **Colposcopic assessment**
  - Satisfactory & normal
  - Satisfactory & abnormal
  - Unsatisfactory

- **Target biopsy**
  - **CIN1**
  - **CIN2/3**

- **Cytology review recommended**
  - **LSIL confirmed**

- **Treatment**
  - see special circumstances for pregnancy and under 20 years

- **Management** may be individualised based on age, reproductive status and clinical risk.
  - Treatment is not usually indicated.
High-grade Squamous Abnormalities: ASC-H/HSIL

Introduction

This category encompasses CIN2 and CIN3 (moderate dysplasia, severe dysplasia/carcinoma in situ) as well as changes that are suspicious of high-grade squamous intraepithelial lesions.

The finding of a high-grade result on cytology carries a high risk of significant cervical disease. The main objective of the NCSP is to detect high-grade abnormalities in order to treat these effectively and prevent cervical cancer.

Management of women with a cervical smear report of ASC-H/HSIL

Women with untreated CIN3 lesions are at high risk of cervical cancer.\(^{18,19}\) CIN2 lesions are more heterogeneous and variable in cancer potential than CIN3,\(^ {19,20}\) but in New Zealand these abnormalities are usually reported as CIN2/3.

The histological differentiation between CIN2 and CIN3 is subjective and not sufficiently reliable to permit clear stratification of risk.\(^ {21}\) Recommendations for management are in most cases combined, with CIN2 being seen as the threshold for treatment. Exceptions to this are women under 20 years with CIN2, where the likelihood of regression is high, and pregnant women.

Guideline 6: Cervical smear report ASC-H or HSIL

<table>
<thead>
<tr>
<th>CERVICAL SMEAR REPORT</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASC-H or HSIL</td>
<td>Refer for colposcopy and targeted biopsy, where indicated.</td>
<td>Grade B</td>
</tr>
</tbody>
</table>
Colposcopic assessment of women with ASC-H/HSIL

A significant number of lesions can be missed on colposcopic impression. Where cytology is ASC-H or HSIL but colposcopic examination of the cervix shows no sign of any abnormality, there should be careful clinical inspection and colposcopy of the entire lower genital tract and a review undertaken of possible sites of origin for neoplastic cells in the upper genital tract.

Guideline 7: Colposcopic assessments of women with ASC-H/HSIL (See Flowchart 3)

<table>
<thead>
<tr>
<th>COLPOSCOPIC ASSESSMENT</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
</table>
| Satisfactory and abnormal | Undertake targeted biopsy for histology.  
*Note: For ‘See and treat’ see Guideline 8.*  
Where the biopsy confirms CIN1, manage based on a multidisciplinary team review. | Grade B |
| Satisfactory and normal colposcopy or negative biopsy | Cytology review is recommended.  
If the review confirms high-grade, repeat colposcopy and cytology within 3 months.  
1. If colposcopy and cytology are normal at 3 months, repeat cytology in 12 months.  
2. If colposcopy or cytology is LSIL at 3 months, individualise management based on a multidisciplinary team review.  
3. If colposcopy or cytology is HSIL at 3 months, treatment is indicated (see Guideline 8). | Grade C  
✓ |
| Unsatisfactory colposcopy | Cytology review is recommended.  
1. If the review confirms ASC-H/HSIL, then cold knife cone biopsy is recommended.  
2. If the review confirms normal or ASC-US or LSIL, manage based on a multidisciplinary team review. | Grade C  
✓ |
Flowchart 3: Management of women with high-grade abnormalities: ASC-H or HSIL

ASC-H/HSIL

Colposcopic assessment

Unsatisfactory

Cytology review

- Negative ASC-US/LSIL
  - Management based on multidisciplinary team review

- Confirmed ASC-H/HSIL
  - Cone biopsy
  - Management based on multidisciplinary team review

Satisfactory

Normal (negative biopsy)

- Cyto-histo review
  - ASC-US/LSIL
    - Repeat colposcopy in 3 months (see summary table)
    - Management based on multidisciplinary team review
  - ASC-H/HSIL
    - Target biopsy
    - CIN1
      - Treatment
        - See special circumstances for pregnancy and under 20 years
    - CIN2/3

Abnormal

Target biopsy

CIN1

CIN2/3

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Management of women with histologically confirmed CIN2 or 3

No substantial differences have been found between the different treatment modalities in terms of reducing cancer risk.\textsuperscript{25,26,27} Recent evidence suggests that all excisional treatment methods are associated with a small but real increase in long-term adverse obstetric outcomes, including pre-term delivery, low birth weight and premature rupture of the membranes.\textsuperscript{28,29,30} One review recorded a significantly increased risk if the excision depth exceeded 10mm.\textsuperscript{28} This evidence reinforces the need for caution when treating young women with mild cervical abnormalities and supports management by surveillance.

Follow-up after treatment serves to identify both complications of treatment and recurrent disease, which may be the result of inadequately treated disease, persistent disease or new infection. Women treated for HSIL are at increased risk of developing further high-grade disease and invasive cancer.\textsuperscript{31,32} Persistence and recurrence rates are greatest in the initial two years following treatment, but the risk has been found to persist for at least 10 years after the initial treatment.\textsuperscript{31,33,34,35}

Treatment failure rates have been reported to average around 10%.\textsuperscript{35} Involved excision margins after large loop excision of the transformation zone (LLETZ) or cold knife cone biopsy are a risk factor for treatment failure.\textsuperscript{34} The risk of further high-grade disease and invasive cervical cancer increases with age.\textsuperscript{32,34}
### Guideline 8: Histologically confirmed CIN2 or CIN3

<table>
<thead>
<tr>
<th>HISTOLOGY REPORT</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIN2 or 3</td>
<td>Treat in order to reduce the risk of developing invasive cervical carcinoma. (Also see Guidelines 14 and 15)</td>
<td>Grade A</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TREATMENT</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
</table>
| Ablative therapy | Ablative therapy may be considered provided:  
• colposcopic assessment is satisfactory  
• a targeted biopsy has confirmed the diagnosis  
• there is no evidence of an invasive cancer on cytology, colposcopic assessment or biopsy  
• there is no evidence of a glandular lesion on cytology, biopsy or colposcopy  
• the entire lesion can be visualised. | Grade C |
| Cryotherapy | Cryotherapy is not recommended. | Grade B |
| Loop electro-excisional procedure (LEEP) or large loop excision of the transformation zone (LLETZ) | Excess diathermy artefact should be avoided when using diathermy loops in order to allow comprehensive pathological examination, including margin status. | Grade C |
| Cone biopsy | Cold knife cone biopsy may be necessary to treat women with high-grade squamous lesions. Indications include:  
• failure to visualise the upper limit of the cervical transformation zone in a woman with high-grade squamous abnormality on her referral cervical smear (ie, unsatisfactory colposcopy)  
• suspicion of an early invasive cancer on cytology, biopsy or colposcopic assessment  
• the suspected presence of an additional glandular abnormality (eg, adenocarcinoma in situ) on cytology or biopsy (ie, a mixed lesion).  
Careful attention should be paid to tailoring treatment to the individual woman, taking into account the size, extent, situation and severity of the lesion. | Grade C |

Table continues on next page.
### Guideline 8: Histologically confirmed CIN2 or CIN3 (continued)

<table>
<thead>
<tr>
<th>TREATMENT</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
</table>
| Hysterectomy                       | Hysterectomy is not generally indicated for the management of CIN2 or 3 alone. If performed for concurrent clinical indications, the following conditions must be met:  
  • colposcopic assessment is satisfactory  
  • a targeted biopsy has confirmed the diagnosis  
  • there is no evidence of an invasive cancer on cytology, colposcopic assessment or biopsy  
  • there is no evidence of a glandular lesion on cytology or biopsy or colposcopy  
  • the entire lesion can be visualised.                                                                                                                                   | Grade B  |
| See and treat                      | Note: ‘See and treat’ should only be considered if it is thought this may be the only opportunity to undertake treatment and:  
  • circumstances are appropriate or immediate treatment is necessary  
  • the colposcopic examination is consistent with the referral  
  • the limits of the lesion are visible  
  • the whole abnormality can be excised  
  • there is no suspicion of invasion  
  • there is an excisional specimen available for histological examination (ie, no ablative therapy).                                                                 | Grade C  |
| In women who plan to have children | Local ablative or excisional treatments should destroy or remove abnormal tissue to a depth of at least 7 mm. There is no clearly superior method of fertility-sparing treatment of CIN2 and 3.                                                        | Grade B  |
Management of women previously treated for CIN2 or 3

HrHPV testing has a high sensitivity for detecting persistent CIN2/3 post-treatment and allows for shortening of the surveillance period (see NCSP Best Practice Guidance on HPV Testing, page 47).

There has been little research done on the role of post-treatment HrHPV testing long-term (more than two years), therefore this management strategy will be closely monitored.

**Guideline 9: Follow-up of women previously treated for CIN2/3**

<table>
<thead>
<tr>
<th>FOLLOW-UP</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routine follow-up</td>
<td>A woman treated for CIN2 or 3 should have a colposcopy and smear in 6–12 months. Any symptoms should be appropriately managed. A cervical smear should be taken 12 months after treatment and annually thereafter until the age of 70. From 1 July 2009 HrHPV testing as per the NCSP Best Practice Guidance on HPV Testing (2008) can be used to help identify women at risk of persistent or recurrent lesions. See Flowchart HPV Testing Guidance 2: Follow-up of women treated for high grade lesions, page 51.</td>
<td>Grade B</td>
</tr>
</tbody>
</table>

Management of women with suspected invasion/SCC

**Guideline 10: HSIL with suspected invasion or SCC**

<table>
<thead>
<tr>
<th>CERVICAL SMEAR REPORT</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSIL with suspected invasion or squamous cell carcinoma (SCC)</td>
<td>Urgent referral to a specialist colposcopist or an oncologist.</td>
<td>Grade B</td>
</tr>
</tbody>
</table>
Cervical Glandular Abnormalities: AGC/AIS /AC

Introduction

In New Zealand, and internationally, glandular lesions are now estimated to represent 15–20% of invasive cervical cancers.38-40

Cervical screening is less effective at preventing cervical adenocarcinoma compared to squamous carcinoma because of the limitations of the cervical smear test.41,42

Infection with HrHPV types has been reported to be associated with cervical adenocarcinoma and adenocarcinoma in situ (AIS) in approximately 90% of cases.43,44

It is not uncommon for atypical glandular cells (AGC) to be associated with an underlying neoplastic condition, including adenocarcinoma of the cervix, endometrium, ovary and fallopian tube.45,46-48

Because of this, all women with glandular abnormalities should be referred to colposcopy or a gynaecological oncologist for assessment.

It is common for both squamous and glandular lesions to co-exist, and a significant number of cytology detected glandular abnormalities result in either a squamous or coexisting squamous/glandular lesion.49-51

Because of the high incidence of neoplasia and poor sensitivity of testing methods, diagnostic excisional procedures may be necessary.52,53

HrHPV testing may have an ancillary role in the management of cytological cases in which a lesion is suspected but not confirmed on colposcopy/histology.48,51,53

Management of women with a smear report of cervical glandular abnormalities

Guideline 11: Cervical cytology report AGC, AIS or AC

<table>
<thead>
<tr>
<th>CERVICAL CYTOLOGY REPORT</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGC or AIS or AC</td>
<td>Refer to a specialist colposcopist or to a gynaecological oncologist.</td>
<td>Grade B</td>
</tr>
</tbody>
</table>
Cervical Glandular Abnormalities: AGC/AIS /AC

Introduction
In New Zealand, and internationally, glandular lesions are now estimated to represent 15−20% of invasive cervical cancers.\(^{38-40}\) Cervical screening is less effective at preventing cervical adenocarcinoma compared to squamous carcinoma because of the limitations of the cervical smear test.\(^{41,42}\) Infection with HrHPV types has been reported to be associated with cervical adenocarcinoma and adenocarcinoma in situ (AIS) in approximately 90% of cases.\(^{43,44}\) It is not uncommon for atypical glandular cells (AGC) to be associated with an underlying neoplastic condition, including adenocarcinoma of the cervix, endometrium, ovary and fallopian tube.\(^{45,46-48}\) Because of this, all women with glandular abnormalities should be referred to colposcopy or a gynaecological oncologist for assessment.

It is common for both squamous and glandular lesions to co-exist, and a significant number of cytology detected glandular abnormalities result in either a squamous or coexisting squamous/glandular lesion.\(^{49-51}\) Because of the high incidence of neoplasia and poor sensitivity of testing methods, diagnostic excisional procedures may be necessary.\(^{52,53}\) HrHPV testing may have an ancillary role in the management of cytological cases in which a lesion is suspected but not confirmed on colposcopy/histology.\(^{48,51,53}\)

Management of women with a smear report of cervical glandular abnormalities

Guideline 11: Cervical cytology report AGC, AIS or AC

CERVICAL CYTOLOGY REPORT GUIDELINE EVIDENCE

AGC or AIS or AC Refer to a specialist colposcopist or to a gynaecological oncologist.

Grade B

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Guideline 12: Colposcopic assessment and treatment of glandular abnormality (see Flowchart 4)

<table>
<thead>
<tr>
<th>TREATMENT</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
</table>
| Assessment | Colposcopic assessment is mandatory in the presence of cervical cytology suggesting glandular abnormalities (AGC or AIS).  
1. If the colposcopy is satisfactory and normal, it is recommended that cytology be reviewed.  
   • If abnormal glandular cytology is confirmed on review, cold knife cone biopsy and dilatation and curettage (D&C) are recommended.  
   • If abnormal glandular cytology is not confirmed on review, management should be based on a multidisciplinary team decision.  
2. If the colposcopy is satisfactory and abnormal, and consistent with cancer, punch biopsy and refer to a gynaecological oncologist.  
3. If colposcopy is satisfactory and abnormal, and suspicious of a neoplastic process, cold knife cone biopsy and D&C are recommended.  
4. If colposcopy is unsatisfactory, it is recommended that cytology be reviewed.  
   • If cytology is confirmed as favouring a neoplastic process, cold knife cone biopsy and D&C are recommended.  
   • If cytology is not confirmed on review, management should be based on a multidisciplinary team decision. |
| Cone biopsy | Cold-knife cone biopsy should be considered the ‘gold standard’ for the assessment of glandular abnormalities. |
| Referral for women with adenocarcinoma on cone or punch biopsy | Refer to a gynaecological oncologist or an oncology unit for subsequent management. |

From 1 July 2009 HrHPV testing should be considered as a useful adjunct for further management, as per the NCSP Best Practice Guidance on HPV Testing (2008).

Grade B

Cone biopsy Cold-knife cone biopsy should be considered the ‘gold standard’ for the assessment of glandular abnormalities. Grade B

Referral for women with adenocarcinoma on cone or punch biopsy Refer to a gynaecological oncologist or an oncology unit for subsequent management. Grade B

table continues on next page
### Guideline 12: Colposcopic assessment and treatment of glandular abnormality (continued)

<table>
<thead>
<tr>
<th>TREATMENT</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Management of women with a smear report of AIS</td>
<td>If invasive carcinoma is not identified at colposcopic assessment, a cold knife cone biopsy should be undertaken. Hysterectomy should not be undertaken without prior cone biopsy to exclude invasive carcinoma.</td>
<td>Grade C</td>
</tr>
<tr>
<td>Management of women with a cone biopsy report of AIS</td>
<td>The management of these women will depend on the age and fertility expectations of the woman and the status of the excision margins. Hysterectomy should be discussed, and may be recommended for women who have completed childbearing because of the difficulties of reliable cytological follow-up, a high recurrence rate, and the reported multi-focal nature of the disease.</td>
<td>Grade B</td>
</tr>
</tbody>
</table>
| AIS treatment (with cone) follow-up | 1. If the cone biopsy has positive margins on the results, further treatment should be considered.  
2. If the margins are clear, follow-up colposcopy and cytology should be undertaken by endocervical brush 6 months after treatment.  
3. Repeat cytology at 12 months, then annually if both smears and examinations are normal.  
4. Early follow-up of symptoms is recommended. | Grade B |

### Colposcopy

<table>
<thead>
<tr>
<th>Flowchart 4: Colposcopic assessment and treatment of women with glandular abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glandular Abnormalities</strong></td>
</tr>
<tr>
<td>Atypical glandular cells (AGC) (AG1-5)</td>
</tr>
<tr>
<td>Adenocarcinoma in situ (AIS)</td>
</tr>
<tr>
<td>Adenocarcinoma (AC 1-4)</td>
</tr>
<tr>
<td><strong>Cytology</strong></td>
</tr>
<tr>
<td><strong>Cytology confirmed</strong></td>
</tr>
<tr>
<td><strong>Not confirmed</strong></td>
</tr>
<tr>
<td><strong>Multidisciplinary team review</strong></td>
</tr>
<tr>
<td><strong>Cone biopsy and D&amp;C</strong></td>
</tr>
<tr>
<td><strong>Consistent with cancer</strong></td>
</tr>
<tr>
<td><strong>Favouring a neoplastic process (AIS)</strong></td>
</tr>
<tr>
<td><strong>Punch biopsy and refer to gynaecological oncologist</strong></td>
</tr>
<tr>
<td><strong>As from 1 July 2009</strong></td>
</tr>
</tbody>
</table>

HPV testing should be considered as a useful adjunct to management, as per NCSP Best Practice Guidance on HPV Testing.

**Note:** Atypical glandular cells of undetermined sinificance (AGUS) has been replaced with 'typical glandular cells' (AGC) with specification of cell types: endocervical, endometrial or otherwise specified (see codes left).

**Bethesda 2001 Codes**

- AG1 Atypical endocervical cells present
- AG2 Atypical endometrial cells present
- AG3 Atypical glandular cells present
- AG4 Atypical endocervical cells favouring a neoplastic process
- AG5 Atypical glandular cells favouring a neoplastic process
- AIS Adenocarcinoma in situ
- AC1 Abnormal glandular cells consistent with endocervical adenocarcinoma
- AC2 Abnormal glandular cells consistent with endometrial adenocarcinoma
- AC3 Abnormal glandular cells consistent with extrauterine adenocarcinoma
- AC4 Abnormal glandular cells consistent with adenocarcinoma
- AC5 Abnormal glandular cells consistent with malignant neoplasm adenocarcinoma
Guidelines for Cervical Screening in New Zealand

Flowchart 4: Colposcopic assessment and treatment of women with glandular abnormalities

Glandular Abnormalities
Atypical glandular cells (AGC) (AG1-5)
Adenocarcinoma in situ (AIS)
Adenocarcinoma (AC 1-4)

Colposcopy

Satisfactory & normal
Satisfactory & abnormal
Unsatisfactory

Consistent with cancer
Favouring a neoplastic process (AIS)

Cytology review
Punch biopsy and refer to gynaecological oncologist
Cone biopsy and D&C

Cytology confirmed
Not confirmed

Cone biopsy and D&C
Multidisciplinary team review

Confirmed favouring a neoplastic process
Not confirmed

Cone biopsy and D&C
Multidisciplinary team review

As from 1 July 2009 HPV testing should be considered as a useful adjunct to management, as per NCSP Best Practice Guidance on HPV Testing

Bethesda 2001 Codes

AG1 Atypical endocervical cells present
AG2 Atypical endometrial cells present
AG3 Atypical glandular cells present
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AC5 Abnormal glandular cells consistent with malignant neoplasm adenocarcinoma

Note: Atypical glandular cells of undetermined significance (AGUS) has been replaced with “typical glandular cells” (AGC) with specification of cell type: endocervical, endometrial or otherwise specified (see codes left).
Management of Women in Special Clinical Circumstances

Pregnancy

There is no contra-indication to smear-taking during pregnancy, but routine smears may be delayed until after pregnancy unless there is a reason not to, such as if the woman is well overdue for a smear or the previous smear was abnormal.

The risk of progression of CIN 2/3 to invasive cancer during pregnancy is low.\textsuperscript{52,58,59} However, some studies have found a high probability that a high-grade lesion will persist,\textsuperscript{60,61} pointing to the need for continued colposcopic and cytological surveillance during the pregnancy (at about 20–30 weeks) and postpartum (after 6 weeks).\textsuperscript{52, 58} Other studies show a high rate of regression.\textsuperscript{62}

Treatment of CIN during pregnancy has been associated with complications and a high rate of recurrence or persistence.\textsuperscript{52,58,59} Therefore the only indication for treatment in pregnancy is invasive cancer.

It is preferable that the colposcopic assessment of pregnant women with HSIL be undertaken by a colposcopist experienced in assessing the pregnant cervix.\textsuperscript{52}

Guideline 13: Management during pregnancy

<table>
<thead>
<tr>
<th>SITUATION</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy</td>
<td>Take smears according to NCSP guidelines. It is not necessary to do routine cervical smears during pregnancy, although cervical smears and colposcopy are not contra-indicated.</td>
<td>Grade B</td>
</tr>
<tr>
<td>Evaluation of an abnormal cervical cytology result during pregnancy</td>
<td>Low-grade cytologic lesions should be managed in the same way as a low-grade squamous abnormality ie, with a repeat smear after 12 months. Refer high-grade lesions for colposcopy.</td>
<td>Grade B</td>
</tr>
<tr>
<td>Colposcopy during pregnancy</td>
<td>The aims of colposcopy in the pregnant woman are to exclude the presence of invasive cancer and to reassure the woman that her pregnancy will not be affected by an abnormal cervical smear result. Biopsy of the cervix in pregnancy is indicated if invasion is suspected at colposcopy. If invasion is not suspected, it may be appropriate to defer biopsy of the cervix until after delivery. \textit{Note: Following initial colposcopy, further evaluation may be indicated during the pregnancy.}</td>
<td>Grade C</td>
</tr>
</tbody>
</table>
Guideline 13: Management during pregnancy (continued)

<table>
<thead>
<tr>
<th>SITUATION</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of a high-grade lesion during pregnancy</td>
<td>Definitive treatment of a high-grade lesion, with the exception of invasive cancer, may be safely deferred until after delivery.</td>
<td>Grade B</td>
</tr>
</tbody>
</table>

Women aged under 20 years

CIN lesions are common among sexually active women in this age group and frequently regress.\(^63\) The risk of invasive cancer is very low and therefore does not warrant routine screening.\(^2,5\) In New Zealand the recent rate of invasive cervical cancer in women under 20 years has been less than 1 per 100,000 women.\(^3\)

**NCSP Policy:** Routine screening is not recommended for women younger than 20 years.

Guideline 14: Women aged under 20 years

<table>
<thead>
<tr>
<th>SITUATION</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Management of CIN2 only (not CIN3)</td>
<td>If a woman aged under 20 years is screened (contrary to NCSP policy) and CIN2 is found, management should be individualised and include multidisciplinary team review of cytology and histology results. If agreed by the multidisciplinary review, careful specialist colposcopic observation at 4 to 6 month intervals for up to 12 months may be appropriate, provided colposcopy is satisfactory, given the high rate of resolution of CIN2 in this age group. This applies for histologically confirmed CIN2 lesions only (not CIN3). If the colposcopic appearance of the lesion worsens, or if HSIL persists, repeat biopsy is recommended. After 2 consecutive results of ‘negative for intra-epithelial lesions or malignancy’, women under 20 years with normal cytology results can return to routine cytological screening. Treatment is recommended if CIN3 is subsequently identified, or if CIN2 persists for 12 months. <strong>Note:</strong> In New Zealand high-grade histological specimens are often reported as CIN2/3 combined, rather than CIN2.</td>
<td>Grade B</td>
</tr>
</tbody>
</table>
Management of post-menopausal women and women over 40 years with normal endometrial cells

Benign endometrial cells in pre-menopausal women are rarely associated with significant pathology, and if asymptomatic no further evaluation is recommended.\textsuperscript{53} In contrast, benign endometrial cells in post-menopausal women may be associated with significant endometrial pathology, and further assessment is recommended.\textsuperscript{53}

The management of women 40 years or older with benign endometrial cells in a cervical smear, and in the absence of any other cellular abnormality, is clinically driven by the smear-taker/clinician, who should consider other factors such as menstrual history, post-menopausal bleeding, hormone replacement therapy and other relevant clinical conditions.\textsuperscript{51, 54-57}

Guideline 15: Cervical smear report of normal endometrial cells for post-menopausal women and women over 40

<table>
<thead>
<tr>
<th>CERVICAL SMEAR REPORT</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal endometrial cells</td>
<td>Endometrial cells in women over 40 years are rarely associated with endometrial pathology, such as endometrial carcinoma. It is recommended that this finding be correlated with symptoms of uterine pathology eg, abnormal bleeding, and with histology specimens where possible. A woman with symptoms of uterine pathology requires investigation regardless of her cervical smear results.</td>
<td>Grade B</td>
</tr>
<tr>
<td>Atypical endometrial cells</td>
<td>Atypical endometrial cells have a high correlation with endometrial pathology. Urgent referral to a specialist colposcopist is recommended.</td>
<td>Grade B</td>
</tr>
</tbody>
</table>
Immunocompromised women

Immunocompromised women include those women with disorders of the immune system such as HIV/AIDS or other immunodeficiency disorders (such as systemic lupus erythematosis or ulcerative colitis), and those receiving immunosuppressive treatments for cancer or organ transplants, or high-dose steroids. For HIV-positive women, the American Society for Colposcopy and Cervical Pathology (ASCCP) recommends a repeat screen six months after the first, and if the result of the second test is normal, annual screening thereafter.64

Evidence suggests that immunocompromised women are at increased risk of anogenital HPV infection and precancerous intra-epithelial neoplasia compared with healthy immunocompetent women.64 The management of these women is more complex (with higher rates of disease progression, recurrence and persistence of abnormalities) and should be carried out by specialists.

There is limited literature on the efficacy of CIN treatment in women immunocompromised for reasons other than HIV/AIDS or, to a lesser extent, organ transplantation. For this reason, this guideline applies to all immunocompromised women.

**Guideline 16: Immunocompromised women**

<table>
<thead>
<tr>
<th>COLPOSCOPIC ASSESSMENT</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunocompromised women with normal cervical smears</td>
<td>Annual screening is recommended because of the high risk of persistent HPV infection.</td>
<td>Grade B</td>
</tr>
<tr>
<td>Immunocompromised women with abnormal results (ASC-US, LSIL, ASC-H, HSIL, AGC)</td>
<td>Refer for colposcopy, even for a low-grade lesion, because cytological surveillance alone may be inadequate. Assessment and treatment should be by a gynaecological colposcopist. The whole of the lower genital tract will need evaluation, because the same risk factors apply for cervical, vaginal, vulval and perianal lesions.</td>
<td>Grade B</td>
</tr>
<tr>
<td>Treatment of immunocompromised women</td>
<td>Treatment of the cervix should be by excisional methods. Follow-up after treatment should include colposcopy as well as cytology. Follow-up should be annual and indefinite.</td>
<td>Grade B</td>
</tr>
</tbody>
</table>
Women with a previous hysterectomy

The following advice is taken from the RANZCOG statement Pap Smears After Hysterectomy (2007).65

- For women who have had a total hysterectomy, the aim of taking a smear from the vaginal vault is screening for the prevention of vaginal cancer.
- Women who have had a previous total hysterectomy for documented benign reasons (eg, menstrual problems or prolapse), have a history of normal cervical smears and whose histopathology of the cervix shows no premalignant or malignant change, do not require further screening.
- Women treated by hysterectomy for CIN2 or 3 may be at increased risk of vaginal cancer and must continue to have annual vault smears.
- Women with previous smear or cervical biopsy with a low-grade lesion who had reverted to normal cervical cytology prior to hysterectomy do not need vaginal vault smears, unless they are symptomatic. (Note that this varies from the current guideline below.)
- Women previously treated for vaginal intra-epithelial neoplasia (VAIN) are at risk for the development of VAIN. They should continue to have vault smears every 1–2 years or at the discretion of the treating specialist.
- Women who are immunocompromised who have had a hysterectomy for benign disease should have vault smears every 3 years.

Guideline 17: Women with a previous hysterectomy

<table>
<thead>
<tr>
<th>SITUATION</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-total hysterectomy (cervix remains) for documented benign reasons</td>
<td>Routine screening as per these guidelines.</td>
<td>Grade B</td>
</tr>
</tbody>
</table>
| Total hysterectomy (removal of uterus and cervix) for documented benign reasons. | Women who have a normal cytology/histology history in the 5 years preceding the hysterectomy do not require routine vaginal vault cytology.  
Women who have an unknown smear history should have baseline vaginal vault cytology. If this is normal, no further vaginal vault cytology is required. | Grade B  |
| Total hysterectomy previous CIN1       | Women with histological evidence of CIN1 at any time in the past should have 3-yearly vaginal vault cytology until age 70 years. | Grade C  |

Table continues on next page
Guideline 17: Women with a previous hysterectomy (continued)

<table>
<thead>
<tr>
<th>SITUATION</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total hysterectomy previous CIN2 or 3</td>
<td>Guidelines for high-grade abnormality apply. Women with histological evidence of a high-grade lesion at any time in the past should have annual vaginal vault cytology until age 70 years. <strong>From 1 July 2009</strong> HrHPV testing can be used to help identify women at risk as per the <em>NCSP Best Practice Guidance on HPV Testing</em> (2008) (ie, follow up with cytology and HPV testing annually until the woman has tested negative in both tests on 2 consecutive occasions, 12 months apart).</td>
<td>Grade B</td>
</tr>
<tr>
<td>Hysterectomy for genital malignancy</td>
<td>These women should be under ongoing surveillance from an oncologist. Therefore, they will be guided by this specialist about appropriate surveillance and care, and will no longer be the subject of these guidelines.</td>
<td>Grade C</td>
</tr>
</tbody>
</table>

**Women exposed in utero to diethylstilboestrol (DES)**

Diethylstilboestrol (DES) was given to pregnant women between 1940 and about 1970 to improve pregnancy outcomes, particularly in diabetic women. The critical period of exposure was before 18 weeks’ gestation. These women are at increased risk of clear cell adenocarcinoma of the vagina and cervix, and there is some evidence of increased risk of HSIL and cervical cancer.66

DES has not been used in pregnancy for over 30 years, so the problem is diminishing.

**Guideline 18: Women exposed in utero to diethylstilboestrol (DES)**

<table>
<thead>
<tr>
<th>SITUATION</th>
<th>GUIDELINE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>DES-exposed women</td>
<td>DES-exposed women should be offered annual cytological screening and colposcopic examination of both the cervix and vagina. Screening should begin any time at the woman’s request and continue indefinitely.</td>
<td>B</td>
</tr>
<tr>
<td>DES-exposed women with an abnormal smear report</td>
<td>These women should be managed in a specialist centre by a specialist colposcopist.</td>
<td></td>
</tr>
</tbody>
</table>
Summary of Indications for Cytological Review

Some cases may require cytology review or cyto-histo correlation at multidisciplinary case review meetings to determine best clinical management, treatment and follow-up.

Factors such as marked inflammatory/reactive change, infection or few abnormal cells contribute to the subjectivity that may occasionally occur with cervical cytology.

A review of cytology is usually undertaken where the cytological interpretation suggests either a more significant lesion than subsequently detected by colposcopy/histology (false positive), or a negative cytology with a subsequent confirmed abnormality (false negative).

Cytological review is a key component of quality and educational improvement.

**Guideline 19: Summary of indications for cytological review**

<table>
<thead>
<tr>
<th>CASE REVIEW</th>
<th>GUIDELINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytology/case review</td>
<td>In cases of ‘apparent discrepancy’ (discordance) between cytology and colposcopy, discussion with the reporting pathologist regarding an individual case is strongly recommended. Multidisciplinary case review is recommended in the following situations: • HSIL in women aged under 20 years • HSIL cytology and normal findings at colposcopic assessment • abnormal glandular cytology and normal findings at colposcopic assessment • persistent LSIL and normal findings at colposcopic assessment • unsatisfactory colposcopic assessment of women with suggested high-grade disease. Note: For further information on cyto-histo correlations, refer to Standard 521 Section 5: Providing a Laboratory Service (NCSP Operational Policy and Quality Standards).</td>
</tr>
</tbody>
</table>
Cytological review is a key component of quality and educational improvement. A review of cytology is usually undertaken where the cytological interpretation suggests either a more significant lesion than subsequently detected by colposcopy/histology (false positive), or a negative result. Factors such as marked inflammatory/reactive change, infection or few abnormal cells contribute to the situation where a review of cytology is recommended. Some cases may require cytology review or cyto-histo correlation at multidisciplinary case review.

**Summary of Indications for Cytological Review**

**Guideline 19: Summary of indications for cytological review**

Cytology/case

Multidisciplinary case review is recommended in the following situations:

- unsatisfactory colposcopic assessment of women with suggested high-grade disease.
- persistent LSIL and normal findings at colposcopic assessment.
- abnormal glandular cytology and normal findings at colposcopic assessment.
- HSIL in women aged under 20 years.

Disease.

**References**

46. DeSimone CP, Day ME, Tovar MM, et al. 2006. Rate of pathology from atypical glandular cell Pap test classified by


34. Dias-Montes TP, Farinola MA, Zahurak ML, et al. 2006. Clinical utility of atypical glandular cells (AGC) classification:


20. 73: 348−53.


18. 390: 244−51.

17. 102: 228−32.


13. 118: 2048−55.


10. 93: 8−15.


7. 367: 489−98.


5. 193: 559−67.

4. atypical glandular cells or adenocarcinoma in situ in their Pap smears. Gynecologic Oncology 95: 618−23.


2. 19: 34−43.


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PART C: Guidance on HPV Testing
Purpose

There is good evidence that appropriately applied testing for high risk (oncogenic) types of human papillomavirus (HPV) can play a useful and cost-effective role in the management of women with abnormal cervical smears.

This document is intended to provide guidance for health professionals in the use of HPV testing. It has been developed in consultation with a multidisciplinary advisory group on HPV testing. It is based on studies that have used HPV tests that have been validated by a local or internationally recognised accreditation body and/or an accredited laboratory.

Introduction

HPV is a very common transient sexually transmitted infection. In women under 30 years, the prevalence is very high, however the vast majority of high-risk HPV (HrHPV) infections clear within two years of infection and are of little clinical significance. HPV testing for the triage of low-grade smear results is therefore of limited usefulness in women under 30 years, where it would lead to unnecessary testing and anxiety. As age increases, persistence of infection with HrHPV subtypes increases the risk of developing a high-grade lesion.

HrHPV testing has been repeatedly found to have a high negative predictive value (~99%) and to be more sensitive for detecting risk of high grade abnormalities than conventional cytology, which is generally a more specific test. It is the strong negative predictive value of HrHPV testing that has most clinical use.

For HrHPV testing, liquid-based cytology (LBC) has practical advantages in that it offers a platform for combined cytology and HrHPV testing on one cervical smear sample, however, co-collection in an appropriate transport medium at the time of the conventional smear is an acceptable alternative.

‘Reflex testing’ ie, testing either the original LBC sample for HrHPV or a separate sample co-collected at the time of the screening visit should the cytology be ASC-US/LSIL (atypical squamous cells of undetermined significance/low-grade squamous intraepithelial lesion), eliminates the need for a woman to return for repeat testing, and has been shown to be cost-effective.

Note HPV testing as a primary screening test is not recommended, as the evidence for this is not yet conclusive.
NCSP Best Practice Guidance on HPV Testing

Purpose

There is good evidence that appropriately applied testing for high risk (oncogenic) types of human papillomavirus (HPV) can play a useful and cost-effective role in the management of women with abnormal cervical smears.

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‘Reflex testing’ ie, testing either the original LBC sample for HrHPV or a separate sample co-collected at the time of the screening visit should the cytology be ASC-US/LSIL (atypical squamous cells of undetermined significance/low-grade squamous intraepithelial lesion), eliminates the need for a woman to return for repeat testing, and has been shown to be cost-effective.

Note HPV testing as a primary screening test is not recommended, as the evidence for this is not yet conclusive.
HPV testing in the National Cervical Screening Programme (NCSP)

The areas of management of asymptomatic women with abnormal cervical smears within the NCSP that may benefit from HrHPV testing include the following:

1. The triage of women 30 years and over with ASC-US or LSIL cytology (without an abnormal smear in the last five years).

   ‘Reflex’ testing of women with ASC-US/LSIL eliminates the need for shorter interval repeat cytology testing. A normal test can reassure a woman that she is very unlikely to have a significant lesion and can reduce the need for colposcopy.

   Women with ASC-US/LSIL smears who test positive for HrHPV should be referred to colposcopy.

   Women who are found to be HrHPV negative can be followed up with repeat cytology testing at 12 months.

   Following a negative cytology result at 12 months, a woman can return to normal three yearly screening.

   *See Flowchart HPV Testing Guidance 1*

2. The follow-up of women who have been treated for a high-grade lesion.

   Women who have been previously treated for CIN2/3 are at increased risk of further high grade disease and cervical cancer. Recurrence may be due to limitations of colposcopy, inadequate treatment, persistent disease, or new infection.

   HrHPV testing allows better identification of women at risk of persistent or recurrent lesions, while enabling many women to return to normal screening intervals.

   Women treated for CIN2/3 should in the first instance undergo follow-up colposcopy and cytology within six to twelve months after treatment as is usual practice.

   HrHPV testing and cytology should then be carried out 12 months after treatment and annually thereafter until a woman has tested negative by both tests on two consecutive occasions, 12 months apart. A woman can then return to a normal three-yearly screening interval.

   It should be noted that HrHPV testing should not be carried out sooner than 12 months after treatment of high grade lesions, as viral clearance may take more than 12 months to occur.

   *See Flowchart HPV Testing Guidance 2*
3. Post colposcopy management of women with discordant results: eg high-grade cytology and negative, satisfactory colposcopy.

A single colposcopic examination can miss significant lesions. Where findings on colposcopy/histology are negative or show low-grade changes only and the discordance persists following case review, HRHPV testing can be a useful adjunct to further management.

The NCSP recommends a woman return to three-yearly screening only after two negative sets of HRHPV plus cytology tests 12 months apart.

Failure to detect CIN2/3 lesions in a woman with high-grade cytology (following review of the smear) should lead to consideration of a diagnostic excisional procedure, or observation for one year with colposcopy, cytology and HPV testing.

Implementation and monitoring

For logistical reasons, HRHPV testing will not be part of the new NCSP guidelines for the management of women with abnormal cervical smears until 1 July 2009. Prior to this, an information and training programme will be run for practitioners.

The introduction of HRHPV testing as an integral part of the management of asymptomatic women with abnormal cervical smears is also compatible with the changes that will become necessary for the NCSP as the population increasingly becomes HPV vaccinated.

The impact of introducing HRHPV testing into the above areas of management will require ongoing monitoring. A review of this best practice guidance will be undertaken within five years.

Terminology

Triage – the clinical process of sorting people based on their need for or likely benefit from treatment.

Sensitivity – the proportion of persons with the disease who test positive with the screening test ie, the test correctly identifies the condition. A test with a high sensitivity has few false negatives ie, people with the disease escaping detection.

Specificity – the proportion of non-diseased persons who test negative with the screening test. A highly specific test means that there are few false positive results.

Negative predictive value – the proportion of the screened population with negative test results that do not have the disease ie, it assesses the reliability of a negative test.
**Flowchart HPV Testing Guidance 1:** Triage of women 30 years and over with ASC-US or LSIL (who have not had an abnormal smear within the last 5 years)

1. **Women ≥ 30 years ASC-US/LSIL**
   - HrHPV reflex test

   1. **HrHPV positive**
      - Refer to colposcopy

   2. **HrHPV negative**
      - Repeat cytology at 12 months

         1. **Cytology ≥ ASC-US**
            - Refer to colposcopy

         2. **Cytology negative**
            - Return to 3 yearly screening

---

**Histologically confirmed and treated HSIL**

1. **HrHPV negative**
   - Cytology negative on both testing occasions

2. **HrHPV positive or cytology > ASC-H** at either event
   - Refer to colposcopy

**Colposcopy follow-up with cytology at 6-12 months**

**Return to 3 yearly screening**
Flowchart HPV Testing Guidance 2: Follow-up of women treated for high-grade lesions

Histologically confirmed and treated HSIL

Colposcopy follow-up with cytology at 6-12 months

Cytology and HrHPV test 12 months post-treatment and again at 24 months post-treatment

HrHPV negative

cytology negative on both testing occasions

Return to 3 yearly screening

HrHPV positive or cytology ≥ ASC-H at either event

Refer to colposcopy

12 months result:

HrHPV negative cytology ASC-US/LSIL

Repeat cytology and HrHPV testing 24 months post-treatment

- HrHPV negative, cytology negative, repeat cytology in 12 months
- HrHPV negative, cytology ASC-US/LSIL, consider referral to colposcopy or continue annual screening
- HrHPV negative, cytology ≥ ASC-H, refer to colposcopy
- HrHPV positive, refer to colposcopy irrespective of cytology result
Flowchart HPV Testing Guidance 2 EXTENDED: Follow-up of women treated for high-grade lesions

Discharged from colposcopy

- Cytology and HrHPV test
- 12 months post-treatment

HrHPV negative
- Cytology negative
  - ASC-US/LSIL
    - Repeat cytology & HrHPV testing at a further 12 months
  - ASC-US/LSIL
    - Repeat cytology (12 months)
    - Annual screening

HrHPV negative
- Cytology positive
  - ASC-US/LSIL
    - Repeat cytology & HrHPV testing at a further 12 months
  - ≥ ASC-H
    - Colposcopy

HrHPV positive
- Cytology negative
  - ≥ ASC-H
    - Colposcopy
  - ASC-US/LSIL
    - Repeat cytology (12 months)
  - ≥ ASC-H
    - Colposcopy

HrHPV positive
- Cytology positive
  - ≥ ASC-H
    - Colposcopy

Note: HrHPV negative, cytology negative, repeat cytology in 12 months
HrHPV negative, cytology ASC-US/LSIL, consider referral to colposcopy or continue annual screening
HrHPV negative, cytology ≥ ASC-H, refer to colposcopy
HrHPV positive, any cytology result, refer to colposcopy

Guidelines for Cervical Screening in New Zealand
Bibliography (Guidance on HPV Testing)


Guidelines for Cervical Screening in New Zealand

Guidance on HPV Testing Update 1: April 2010

Introduction
This is the first in an ongoing series of updates of the Guidelines for Cervical Screening in New Zealand, released by the National Cervical Screening Programme (NCSP) in August 2008 and available on www.nsu.govt.nz/Health-Professionals/2747.asp

Note that guidelines are intended only as an aid to clinical practice, not as a substitute for clinical judgment. Clinicians should continue to manage patients on the basis of personal and family medical history, and clinical signs and symptoms, as well as formal guidelines.

Testing for high risk (oncogenic) HPV types (HrHPV) was introduced in New Zealand in October 2009. This reflects accumulating evidence on the clinical utility and cost effectiveness of HrHPV testing alongside cervical cytology in the management of women with cervical abnormalities.\(^{(1,13,15)}\)

The addition of HrHPV testing to cytology and colposcopy offers several advantages,\(^{(2-9)}\) including both greater sensitivity for the detection of CIN2/3 or cancer and a higher predictive value of a negative test. That is, testing negative for HrHPV implies a very low risk of CIN2/3 or cancer. HrHPV testing thus helps to clarify the risk of having significant cervical disease against the harm of having unnecessary interventions.\(^{(10-12)}\)

HrHPV testing is currently recommended in the Guidelines in three clinical situations:

<table>
<thead>
<tr>
<th>Situation</th>
<th>Who usually initiates the HPV test</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Women 30 years and older with ASC-US or low-grade changes, to help assess risk of progression</td>
<td>Laboratories (the HrHPV result is reported at the same time as the ASCUS /LSIL result) Smear takers are required to ensure that all women over 30 years are informed about HPV testing.</td>
</tr>
<tr>
<td>2. Women (all ages) treated for a high-grade lesion, to help assess whether the lesion has been completely resolved. Includes ‘historical testing’ for women on annual smears for previous high-grade lesions and with negative smears since, to assess whether they can return to routine 3 yearly screening - refer page 3.</td>
<td>The smear taker, after discussing with the woman.</td>
</tr>
<tr>
<td>3. Where colposcopy has shown discordant results from cytology, to help interpret these results.</td>
<td>Colposcopists</td>
</tr>
</tbody>
</table>

Who should not be offered HrHPV testing as part of the NCSP?
Women under 30 years (unless they have had a previous high-grade (HSIL/ASC-H) lesion). Note that where HrHPV testing is requested outside the Guidelines, women may be asked to pay for it.

The following interim advice relates to situation (2) above.
NCSP Interim Advice: HrHPV testing for women with previous high-grade lesions

1. HrHPV testing of women treated for high-grade lesions (HSIL/ASC-H) within the last 3 years

The 2008 guidelines for HrHPV testing following colposcopy refer to women who have been recently treated at colposcopy. In this context, ‘recent’ can be interpreted as meaning within the past 3 years. Women in this situation who test HrHPV positive, despite having cytology assessed as negative on one or two occasions post colposcopy, should be referred back to colposcopy. The reason for this is the risk of residual disease requiring assessment and further treatment, despite the apparently negative cytology.

Follow-up of women treated for high-grade lesions in the last 3 years
As indicated in Flowchart HPV Testing Guidance 2 (pgs 51 and 52 of Guidelines for Cervical Screening in New Zealand), summarised below

1 3 years has been recommend in order to distinguish failure of colposcopic treatment from a new infection

Please Note:
• This NCSP update should assist clinicians to determine future management, based on a woman’s risk of CIN2/3+.
• As with all tests, it is important to explain to women the reason for the test, gain her consent, and explain the implications of results.
• The practice of offering HrHPV testing to women already undergoing annual cytological review for a previously treated HSIL follows that published in the Australian NHMRC guideline (9 June 2005).
• A further update will be provided on the use of HrHPV testing in the management of glandular abnormalities and post hysterectomy.
2. HrHPV testing of women with a high-grade lesion (HSIL/ASC-H) followed by colposcopy (or no treatment) more than 3 years previously, with subsequent repeated negative cytology tests (historical testing)

Women with previous high-grade lesions (HSIL/ASC-H), treated or not treated colposcopically, and currently managed by annual cytology for more than three years, with all tests assessed as negative, may benefit from dual cytology and HrHPV testing. This is because the high negative predictive value of HrHPV testing together with a double negative (cytology and HrHPV) implies a low risk of CIN2/3+. If these women test negative by both tests over two years, they can be screened with cytology alone every three years until 70 years of age.

However, some women will test positive for HrHPV despite the repeated negative cytology tests. These women also are likely to be at very low risk of CIN2/3 or worse and can be retested with cytology and HrHPV testing annually. A positive HrHPV test where cytology remains negative is not a cause for immediate concern in these circumstances, however contributes to the overall assessment of a woman’s risk status.

**Please Note:**

- This NCSP update should assist clinicians to determine future management, based on a woman’s risk of CIN2/3+. The NCSP plans to review data held on the NCSP Register and to further refine this advice within six months.
- As with all tests, it is important to explain to women the reason for the test, gain her consent, and explain the implications of results.
- The practice of offering HrHPV testing to women already undergoing annual cytological review for a previously treated HSIL follows that published in the Australian NHMRC guideline (9 June 2005).
- A further update will be provided on the use of HrHPV testing in the management of glandular abnormalities and post hysterectomy.
References


Appendices
Appendix 1: Advisory Group Members

Guidelines Development Team

Professional/sector group representatives

- Dr Gary Fentiman (Chair), Obstetrician & Gynaecologist
- Barbara Beckford, NSU Consumer Reference Group
- Naomi Brewer, Epidemiologist
- Dr Alison Denyer, General Practitioner
- Dr Peter Fitzgerald, Cytopathologist
- Dr Donna Hardie, Obstetrician & Gynaecologist
- Mr Torben Iversen, Obstetrician & Gynaecologist
- Dr Mona Jeffreys, Epidemiologist
- Dr Peter Sykes, Gynaecological Oncologist
- Dr Ailing Tan, Gynaecological Oncologist
- Dr Mee-ling Yeong, Cytopathologist

National Cervical Screening Programme (NCSP) representatives

- Dr Hazel Lewis, Clinical Leader, NCSP
- Dr Debbie Holdsworth, Project Manager, NCSP
- Diane Casey, Senior Analyst, NCSP
- Jane McEntee, Programme Manager, NCSP

New Zealand Guidelines Group representatives

- Anne Lethaby
- Jane Marjoribanks

HPV Testing Working Group

Professional/sector group representatives

- Dr Peter Bethwaite (Chair), Pathologist
- Barbara Beckford, NSU Consumer Reference Group
- Dr Collette Bromhead, Virologist
- Dr Kitty Croxson, Virologist
- Dr Gary Fentiman, Obstetrician & Gynaecologist
- Dr Helen Gemmell, General Practitioner
- Dr Lance Jennings, Virologist
- Jennifer Lindeman, Medical Laboratory Science Board
- Dr Richard Lloydd, Pathologist
- Dr Richard Massey, Pathologist
- Marilyn Rosewarne, Registered Nurse
- Dr Andre Smith, Obstetrician & Gynaecologist
- Dr David Wilde, Obstetrician & Gynaecologist

NSU representatives

- Dr Hazel Lewis, Clinical Leader, NCSP
- Dr Harold Neal, Scientific Advisor, NCSP
- Diane Casey, Programme Manager, NCSP
- Anna Maxwell, Senior Policy Analyst, Cancer Screening

Lead colposcopist participants at a combined meeting also included: Dr Nasser Shehata, Dr Jay Siresa, Dr Edwin Ozumba and Dr Helene McNab.
Appendix 2: AGREE Tool

This tool was used for the appraisal of five evidence-based guidelines on the management of cervical abnormalities.

<table>
<thead>
<tr>
<th></th>
<th>UK</th>
<th>ICSI*</th>
<th>Aus</th>
<th>ASCCP*</th>
<th>Ontario</th>
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</thead>
<tbody>
<tr>
<td>1. The overall objectives of the guideline are specifically described</td>
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<td>2. The clinical questions covered by the guideline are specifically described</td>
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<tr>
<td>3. The patients to whom the guideline is meant to apply are specifically described</td>
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<td>4. The guideline development group includes individuals from all the relevant professional groups</td>
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<td>5. The patients’ views and preferences have been sought</td>
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<td>6. The target users of the guideline are clearly defined</td>
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<tr>
<td>7. The guideline has been piloted among target users</td>
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<td>8. Systematic methods were used to search for evidence</td>
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<td>9. The criteria for selecting the evidence are clearly described</td>
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<td>10. The methods used for formulating the recommendations are clearly described</td>
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<td>11. The health benefits, side effects and risks have been considered in formulating the recommendations</td>
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<td>12. There is an explicit link between the recommendations and the supporting evidence</td>
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<td>13. The guidelines has been externally reviewed by experts prior to its publication</td>
<td>*</td>
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<td>14. A procedure for updating the guideline is provided</td>
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<td>15. The recommendations are specific and unambiguous</td>
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<td>16. The different options for management of the condition are clearly presented</td>
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<td>17. Key recommendations are easily identifiable</td>
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<td>18. The guideline is supported with tools for application</td>
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<td>19. The potential organisational barriers in applying the recommendations have been discussed</td>
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<td>20. The potential cost implications of applying the recommendations have been considered</td>
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<tr>
<td>21. The guideline presents key review criteria for monitoring and/or audit purposes</td>
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<td>22. The guideline is editorially independent from the funding body</td>
<td>NR</td>
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<tr>
<td>23. Conflicts of interest of guideline development members have been recorded</td>
<td>*</td>
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<td>****</td>
</tr>
</tbody>
</table>

Source: The AGREE Collaboration, 2001

*Institute of Clinical Systems Improvement, Minnesota
*American Society for Colposcopy and Cervical Pathology
The scoring system ranges from 1 to 4, with 1 being strongly disagree and 4 being strongly agree. The document uses stars, which correspond to the numbers. AGREE questions 8–14 represent the ‘Rigour of Development’ domain, and the percentage scores for each guideline have been graphed in Figure A1 (below).

**Figure A1: Rigour score – Cervical Cancer Screening Guidelines**
Appendix 3: Bethesda 2001 New Zealand modified (2005) in brief

SPECIMEN TYPE
- Conventional smear
- Liquid-based cytology (LBC)
- Combined (LBC and conventional)

SPECIMEN SITE
- Cervical
- Vault
- Vaginal

SPECIMEN ADEQUACY
- Satisfactory for evaluation (note presence/absence of endocervical/transformation zone component)
- Unsatisfactory for evaluation (specify reason)

GENERAL CATEGORISATION
- Negative for intraepithelial lesion or malignancy
- Epithelial cell abnormality
- Other abnormality (non-epithelial malignancy)

INTERPRETATION
Negative for intra-epithelial lesion or malignancy
- Organisms
  - Trichomonas vaginalis
  - Fungal organisms morphologically consistent with Candida species
  - Shift in flora suggestive of bacterial vaginosis
  - Bacteria morphologically consistent with Actinomyces species
  - Cellular changes consistent with herpes simplex virus
- Other non-neoplastic findings (optional to report, list not comprehensive)
  - Reactive cellular changes eg, associated with inflammation (includes repair), radiation, intra-uterine contraceptive device
- Other
  - Endometrial cells in women, aged >40 years
  - Atrophy

Epithelial cell abnormalities

SQUAMOUS CELL
- Atypical squamous cells
  - of undetermined significance (ASC-US)
  - cannot exclude HSIL (ASC-H)
- Low-grade squamous intraepithelial lesion (LSIL) (encompassing: HPV/mild dysplasia/CIN 1)
- High-grade squamous intraepithelial lesion (HSIL) (encompassing: moderate and severe dysplasia, carcinoma in situ; CIN2, CIN3)
  - with features suspicious for invasion (if invasion is suspected)
- Squamous cell carcinoma

GLANDULAR CELL
- Atypical
  - endocervical
  - endometrial
  - glandular cells (not otherwise specified)
  - endocervical, favour neoplastic
  - glandular cells, favour neoplastic (not otherwise specified)
- Endocervical adenocarcinoma in situ
- Adenocarcinoma – endocervical, endometrial, extra-uterine, glandular (not otherwise specified)

RECOMMENDATIONS